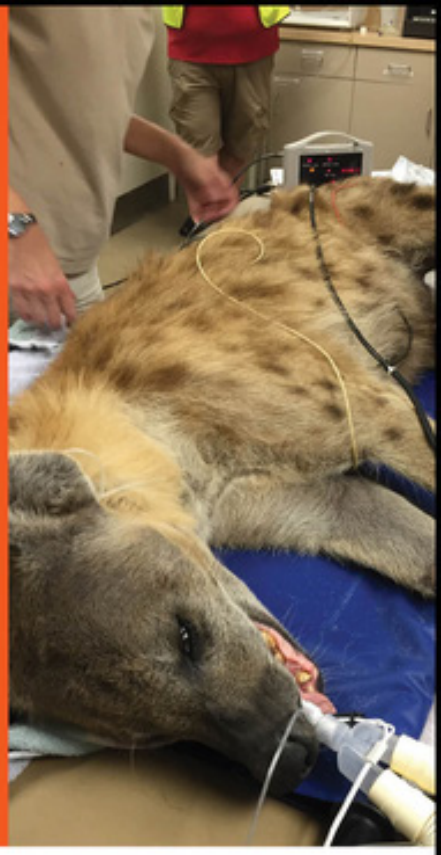
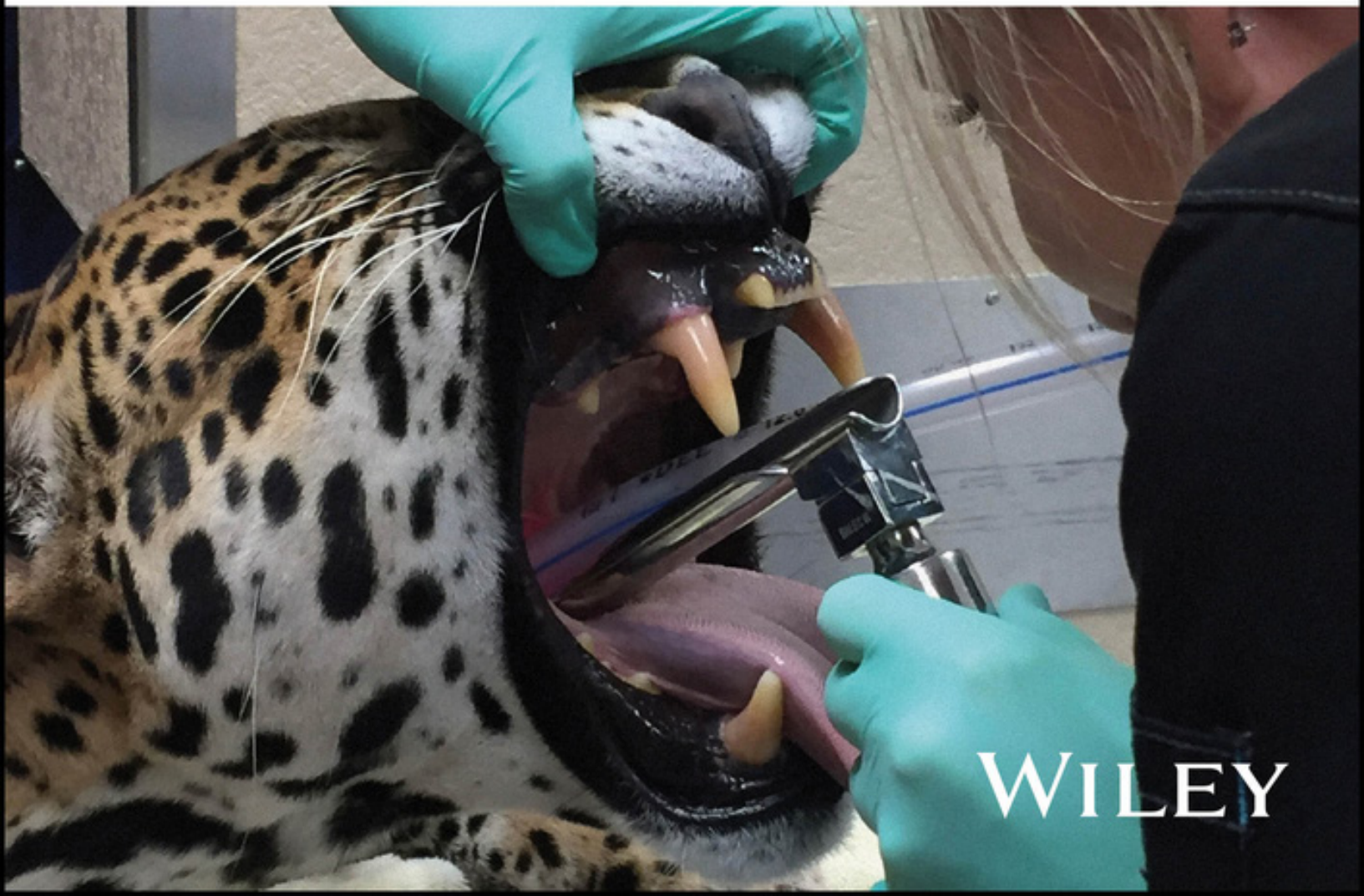
Third Edition

Zoo Animal and Wildlife Immobilization and Anesthesia



Edited by
Gary West | Darryl Heard | Nigel Caulkett



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Edited by

Gary West, DVM, DACZM
Senior Vice-president of Animal Health and Living Collections
Arizona Center for Nature Conservation/Phoenix Zoo

Darryl Heard, BSc, BVMS, DACZM, PhD
Department of Comparative Diagnostic and Population Medicine
College of Veterinary Medicine, University of Florida, Gainesville, Florida

Nigel Caulkett, DVM, MVetSc, DACVAA
VCA Western Veterinary Specialists, Calgary
Adjunct Professor, University of Calgary Faculty of Veterinary Medicine

WILEY

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Contributors

Noha Abu-Madhi, DVM
Cornell University College of Veterinary Medicine
Rosamond Gifford Zoo

and

Associate Clinical Professor
Cornell University
College of Veterinary Medicine
Ithaca, NY 14853, USA
Email: na24@cornell.edu

Amy B. Alexander, DVM, DACZM
College of Veterinary Medicine
University of Florida, USA

Gen Anderson
General Curator
Saint Augustine Alligator Farm Zoological Park
Saint Augustine, FL, USA
Email: ganderson@alligatorfarm.com

Frederick B. Antonio
Director
Orianne Center for Indigo Conservation
The Orianne Society
30931 Brantley Branch Road
Eustis, FL 32736, USA
Email: fantonio@oriannesociety.org

Jon M. Arnemo, DVM, PhD
Inland Norway University of Applied Sciences
Campus Evenstad
Norway

and

Swedish University of Agricultural Sciences
901 83 Umeå, Sweden
Email: jon.arnemo@inn.no

James E. Bailey, DVM, MS, DACVAA
Innovative Veterinary Medicine, Inc.
101 Marketside Ave, STE 404-402
Ponte Vedra, FL 32081-1541, USA
innovative.veterinary.medicine@gmail.com
(325) 226-1111

Eric Baitchman, DVM, DACZM
Vice President of Animal Health and Conservation
Zoo New England

Mads F. Bertelsen, DVM, DVSc, DECZM (Zoo Health Management), DACZM
Zoological Director
Centre for Zoo and Wild Animal Health
Copenhagen Zoo
Roskildevej 38
DK-2000 Frederiksberg
Denmark
Phone: +45 72200227
E-mail: mfb@zoo.dk

Kate Bodley, BSc (Vet), BVSc (Hons), MVS
Melbourne Zoo
Elliott Ave.
Parkville, VIC
Australia
Email: kbodley@zoo.org.au

Søren Boysen, DVM, DACVECC
Professor
Faculty of Veterinary Medicine
University of Calgary
11877-85th Street NW
Calgary, AB T3R1J3, Canada
Email: srboysen@ucalgary.ca

David B. Brunson
Senior Veterinary Specialist
Companion Animal Division
Zoetis Adjunct Associate Professor
Department of Surgical Sciences in the School of Veterinary Medicine
University of Wisconsin
Madison, WI 53706, USA
2780 Waubesa Ave.
Madison, WI 53711
Email: david.brunson@zoetis.com

Charlene Burns, CVT
Disney's Animals Science and Environment
Department of Animal Health
1200 North Savannah Circle
East Bay Lake, Fl 32830, USA

Mitchell Bush, DVM, Dipl. ACZM
Senior Veterinarian Emeritius
Smithsonian Conservation Biology Institute
Front Royal, VA, USA

Peter E. Buss, BVSc, MMedVet (Wildlife), PhD
Veterinary Senior Manager
Veterinary Wildlife Services
Kruger National Park
South African National Parks
Skukuza, South Africa

Nigel Caulkett, DVM, MVetSc, DACVAA
Veterinary Anaesthesiologist
VCA Western Veterinary Specialists
1802 10 Ave SW
Calgary, AB T3C 0J8, Canada

and

Adjunct Professor
Faculty of Veterinary Medicine
University of Calgary 11877–85th Street NW
Calgary, AB T3R1J3, Canada
Email: nacaulke@ucalgary.ca

Sathya Chinnadurai, DVM, MS, DACZM, DACVAA, DACAW
Chicago Zoological Society
Senior Vice President for Animal Health
3300 Golf Road
One Government Drive
Brookfield, IL 60513, USA
Email: skchinnadurai@gmail.com

Scott B. Citino, DVM., Dipl. ACZM
Senior Veterinarian
White Oak Conservation
581705 White Oak Road
Yulee, FL 32097, USA
Phone: 904-225-3387
Email: scitino@white-oak.org

Tonya Clauss, DVM, MS
Vice President, Animal & Environmental Health
Georgia Aquarium
225 Baker Street Northwest
Atlanta, GA 30313, USA
Email: tclauss@georgiaaquarium.org

David V. Cooper
Retired Veterinarian
Ezemvelo KwaZulu-Natal Wildlife
PO Box 25, Mtubatuba 3935, South Africa

Andrew Cushing, BVSc, Cert AVP (Zoo Med) MRCVS Dip. ACZM
Associate Professor of Zoological Medicine
University of Tennessee, Knoxville, TN, USA
Email: acushin1@utk.edu

Jennifer D'Agostino, DVM, DACZM
Chief Animal Program Officer
Oklahoma City Zoo
Oklahoma City, OK 73111, USA
Email: jdagostino@okczoo.org

Chris Dold
SeaWorld Parks & Entertainment
9205 South Park Center Loop
Suite 400
Orlando, FL 32819, USA

Dana Franzen-Klein, DVM, MS
Medical Director
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108, USA

Whitney Greene, DVM, MS
Disney's Animals Science and Environment
Department of Animal Health
1200 North Savannah Circle, East
Bay Lake, Fl 32830, USA.
Phone: 407-938-3277
Email: natalie.mylniczenko@disney.com

Kurt A. Grimm, DVM, MS, PhD, DACVAA, DACVCP
Owner Veterinary Specialist Services, PC
PO Box 504
Conifer, CO 80433, USA
Phone: 303-918-1321
Email: grimm.dvm@gmail.com

Holly J. Haefele, DVM
Director of Animal Health
Fossil Rim Wildlife Center
2155 County Road 2008
Glen Rose, TX 76043, USA

Nina Hahn
California Department of Public Health
3701 N Freeway Blvd
Sacramento, CA 95834, USA
Phone: (925) 313-6100

Elizabeth E. Hammond, DVM, DACZM
Senior Veterinarian
Lion Country Safari
2003 Lion Country Safari Rd
Loxahatchee, FL 33470, USA

Craig A. Harms, DVM, PhD, Dipl. ACZM, Dipl. ECZM (ZHM)
North Carolina State University
College of Veterinary Medicine and Center for Marine Sciences and Technology
303 College Circle
Morehead City, NC 28557, USA
Phone: 252-222-6339
Email: craig_harms@ncsu.edu

Michelle G. Hawkins, VMD DABVP (Avian Practice)
Professor, One Health Institute
School of Veterinary Medicine
University of California, Davis
Davis, CA 95616

Darryl Heard, BSc, BVMS, PhD, DACZM
Associate Professor Zoological Medicine
Department of Comparative Diagnostic and Population Medicine
College of Veterinary Medicine
University of Florida
Gainesville, FL 32610-0126, USA
Email: heardd@ufl.edu

Peter Holz, BVSc, DVSc, MACVSc, DACZM
Tidbinbilla Nature Reserve
RMB 141
Via Tharwa, ACT 2620
Australia
E-mail: holz@megalink.com.au

Ramiro Isaza, DVM, MS, MPH, DACZM
Professor of Zoological Medicine
Department of Large Animal Clinical Sciences
College of Veterinary Medicine
Gainesville, FL, USA

James G. Johnson III, DVM, MS, CertAqV, DACZM
Denver Zoological Foundation
Head Veterinarian
2300 Steele Street
Denver, CO 80205, USA
Email: johnson.4013@gmail.com

Shawn Johnson
Director of Innovative Medicine
Sea Change Health
596 W. McKinley Ave
Sunnyvale, CA, USA
Phone: 415-480-9664
Email: shawn@seachangehealth.org

Randall E. Junge, MS, DVM, DACZM
Vice President for Animal Health
Columbus Zoo and the Wilds
Cumberland, OH, USA
Email: Randy.Junge@columbuszoo.org

Matthew Kinney, DVM, DACZM
Director of Veterinary Services
San Diego Zoo Safari Park

Felicia Knightly, DVM
Senior Veterinarian
Memphis Zoo
2000 Prentiss Place
Memphis, TN 38112
Cell: 901-238-0721
Office: 901-333-6644
Email: fknightly@memphiszoo.org

Jeff C. Ko, DVM, MS
Professor of Anesthesiology
Diplomate
American College of Veterinary Anesthesia
and Analgesia
Lynn Hall of Veterinary Medicine
625 Harrison Street
West Lafayette, IN 47907, USA
Phone: 765-496-9329
Email: jcko@purdue.edu

Leigh A. Lamont, DVM, MS, DACVAA
Department of Companion Animals
Atlantic Veterinary College
University of Prince Edward Island
Charlottetown, PE, Canada

R. Scott Larsen, DVM, MS, Dipl ACZM
Wildlife Futures Program – University of Pennsylvania
School of Veterinary Medicine
Wildlife Veterinary Liaison
Pennsylvania Game Commission Headquarters
2001 Elmerton Avenue
Harrisburg, PA 17110, USA
Email: rscottlarsen@gmail.com

Gregory A. Lewbart, MS, VMD, Dipl. ACZM, Dipl. ECZM (ZHM)
North Carolina State University
College of Veterinary Medicine
1060 William Moore Drive
Raleigh, NC 27607, USA
Phone: 919-513-6439
Email: galewbar@ncsu.edu

Khursheed R. Mama, DVM, Board Certified Specialist in Veterinary Anesthesia and Analgesia™
Professor, Veterinary Anesthesiology
Department of Clinical Sciences
Colorado State University
Fort Collins, CO 80523-1678, USA
Phone: 970-297-4124
Email: kmama@colostate.edu

Paulo Rogerio Mangini
Pro-Tapir Institute for Biodiversity and
Brazilian Institute for Conservation Medicine-Triade

Michele A. Miller, DVM, MPH, PhD, DECZM (ZHM)
National Research Foundation South African Research
Chair in Animal Tuberculosis
SAMRC Centre for Tuberculosis Research
Division of Molecular Biology and Human Genetics
Faculty of Medicine and Health Sciences
Stellenbosch University
Cape Town, South Africa
Email: miller@sun.ac.za

Anneke Moresco, DVM, PhD
CMU-Tech
2508 Blichmann Ave
Grand Junction CO 81505, USA
Email: anneke_moresco@hotmail.com

Peter vdB. Morkel, BVSc
Wildlife Veterinarian
Independent Consultant
PO Box 294
Karasburg
Namibia

Daniel Mulcahy, PhD, DVM, DACZM
Wildlife Veterinarian (Retired)
Email: drdanielmulcahy@gmail.com

Natalie D. Mylniczenko, MS, DVM, Dipl ACZM
Disney's Animals Science and Environment
Department of Animal Health
1200 North Savannah Circle
East Bay Lake, FL 32830, USA
Phone: 407-938-3277
Email: Natalie.Mylniczenko@disney.com

Julia E. Napier, DVM
345 58th Court
West Des Moines, IA 50266, USA

Elizabeth C. Nolan, DVM, MS, DACZM
Disney's Animals, Science, and Environment
P.O. Box 10,000
Lake Buena Vista, FL 32830, USA
Email: elizabeth.c.nolan@disney.com

Rolf-Arne Ølberg, DVM, DVSc
Director of Animal Care
Kristiansand Dyrepark
4609 Kardemomme By
Norway
Phone: +47 97059860
Email: rolfarne@dyreparken.no

Luis R. Padilla, DVM, DACZM
Director of Animal Health
St. Louis Zoo
1 Government Drive
St. Louis, MO 63110, USA

John M. Parker, DVM
Campus Veterinarian
Laboratory Animal Resource Center
University of California San Francisco
San Francisco, CA, USA

Peter J. Pascoe, BVSc, DVA, DACVAA, DipECVAA, FRCVS.
Emeritus Professor, Department of Surgical and Radiological Sciences
University of California
Davis, CA, 95616

Kristen A. Phair, DVM, Dipl. ACZM
Senior Veterinarian
San Diego Zoo Wildlife Alliance
San Diego Zoo Safari Park
San Diego, CA, USA

Julia Ponder, DVM, MPH
Associate Dean for External Partnerships and Engagement
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108, USA
Email: wille203@umn.edu

Dr. Budhan Pukazhenthi, B.V.Sc., Ph.D.
Research Physiologist
Smithsonian's National Zoo and Conservation Biology Institute
1500 Remount Road
Front Royal, VA 22630
USA
Email: pukazhenthib@si.edu

Robin W. Radcliffe, DVM, DACZM
Associate Professor of Practice of Wildlife and Conservation Medicine
Board Certified Specialist in Zoological MedicineTM
Director, Cornell Conservation Medicine Program
Faculty Fellow, Cornell Atkinson Center for Sustainability
Partnerships For The Planet
Email: partnershipsfortheplanet.or

Patrick Redig, DVM, PhD
Professor/Director Emeritus
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108, USA

Rebecca Richards
Wildlife Veterinary Services, CA

Gianmarco Rojas Moreno, DVM, Esp.
Veterinary Anesthesiologist
Zoo and Wild Animal Medicine and Anesthesia
Escuela de Medicina Veterinaria - Universidad Ricardo Palma
Lima - Peru
Email: gianmarco_rojas@yahoo.com

Marta Romano, DVM, MSc, PhD, Diplomate ACVAA
Clinical Assistant Professor of Anesthesia and Pain Management
Department of Comparative, Diagnostic and Population Medicine
College of Veterinary Medicine, University of Florida
Gainesville, FL 32610, USA
Email: marta.romano@ufl.edu

Todd L. Schmitt, DVM
SeaWorld San Diego
500 SeaWorld Dr.
San Diego, CA 92109, USA
E-mail: todd.schmitt@seaworld.com

Jessica Siegal-Willott, DVM, DACZM
Center for Animal Care Sciences
Smithsonian's National Zoological Park
Smithsonian Conservation Biology Institute
P.O. Box 37012, MRC 5502
Washington, DC 20013-7012, USA
Email: Siegal-WillottJ@mail.vetmed.ufl.edu

Melissa Sinclair
OVC Clinical Studies
Department of Clinical Studies
Ontario Veterinary College
University of Guelph
Guelph, ON N1G 2W1, Canada
Phone: +1-226-924-5872
Email: msinclai@ovc.uoguelph.ca

Kurt K. Sladky, MS, DVM, DACZM, DECZM (Zoo Health Management), DECZM (Herpetology)
Clinical Professor (Zoological Medicine/Special Species Health)
Department of Surgical Sciences
School of Veterinary Medicine
University of Wisconsin
2015 Linden Drive West
Madison, WI 53706, USA
Email: kurt.sladky@wisc.edu

Wm. Kirk Suedmeyer, DVM, DACZM
Director of Animal Health
The Kansas City Zoo
6800 Zoo Drive
Kansas City, MO 64132, USA

Gregory Timmel, DVM, MS, DACLAM
Attending Veterinarian
Legacy Research
Portland, OR, USA

Alessio Vigani, DVM, PhD, ACVECC, ECVECC, ACVAA
University of Zurich Veterinary Hospital
Winterthuerstrasse 260
Zurich, Zurich 8057, Switzerland
Phone: 0041 44 635 8112
Email: avigani@vetclinics.ush.ch

Kent A. Vliet
University of Florida
Department of Zoology
Gainesville, FL, USA
Email: kvliet@ufl.edu

Sarah J. Wahltinez, DVM
University of Florida
College of Veterinary Medicine
2015 Southwest 16th Avenue
Gainesville, FL 32608, USA
Email: sjwahltinez@gmail.com

Michael T. Walsh, DVM, DECZM
Clinical Associate Professor
Department of Comparative Diagnostic
and Population Medicine
College of Veterinary Medicine
University of Florida 32610
2015 SW 16th Ave
Gainesville, FL 32610, USA
Phone: 352-222-4948
Email: mtwdsm@earthlink.net

Chris Walzer, Dr. med. vet., Dipl. ECZM (wph)
Professor
Research Institute of Wildlife Ecology Conservation
Medicine Unit
Department of Interdisciplinary Life Sciences
University of Veterinary Medicine
Savoyenstrasse 1, A-1160 Vienna, Austria

and

Executive Director Health Wildlife Conservation
Society – Global

Tobias Wang
Professor
Department of Biology – Zoophysiology
Aarhus University, Denmark

Mary L. Weldele, BA
Associate Research Specialist
Department of Psychology
University of California Berkeley
Berkeley, CA, USA

Douglas P. Whiteside, DVM, DVSc, DACZM, DECZM
(Zoo Health Management)
Associate Professor (Conservation Medicine)
University of Calgary Faculty of Veterinary Medicine
Head Veterinarian and Senior Manager – Animal Health
and Welfare
Wilder Institute-Calgary Zoo
3280 Hospital Dr. NW
Calgary, AB T2N 4Z6, Canada
Email: dpwhites@ucalgary.ca

Michelle Willette, DVM, MPH, Dipl. ACVPM
Assistant Clinical Professor/Senior Veterinarian
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108, USA
Email: wille203@umn.edu

Catherine Williams, DVM
Senior Veterinarian
Duke Lemur Center
Duke University
Durham, NC, USA

and

Adjunct Assistant
Professor of Zoological Medicine
College of Veterinary Medicine
North Carolina State University
Raleigh, NC, USA

Catherine J.A. Williams, PhD, vetMB
Assistant Professor
Dept. of Animal and Veterinary Sciences
Aarhus University
Blichers Allé 20, Postboks 50
DK-8830 Tjele
Email: catherine.williams@anivet.au.dk

Dawn Zimmerman
Veterinary Initiative for Endangered Wildlife and
Yale School of Public Health

Jeffery R. Zuba, DVM
Senior Veterinarian (retd.)
San Diego Zoo Wildlife Alliance
In Case of Anesthesia Zoo and Wildlife Consultants
Email: doczooba@gmail.com

Preface

Welcome to the third edition of *Zoo Animal and Wildlife Immobilization and Anesthesia*. This edition was developed at a time of great clinical and research advances in the anesthesia of wildlife. The goal of this work was to develop a textbook that promotes best practices in anesthesiology and supports the efficient acquisition and sharing of knowledge. We realize there is some redundancy, but we have tried to reduce repetition wherever possible. Clinical problems are often managed differently, and we understand that clinical experience may influence the decision-making process in anesthesia. We hope that this textbook will also continue to help practitioners prepare for board certification.

We have many new contributors in the third edition, and this has offered a fresh point of view on many subjects.

We want to express our sincere appreciation to all of our contributors who have allowed us to deliver an outstanding new edition.

Gary West, Darryl Heard, and Nigel Caulkett

1

Clinical Pharmacology

Leigh A. Lamont and Kurt A. Grimm

Introduction

Pharmacology is the study of drugs and their interactions with organisms (Page & Maddison 2002). Pharmacology incorporates aspects of statistics, biochemistry, biology, pathology, and medicine. Failure to interpret the description of drugs' pharmacological properties in the context of the clinical picture (i.e., clinical pharmacology) can result in unintended outcomes.

The pharmacological data available for most drugs are mean values derived from a relatively small number of individuals (usually healthy individuals). While this approach provides a starting point for clinical use of drugs, individual responses can vary greatly due to disease states, body condition, environment, genetics, coadministered drugs, and many other factors. When the toxic dose is close to the therapeutic dose (as is often the case with drugs used for immobilization and anesthesia), careful titration of dose and patient monitoring are required. However, the nature of working with wildlife and captive nondomestic species often precludes baseline health assessment, individualization of dosing, and intensive patient monitoring. This is one factor associated with increased risk of adverse outcomes when capturing or anesthetizing nondomestic species. It should also be appreciated that advances in drug safety will likely result in only limited improvement of the safety of anesthesia and immobilization. Management of other risk factors through airway management, reduction of stress, and improvements in supportive care will also be beneficial.

Pharmacokinetics

Pharmacokinetics can be generally defined as what an organism does to a drug. Absorption, distribution, biotransformation, and elimination are processes which determine the concentration of drug at the site of action (i.e., biophase). Pharmacokinetic parameters are estimates of these processes in the group of animals studied. These estimates can be used to predict or understand the way a drug interacts with an organism. It is important to understand that pharmacokinetic parameters can vary between individual animals and can be influenced by many different drug- and organism-related factors. Additionally, pharmacokinetic parameters are derived using mathematical models selected by the investigator. There is usually no correlation between model components and anatomical structures.

Pharmacodynamics

Pharmacodynamics can be generally defined as what a drug does to an organism. Pharmacodynamics includes intended drug effects as well as adverse drug actions. Drugs such as opioids, alpha-2 adrenergic agonists, and antimuscarinics act by binding to relatively well-characterized receptor complexes located on cellular membranes and produce well-characterized effects. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin production by binding to cyclooxygenase enzyme isoforms. Relating plasma drug concentrations to observed NSAID actions can be complex in comparison to other drugs (e.g., opioids) due to the different nature of the action. Preexisting prostaglandins, as well as the slower process of inhibiting an enzyme system, confound the relationship between drug concentration and effect. The molecular and neurophysiologic actions of inhalant anesthetics, in contrast, have not been completely characterized even though the drugs have been used clinically for many years and their pharmacodynamic effects have been well described (Steffey et al. 2015).

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Pharmacodynamic effects are predictable for most clinically used drugs. However, individual animal responses can vary considerably. Additionally, the nature of capture of free-ranging and captive wildlife often makes accurate dosing and drug delivery difficult or impossible. Therefore, close monitoring of patient response and preparation for supportive care are paramount to safe immobilization and anesthesia.

Inhalant Anesthetics

Inhalant anesthetics are commonly used in companion animal veterinary practice. Their use under field conditions is limited due to the requirement for specialized delivery devices and a supply of delivery gas (e.g., oxygen). However, inhalant anesthetics are used commonly in controlled settings such as zoological parks and research laboratories because of the ease of titration of anesthetic depth and rapidity of recovery. Inhalant anesthetics should be delivered by a well-maintained anesthetic machine and properly trained individuals. While inhalant anesthetics are relatively safe, their low therapeutic index mandates frequent and careful monitoring of anesthetic depth.

Physics of Gases and Vapors

An understanding of the processes which influence the uptake and delivery of inhalant anesthetics allows the anesthetist to predict and respond to individual circumstances.

Brief Review of Molecular Theory

Molecules in a liquid state have more vibrational energy than when in a solid state, and each molecule can move through the liquid. If heat is added to a liquid, each molecule gains more kinetic energy and eventually some overcome the forces exerted by their neighbors and escape into the space above the liquid. This state is that of a gas or a vapor. A gas is a phase of matter that expands indefinitely to fill a containment vessel. A vapor is the gaseous state of a material below its boiling point.

A vapor is in equilibrium with the liquid beneath it. Because both gaseous and liquid molecules have kinetic energy, they are in constant motion. The molecules in the vapor phase are striking the liquid–gas interface and returning to the liquid, while liquid molecules are leaving the interface to become vapor. The relationship between these two phases depends mainly on the physicochemical properties of the molecules and the temperature of the system.

Vapor Pressure

Molecules in a gaseous state possess kinetic energy and collide with the walls of the containment vessel. These collisions produce a force on the walls. This force is spread over a surface area and therefore is a pressure (pressure = force/area). This pressure is called the vapor pressure. Since kinetic energy increases directly with temperature, vapor pressure must always be given with reference to the temperature it was measured at (e.g., vapor pressure of water is 47 mmHg at 37°C).

When many gases are present in a mixture, such as with atmospheric air or during delivery of inhalant anesthetics, each gas has a vapor pressure that is independent of the other gases (Dalton's law of partial pressures). It is convention to refer to vapor pressure as partial pressure under these conditions. Partial pressure of an anesthetic agent is analogous to the concept of "free drug" and is important for determining the effect of the anesthetic (e.g., the level of central nervous system (CNS) depression correlates directly with the partial pressure of isoflurane within the brain) (see Table 1.1) (Steffey et al. 2015).

Vapor Concentration

Vapor (i.e., partial) pressure is important for the observed pharmacological effect of inhalant anesthetics. However, almost all anesthesiologists refer to the amount of anesthetic delivered in units of volumes % (said as volumes-percent), or just percent, which is a concentration. The fundamental difference between anesthetic partial pressure and anesthetic concentration is that partial pressure relates to the absolute number of molecules and their kinetic energy whereas concentration refers to the number of molecules of anesthetic relative to the total number of molecules present.

Table 1.1 Anesthetic agent vapor pressures at 20 and 24°C.

Anesthetic Agent	Vapor Pressure @ 20°C in mmHg	Vapor Pressure @ 24°C in mmHg
Methoxyflurane	23	28
Sevoflurane	160	183
Enflurane	172	207
Isoflurane	240	286
Halothane	243	288
Nitrous oxide	Gas	Gas

Source: Adapted from Steffey EP, Mama KM, Brosnan RJ. 2015. Inhalation anesthetics. In: *Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones* (KA Grimm, KA Lamont, WJ Tranquilli, SA Greene, SA Robertson, eds.). Ames: Wiley Blackwell.

Critical Temperature

The critical temperature is the temperature above which a substance cannot be liquefied no matter how much pressure is applied. The critical temperature of nitrous oxide is 36.5°C. Consequently, nitrous oxide can be (and is) a liquid below this temperature, but is a gas at greater temperatures. Placing a nitrous oxide tank near a heat source will result in volatilization of liquid nitrous oxide, resulting in a high tank pressure and danger of explosion or tank venting.

The critical temperature of oxygen is −119°C, therefore at room temperature oxygen cannot be liquefied. All compressed cylinders of medical oxygen contain only gas. There are liquid oxygen tanks, but the internal tank temperature is below −119°C.

Henry's Law

Henry's law states the solubility of a gas in a liquid is proportional to the pressure of the gas over the solution. It describes the solubility of an anesthetic in body fluids or other liquids. From it you can derive the formula $c = k \cdot P$, where c is the molar concentration (mol/L) of the dissolved gas and P is the pressure (in atmospheres) of the gas over the solution. For a given gas k is the Henry's law constant and is dependent on temperature.

Partition Coefficient

A partition coefficient is the ratio of the concentration of a substance in one medium relative to another at equilibrium. It is related to the solubility of an agent. At equilibrium the partial pressure is the same throughout the body, including the alveolar gas, but the concentration of total drug may be very different due to partitioning into tissues or body fluids (Table 1.2) (Steffey et al. 2015). Partition coefficients are not absolute constants for an anesthetic agent. Tissue composition may change as a function of age, sex, body condition, etc. and these changes may influence partitioning.

Table 1.2 Selected partition coefficients of commonly used anesthetic agents.

Anesthetic	Blood:Gas Partition Coefficient	Brain:Blood Partition Coefficient
Nitrous oxide	0.47	1.1
Desflurane	0.42	1.3
Enflurane	2.00	1.4
Sevoflurane	0.68	1.7
Methoxyflurane	15.0	2.0
Isoflurane	1.46	2.7
Halothane	2.54	2.9

Source: Adapted from Steffey EP, Mama KM, Brosnan RJ. 2015. Inhalation anesthetics. In: *Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones* (KA Grimm, KA Lamont, WJ Tranquilli, SA Greene, SA Robertson, eds.). Ames: Wiley Blackwell.

Mechanism of Action of Inhaled Anesthetics

The simplest definition of general anesthesia is a reversible drug-induced loss of consciousness (Franks 2006). All clinically used injectable and inhaled general anesthetics reversibly induce unconsciousness at low concentrations and induce an increasing lack of responsiveness at higher concentrations (Franks 2006). Though there are a number of other desirable clinical end-points including amnesia, analgesia, immobility and muscle relaxation (Brown et al. 2010), commonly used anesthetics vary in their ability to produce these effects. Consequently, any explanation of anesthetic mechanism of action must focus on unconsciousness as the critical end-point.

Despite their longstanding and widespread use, and well-characterized pharmacodynamic effects, the specific molecular and neurophysiologic mechanisms of action of general anesthetics are only now beginning to be elucidated thanks to research accumulated over the past 120 years.

The first widely accepted theory of general anesthesia was published by Meyer and Overton in 1901. They observed that most anesthetics were lipophilic and highly hydrophobic and noted a correlation between an anesthetic's potency and the agent's oil–gas partition coefficient (Meyer 1901; Overton 1901). The so-called Meyer–Overton correlation formed the basis for numerous lipid bilayer hypotheses of anesthetic action that dominated the literature until the 1970s.

Franks and Leib were among the first to question the unitary hypothesis that the lipid bilayer was the sole site of anesthetic action (Franks & Leib 1978). They subsequently published their seminal work demonstrating that the Meyer–Overton correlation was preserved for inhibition of firefly luciferase, a soluble lipid-free model protein (Franks & Lieb 1984), which gave rise to the protein receptor hypothesis of general anesthesia. While many potential protein targets have been studied, strong evidence for direct involvement in anesthetic-induced loss of consciousness currently exists for only three: gamma-aminobutyric acid subtype A ($GABA_A$) receptors, two-pore-domain potassium (2PK) channels, and N-methyl-D-aspartate (NMDA) receptors (Uhrig et al. 2014; Chau 2010; Franks 2008).

The $GABA_A$ family of receptors is responsible for most of the fast neuronal inhibition in the mammalian CNS and enhanced GABA-activated chloride currents cause hyperpolarization of neuronal membranes and reduce neuronal activity. Almost all general anesthetics have been found to potentiate GABA-induced chloride currents but are only

capable of directly activating $GABA_A$ receptors at much higher, clinically irrelevant concentrations. Several different mutations in the alpha subunits of the $GABA_A$ receptor have been shown to eliminate or reduce the effects of volatile anesthetics (Mihic et al. 1997; Krasowski & Harrison 2000; Jenkins et al. 2001, 2002; Nishikawa & Harrison 2003; Forman & Miller 2016), whereas those in the beta subunits can reduce the effects of both intravenous and volatile anesthetic agents (Krasowski & Harrison 2000). Experiments demonstrating a correlation between stereoselectivities seen in genetically modified animals in vivo and those found with extrasynaptic $GABA_A$ receptors in vitro provide convincing evidence that these receptors play an important role in volatile anesthetic-induced loss of consciousness (Franks 2008).

The 2PK channels are thought to provide "background" modulation of neuronal excitability. Five members of this channel family (TREK1, TREK2, TASK1, TASK3, and TRESK) can be directly activated by volatile anesthetics (Patel et al. 1999) but anesthetic sensitivity among these channels is not uniform. Anesthetic activation of 2PK channels generally inhibits neuronal activity by either hyperpolarizing the membrane and/or increasing membrane conductance, thus reducing the effects of excitatory currents (Franks 2008). However, these channels are also found presynaptically and their activation here may be inhibitory (if at an excitatory synapse) or excitatory (if at an inhibitory synapse). A growing body of evidence suggests these channels mediate at least some of the effects of volatile anesthetics (Franks 2008).

NMDA receptors mediate the slow components of synaptic transmission in the CNS and may be important targets for certain anesthetics. Both gaseous (i.e., xenon and nitrous oxide) and volatile (i.e., isoflurane, sevoflurane, halothane, and desflurane) inhaled anesthetics inhibit NMDA receptors to some extent but considerable variability exists among agents. Although it is likely that NMDA receptor antagonism plays a role in the actions of xenon and nitrous oxide and, to a lesser extent, the volatile agents, additional targets are required to account for their ability to cause loss of consciousness (Franks 2008).

Determining the cascade of events that follow binding of an anesthetic agent to its molecular target(s) leading to loss of consciousness has proven difficult. Remarkable advances in neuroscience and neuroimaging techniques (e.g., positron emission tomography, functional magnetic resonance imaging [fMRI], magnetoencephalography, and electroencephalography) over the past two decades are beginning to unravel the neural correlates of consciousness which will help answer this longstanding question.

Convergent evidence from multiple studies involving multiple species, multiple neuroimaging modalities, multiple analytic techniques, and diverse drug classes suggests that anesthetic-induced unconsciousness is characterized by a functional fragmentation (also referred to variably as a disconnection or uncoupling) of cortical and thalamocortical networks (Hudetz & Mashour 2016; Li et al. 2017; Mashour & Hudetz 2017). One specific cortical region, known as the lateral frontoparietal network, has received considerable attention over the last decade. Both fMRI and electroencephalographic studies of diverse classes of anesthetics, including volatile inhaled agents, consistently show a functional breakdown in frontoparietal connectivity and surrogates of frontoparietal information transfer (Hudetz & Mashour 2016; Mashour & Hudetz 2017). As our understanding of consciousness continues to evolve, traditional references to the "depth of anesthetic hypnosis" may require revision to reflect the fact that general anesthetics may variably suppress certain higher-order components of consciousness while retaining others (Sleigh et al. 2018).

Inhalant Anesthetic Pharmacokinetics

Anesthetic Uptake and Distribution

A series of partial pressure gradients, beginning at the vaporizer, continuing in the anesthetic breathing circuit, the airways, alveoli, blood, and ending in the tissues will drive the movement of an anesthetic gas. The movement of that gas will continue until equal partial pressures are present throughout the system. Since the lung is the point of entry and exit to the body, the alveolar partial pressure governs the partial pressure of the anesthetic in all body tissues. Therefore, it is most important to understand how to influence the alveolar partial pressure. Increasing alveolar minute ventilation, flow rates at the level of the vaporizer, and inspired anesthetic concentration can speed the delivery of anesthetic and increase the rate of rise of alveolar anesthetic partial pressure. Solubility, cardiac output, and the alveolar-to-venous anesthetic gradient are factors that determine the uptake of the anesthetic from the alveoli into the blood. Solubility describes the affinity of the gas for a medium such as blood or adipose tissue and is reported as a partition coefficient. The blood/gas partition coefficient describes how the gas will partition itself between the two phases (blood and alveolar gas) after equilibrium has been reached. Isoflurane, for example, has a blood/gas partition coefficient of approximately 1.46 (Steffey et al. 2015). This means that if the gas partial pressures are in equilibrium, the concentration in blood will be 1.46 times greater than the concentration in the alveoli. A higher blood/gas partition coefficient means a greater uptake of the gas into the blood, therefore a slower rate of rise of alveolar and blood partial pressure. Since the blood partial pressure rise is slower, it takes longer for the brain partial pressure of the gas to increase, resulting in a longer induction time.

Increased cardiac output exposes the alveoli to more blood per unit time. The greater volume of blood removes more inhalant anesthetic from the alveoli, therefore lowering the alveolar partial pressure. The agent might be distributed faster within the body, but the partial pressure in the arterial blood is lower. It will take longer for the gas to reach equilibrium between the alveoli and the brain, therefore a high cardiac output usually prolongs induction time. The alveolar to venous partial pressure difference reflects the tissue uptake of the inhaled anesthetic. A large difference is caused by increased uptake of the gas by the tissues during the induction phase.

Transfer of the gas from the arterial blood into tissues such as the brain will depend on perfusion and the relative solubility of the gas in the different tissues. The brain/blood coefficient describes how the gas will partition itself between the two phases after equilibrium has been reached. Isoflurane has a brain/blood coefficient of 2.7, therefore when the system is at equilibrium the concentration in the brain will be 2.7 times greater than the concentration in the blood (Steffey et al. 2015). All contemporary inhalation anesthetics have high adipose/blood partition coefficients. This means that most of the gas will accumulate in adipose tissue as times goes by. The partial pressure of the gas in adipose tissue will rise very slowly since this tissue has a high capacity (as indicated by the high adipose/blood partition coefficient). Inhalation anesthetics stored in obese patients may delay awakening at the end of long periods of anesthesia. Fortunately, adipose tissue has a relatively low blood flow and doesn't accumulate significant amounts of anesthetic during the short periods of anesthesia commonly encountered in veterinary medicine.

Elimination of Inhaled Anesthetics

The rate of induction and recovery from anesthesia with inhalant anesthetics differs between agents due to differences in tissue solubility, but general statements can be made. During induction all tissue partial pressures are zero. During recovery, different tissues in the body have different partial pressures of anesthetic, which are governed by the tissue anesthetic content and not the alveolar partial pressure. Recovery is not as controllable as induction of anesthesia. During recovery from anesthesia, elimination occurs due to exhalation and biotransformation.

The enzymes responsible for inhalant anesthetic metabolism are mainly located in liver and kidneys. Anesthetic elimination via metabolism is approximately 50% for methoxyflurane, 10–20% for halothane, 5–8% for sevoflurane, 2.5% for enflurane, about 0.2% for isoflurane, 0.001% for desflurane, and nearly zero for nitrous oxide (Steffey et al. 2015). The amount of anesthetic eliminated from the body during anesthesia due to metabolism is small compared with the amount exhaled. However, anesthetic metabolism accounts for a larger proportion of the anesthetic clearance after anesthetic delivery ceases. The low, but prolonged, blood partial pressure of the anesthetic found after terminating delivery is no longer overwhelming the enzyme systems (enzymes become saturated above ~1 MAC [minimum alveolar concentration]) so metabolism accounts for a larger proportion of clearance than it did during exposure to high partial pressures.

Elimination of the anesthetic via the lungs can be complex. The first point to consider is what effect an increase in alveolar minute ventilation will have on recovery. During recovery, increasing minute ventilation will decrease alveolar anesthetic partial pressure and increase the gradient for diffusion from the blood to the alveoli. This increases elimination, especially for most anesthetic agents with high blood/gas partition coefficients.

Another situation to consider is what effect a change in cardiac output will have on the rate of decrease of partial pressure of the inhalant anesthetic. During induction, high cardiac output will increase the rate at which anesthetic is removed from the lung, slowing the rate of rise of anesthetic partial pressure and slowing induction. When cardiac output is reduced (e.g., cardiogenic shock) there is a slower removal of anesthetic and subsequently a faster rate of rise of alveolar partial pressure and induction occurs. During recovery a high cardiac output will increase the rate at which anesthetic is returned to the lung for excretion. Since the partial pressure of anesthetic in the blood is determined by the tissues, the higher blood flow will shorten recovery. During low cardiac output situations there will be a slower recovery due to the decreased rate at which tissue anesthetic partial pressure decreases.

The last major influence on the rate of induction and recovery is the solubility of the anesthetic agent. Agents with high blood/gas solubility will be partitioned into the blood to a greater extent than agents with low blood/gas solubility. The blood acts as a depot for agent maintaining anesthetic partial pressure. Agents with low blood/gas solubility do not partition into the blood to the extent of highly soluble agents, thus the decrease in partial pressure is faster and recovery time is reduced. Highly soluble agents have high blood concentrations and it will take longer for the partial pressure to decrease if all other factors are equal. In summary, elimination of a volatile anesthetic depends on the ventilation, cardiac output, and solubility of the gas in blood and tissue.

Control of the Partial Pressure of Delivered Anesthetic

Inhalant anesthetics can be classified as either gaseous (nitrous oxide and xenon) or volatile (isoflurane, sevoflurane, halothane, methoxyflurane, and desflurane). Gaseous

anesthetics are usually delivered to the anesthesia machine under pressure and their rate of delivery to the breathing circuit is controlled by a flow meter. Volatile anesthetics are liquids at room temperature and pressure, and are usually delivered by a specialized apparatus that controls the volatilization of the liquid and proportioning of the vapor in the fresh gas delivered to the patient. A vaporizer can be as simple as piece of cotton soaked with agent held near the nose (not recommended) or can be as complex as the desflurane vaporizer, which is an electrically powered device with a heated vaporizing chamber.

The Breathing System

With most modern anesthetic machines the outflow gas from the vaporizer will be delivered to the patient through a set of tubes and machinery collectively called a breathing system. There are many styles of breathing systems, each with a multitude of uses. It is important that the anesthetist understands how the type of breathing circuit used will impact the rate at which the anesthetic concentration can be changed and the relationship between the vaporizer setting and inspired concentration.

Waste Anesthetic Gases

The health effects of chronic exposure to waste anesthetic gases are not completely known. The frequency of inhalant anesthetic use and the lack of significant associations between exposure and most types of chronic toxicities (e.g., cancer, infertility, birth defects, etc.) would suggest there is only a very low risk (if any) associated with chronic exposure. However, certain individuals are highly susceptible to potentially life-threatening reactions, even with trace level exposure (e.g., malignant hyperthermia). In light of this, and with the admission that we do not completely understand all the risks associated with chronic exposure, it is generally agreed that the exposure of personnel be kept as low as reasonably acceptable (ALARA). In the United States, the Occupational Safety and Health Administration requires veterinary hospitals to maintain a system to prevent waste gases from building up in the area of use and can enforce exposure limits that are consistent with guidance from the National Institute of Occupational Safety and Health (NIOSH). Currently, no NIOSH–recommended exposure limits exist for the three most currently used anesthetics (isoflurane, desflurane, and sevoflurane) and at present NIOSH has no published permissible exposure limits regulating these specific agents (American Veterinary Medical Association 2020).

Minimum Alveolar Concentration

Although loss of consciousness is arguably the most critical end-point of general anesthesia (see section on the inhaled anesthetic mechanism of action), it remains challenging to measure in a clinical setting. Immobility in the face of a noxious stimulus is also an important end-point and has formed the basis of the standard unit of inhaled anesthetic potency – minimum alveolar concentration (MAC) – since the 1960s (Merkel & Eger 1963). While our understanding of how inhaled anesthetics produce immobility continues to evolve (Eger et al. 2008), MAC remains the standard measurement of dose in clinical anesthesia. It is defined as the minimum alveolar concentration at 1 atmosphere required to prevent gross purposeful movement in 50% of the subjects tested, following a 60-second application of a supramaximal stimulus (Steffey et al. 2015). One MAC is by definition the EC_{50} (i.e., the effective concentration in 50% of patients) for that agent. Animals awaken from anesthesia at approximately 0.5 MAC, surgical anesthesia occurs at approximately 1.3 MAC, and severe autonomic nervous system depression occurs around 2 MAC.

Birds and many reptiles do not have true alveoli so the concept of MAC has been modified or redefined to be the minimum anesthetic concentration. It is not identical to MAC from other species, but closely approximates it in many ways.

Physiological and Pharmacological Factors That Alter MAC

Minimum alveolar concentration is age-dependent, being lowest in newborns, reaching a peak in infants, and then decreasing progressively with increasing age (Lerman et al. 1983, 1994; Taylor & Lerman 1991). Increases in MAC can also occur from hyperthermia and hypernatremia, and decreases in MAC can result from hypothermia, hyponatremia, pregnancy, hypotension, and drugs such as lithium, lidocaine, opioids, and alpha-2 adrenergic agonists.

General Pharmacological Actions of Inhalant Anesthetics

Inhalant anesthetic agents have more similarities than differences with respect to their effects on vital organ systems. The differences are primarily related to the speed and magnitude with which the changes occur. There are a few classic differences that have been included in the following synopsis.

Central Nervous System

All inhalant general anesthetics alter consciousness, memory, and pain perception by acting on the CNS. Most inhalant anesthetics cause a mild to moderate decrease in the cerebral metabolic requirement for oxygen ($CMRO_2$) and they usually have minimal effects on cerebral blood flow autoregulation at low MAC multiples (Mielck et al.

1998, 1999). Patients with intracranial hypertension should not be anesthetized with nitrous oxide because it may cause an increase in $CMRO_2$ (Roald et al. 1991; Algotsson et al. 1992; Hoffman et al. 1995). Halothane is also a poor choice because of its significant effects on cerebral blood flow autoregulation (Steffey et al. 2015). Isoflurane, sevoflurane, and desflurane are the inhalants of choice.

Cardiovascular System

Most inhalant anesthetic agents cause direct myocardial depression. Halothane is the most depressant on contractility, but it generally has the fewest effects on vascular resistance (Steffey et al. 2015). Isoflurane, enflurane, sevoflurane, and desflurane cause some degree of vasodilatation, which tends to improve forward blood flow and maintain tissue perfusion. The reduction in afterload also tends to offset some of the direct myocardial depressant effects and may result in a net improvement in cardiac output. Nitrous oxide is a sympathomimetic and can improve contractility, blood pressure, and heart rate at light levels of anesthesia. Rapid changes in anesthetic concentration (especially with desflurane) may result in a sympathetic response and temporarily increase cardiac work.

Respiratory System

All anesthetics tend to depress the chemoreceptor response to carbon dioxide, leading to an accumulation of carbon dioxide and a respiratory acidosis unless ventilation is assisted or controlled. The ether derivatives tend to be the most depressant, but all agents may cause significant depression. Most inhalant agents may interfere with hypoxic pulmonary vasoconstriction and may worsen ventilation-perfusion matching in the lung. This is most dramatic in larger animals, where significant pulmonary shunting is often observed.

Genital-Renal Systems

Most anesthetics cause a decrease in renal perfusion and an increase in antidiuretic hormone (ADH) secretion. Inhalant anesthetics may be the safest anesthetic techniques in anuric renal failure since pulmonary excretion is not dependent on renal function.

Inhalant anesthetics may cause an increase in postpartum uterine bleeding. This is a bigger consideration in primate anesthesia due to placentation characteristics. Isoflurane, sevoflurane, desflurane, and nitrous oxide have been advocated for use during Caesarian section because of the rapid onset and termination of effect, and the transient effects on the delivered fetuses. Methoxyflurane and halothane are less desirable due to their greater solubility and slower elimination.

Clinically Useful Inhalant Anesthetics

Nitrous Oxide

Nitrous oxide is commonly used in combination with a primary inhalant or injectable anesthetic drug. The reason it is not useful in veterinary anesthesia as a solo anesthetic is because of its low potency. Nitrous oxide's MAC value has been estimated to be near 100% for humans and closer to 200% for veterinary patients. It is obvious that 200% nitrous oxide cannot be delivered; in fact no more than 79% nitrous oxide can be safely delivered without creating a hypoxic gas mixture. In practice it is common to use a 50% nitrous oxide mixture with the balance of the mix being oxygen. If 50% nitrous oxide is delivered to an animal it is only providing approximately 0.25 MAC of anesthesia. A potent volatile anesthetic, injectable agent, or other sedative/analgesic drug must supply the remaining 0.75 MAC. Because of this limited anesthetic effect, nitrous oxide use for anesthetic maintenance is not widespread in veterinary medicine. Nitrous oxide is used by some anesthetists during induction of anesthesia for the *second gas effect*. Since nitrous oxide is present in the inspired gas mixture in a relatively high concentration and it rapidly diffuses into the body from the alveoli, the rate of rise of partial pressure of a second coadministered inhalant anesthetic is increased and the induction time can be shortened.

Nitrous oxide has a low blood/gas partition coefficient and has a rapid onset and recovery. The gas can diffuse out of the blood so rapidly that if nitrous oxide delivery is suddenly halted and supplemental oxygen is not administered, a situation known as *diffusion hypoxia* may result. Diffusion hypoxia happens when the mass movement of nitrous oxide down its partial pressure gradient results in high alveolar nitrous oxide partial pressure at the expense of oxygen and nitrogen partial pressures. Since breathing room air will result in an alveolar oxygen partial pressure of approximately 100 mmHg under ideal circumstances, any displacement of oxygen by nitrous oxide will result in alveolar hypoxia. Diffusion hypoxia can be minimized or prevented by continuing the administration of oxygen enriched gas for 5–10 minutes following the discontinuation of nitrous oxide. This helps because during normal breathing, 100% oxygen should result in an alveolar oxygen partial pressure close to 500 mmHg. The partial pressure of oxygen can drop a lot further before hypoxia develops.

Nitrous oxide is contraindicated in animals with pneumothorax, gastric dilatation/rumen tympany, gas embolism, and other conditions that are exacerbated by accumulation of gas inside a closed space. This effect is caused by diffusion of nitrous oxide out of the blood into the preexisting gas space in an attempt to establish equilibrium. Nitrous oxide is also contraindicated in animals with

gas diffusion impairment such as interstitial pneumonia. These animals typically have low arterial oxygen partial pressure when breathing oxygen-rich mixtures. The dilution of oxygen by nitrous oxide will lower the inspired oxygen partial pressure and may worsen hypoxemia.

Halothane

Halothane was a major advancement in inhalant anesthesia in its day. It was introduced in the late 1950s and was potent, nonirritating, and nonflammable. Chemically it is classified as a halogenated hydrocarbon and it is not chemically related to the ethers. Halothane was used widely in human anesthesia until it became apparent there were potentially fatal adverse effects associated with its use. Human patients developed a syndrome known as *halothane hepatitis* (Daghfous et al. 2003; Neuberger 1998). This rare, but life-threatening, complication is still somewhat of a mystery, although an immunological etiology is implicated. The disease appears as a fulminant hepatitis, similar to that seen with viral hepatitis, which develops after a short period of apparent recovery. A second, more common, form of hepatitis is less severe and is characterized by a reversible elevation in liver enzymes. The etiology of this second form is thought to be anesthetic-related hepatic hypoxia and does not appear to be immune related. Diagnosis of the correct form is important since repeated exposure to halothane, or any of the volatile agents producing trifluoroacetic acid, is more likely to trigger the immunologically mediated form and result in high morbidity and mortality. Both forms are not commonly documented in veterinary patients; however, transient elevation of liver enzymes may occur postoperatively in some patients. A thorough diagnostic workup is required due to the nonspecific and multifactorial etiology of elevated liver enzymes.

A second complication associated with halothane anesthesia is the development of arrhythmias. Halogenated hydrocarbon anesthetics, especially halothane, can sensitize the myocardium to the arrythmogenic effects of epinephrine. Halothane is generally contraindicated in patients that are predisposed to ventricular arrhythmias (e.g., hypoxia, trauma, or myocardial disease) (Steffey et al. 2015). Arrhythmias that develop during halothane anesthesia may resolve when the anesthetic agent is switched to isoflurane or sevoflurane. Other causes of perianesthetic arrhythmias should also be ruled out.

Halothane undergoes extensive hepatic metabolism (~20%) and is not chemically stable (Steffey et al. 2015). Commercially available halothane contains thymol, a preservative, which does not volatilize to the same degree as halothane. This results in a sticky residue inside the vaporizer that should be cleaned out during periodic maintenance. Veterinary use of halothane is declining due to the increasing popularity of isoflurane and sevoflurane, and its limited availability worldwide.

Isoflurane

Isoflurane is arguably the most widely used veterinary inhalant anesthetic in the world today. It is stable, potent, and undergoes little metabolism. Isoflurane can be irritating to airway tissues at high-inspired concentrations and its use for induction in people has been limited because of patient complaints and complications. However, in veterinary medicine isoflurane mask induction is still common. Isoflurane is a potent agent (MAC ~1.3% in dogs) and has a high saturated vapor pressure (~240 mmHg at room temperature) (Steffey et al. 2015). These characteristics, coupled with the fact that it is possible to cause rapid partial pressure changes in the brain, would suggest that only precision vaporizers located outside the circuit should be used to deliver the agent. However, several reports of the use of modified vaporizer inside circuit (VIC) vaporizers suggest that this type of anesthetic system can be used to safely administer the agent (Bednarski et al. 1993; Laredo et al. 1998).

Isoflurane metabolism is minimal (less than 1%) and fluoride-induced nephrotoxicity is uncommon. Isoflurane and many of the ether-derivative volatile agents are excellent vasodilators and can cause or worsen hypotension.

Desflurane

Desfluane use in veterinary medicine is limited to academic institutions and a very limited number of private practices. The main disadvantage to desflurane use is the cost associated with the agent and the cost associated with a specialized vaporizer that is required to deliver the drug. Desflurane is extremely insoluable and is capable of producing extremely rapid inductions and recoveries (Barter et al. 2004; Clarke 1999). Its main market is for human outpatient anesthesia, where rapid recovery is a large cost savings. It is highly fluorinated, has a very low potency (MAC ~9%), and has a high saturated vapor pressure (~670 mmHg at room temperature) (Steffey et al. 2015). Desflurane boils at 23°C and must be handled using specialized apparatus for vaporizer filling. The vaporizer is specific for desflurane and is electrically heated to boil the desflurane so that a reliable vapor pressure will be produced. Then sophisticated differential pressure transducers and electronic circuits calculate an injection ratio for delivery of the desired anesthetic concentration. Desflurane is very stable and undergoes almost no metabolism.

Sevoflurane

Sevoflurane is the newest volatile inhalant anesthetic approved for veterinary use. Sevoflurane has a low blood/gas partition coefficient (~0.7) which is greater than desflurane and nitrous oxide, but about half of that of isoflurane. Extensive pulmonary elimination of sevoflurane minimizes the amount available for metabolism. Up to 3–8% of the sevoflurane dose is metabolized and appears in the urine as inorganic fluoride (Steffey et al. 2015). This fluoride exposure does not appear to be clinically significant, although serum levels of fluoride can approach those previously reported to be nephrotoxic for methoxyflurane. Factors other than peak serum fluoride concentrations appear important for predicting the incidence of nephrotoxicity (Driessen et al. 2002).

Sevoflurane represents a deviation from the methyl ethyl ether structural theme present in other contemporary volatile anesthetics. Sevoflurane is chemically related to methyl-isopropyl ethers. The structure is significant because an important metabolite of most methyl-ethyl ether volatile anesthetic agents (trifluoroacetic acid) is a suspected trigger of halothane hepatitis. Sevoflurane cannot be metabolized to form this compound. This is not a major consideration in veterinary medicine but is important in human anesthesia. Sevoflurane is also pleasant and nonirritating when used for mask induction and many pediatric anesthesiologists suggest this agent is the drug of choice for pediatric induction via mask. Sevoflurane is less potent than isoflurane (MAC ~2.3% for dogs and horses). When used for induction of anesthesia it is common to use 7–9% sevoflurane.

An early subject of controversy surrounding sevoflurane anesthesia was the production of compound A. Compound A is a degradation product produced when sevoflurane reacts with the carbon dioxide absorbent. Early toxicology studies performed in rats suggested that proximal tubular renal damage could result from clinically relevant exposure to compound A. This led to the suggestion that sevoflurane should not be used in closed-circuit anesthesia or with fresh gas flow rates lower than 2 L per minute. However, since that time little clinical evidence of renal damage in humans and dogs has emerged, even with very low fresh gas flows. Some have suggested that rats have a 10–100 times higher level of the enzyme beta-lyase that is believed to convert the intermediate compounds of Compound A metabolism to a nephrotoxic molecule (Kharasch et al. 2005; Sheffels et al. 2004). Humans and dogs do not appear to have the same level of enzyme conversion and are therefore less susceptible to Compound A toxicity. Safety studies in most other rodents and exotic animals are not published and caution should be used when administering sevoflurane via a breathing system using a carbon dioxide absorbant until further safety data are available (Table 1.3).

Table 1.3 Structure and characteristics of inhalation anesthetics.

Agent	Year Introduced	Structure	Type
Halothane	1956	CF_3–CHClBr	Alkane
Isoflurane	1981	CF_3CHCl–O–CHF_2	Ether
Enflurane	1972	$CHClF$–CF_2–O–CHF_2	Ether
Methoxyflurane	1960	$CHCl_2$–CF_2–O–CH_3	Ether
Desflurane	1992	CF_3CHF–O–CHF_2	Ether

Injectable Anesthetics

Injectable anesthetics are an important family of compounds used for immobilization and anesthesia of wildlife. The dissociative anesthetics in particular are commonly combined with other adjunctive drugs such as alpha-2 adrenergic agonists and opioids to improve the reliability and speed of onset of action.

Barbiturates

Barbiturates can be classified in several ways. One is by chemical structure. Oxybarbiturates are historically important, but not commonly used today due to their slower onset of action, long recovery characteristics, and relatively small margin of safety. Pentobarbital is the prototypical oxybarbiturate. It has been combined with several adjunctive drugs for anesthesia. The thio (i.e., sulfur-substituted) analog of pentobarbital, thiopental, was commonly used in veterinary medicine for intravenous induction of anesthesia for many years but is no longer widley available.

Barbiturates cause anesthesia through global depression of CNS activity. This is accomplished through interference with nervous system impulse conduction. Like many other anesthetics, other excitable tissues can be affected, resulting in commonly encountered side effects, including depression of cardiorespiratory function. Barbiturates decrease cerebral blood flow (CBF) and the $CMRO_2$. $CMRO_2$ decreases progressively until electroencephalographic activity becomes isoelectric (Branson 2007).

Propofol

Propofol (2,6-di-isopropylphenol) is commonly used for sedation, induction, and maintenance of anesthesia in humans and domestic species. Propofol is supplied as a milky white liquid for intravenous injection. It is insoluble in aqueous solution therefore it is usually formulated as an emulsion of 10% soybean oil, 2.25% glycerol, and 1.2% egg phosphatide. Some formulations of propofol (e.g., Diprivan®, Propoflo™) do not contain preservative and will support bacterial and fungal growth should the drug become contaminated. This has led to the label recommendation of discarding unused drug at the end of the procedure or within 6 hours of opening a vial. Other formulations have additives such as benzyl alcohol (e.g., PropoFlo28®) to improve stability or reduce the potential of contamination with storage. Species-sensitivities to these additives should be investigated before their use (Davidson 2001).

Propofol is classified as an ultrashort-acting injectable anesthetic agent. Duration of effect is typically 5–10 minutes in dogs and 5–20 minutes in cats. Its rapid recovery characteristics are maintained in most species following prolonged infusions. Recovery times may be prolonged in the cat (and other species that have reduced capacity for glucuronidation of drugs) following repeated doses or continuous rate infusions.

Propofol has been used in dogs, cats, horses, pigs, goats, sheep, and even birds. Wild turkeys, mallard ducks, pigeons, and chickens have been anesthetized with propofol, but there is significant cardiorespiratory depression in ducks and chickens, indicating birds may need ventilatory support during anesthesia (Machin & Caulkett 1998). Apnea and respiratory depression are the best known side effects of propofol administration. The incidence of apnea may be reduced by administering the drug over 60–90 seconds (Muir & Gadawski 1998). It would be prudent to be prepared to intubate and support ventilation if apnea occurs. Pain is reported on propofol injection by some people. Muscle fasciculations and spontaneous twitching can occur in some animals.

Dissociative Anesthetics

Ketamine

Most veterinary formulations of ketamine are a racemic mixture consisting of two optical enantiomers. However, in many countries (*S*)-ketamine is available as a human or veterinary product. The *S* enantiomer is less cardiodepressant and has a four-fold greater affinity for the phencyclidine site in the NMDA receptor. Serotonin transport is inhibited two-fold by the *R* form. Some of ketamine's effects are not stereoselective. Norepinephrine release is equivalent from the *S* and *R* forms (Kohrs & Durieux 1998).

Ketamine can be administered intramuscularly to anesthetize animals which are not easily given drugs intravenously. Intramuscular administration will produce a longer duration of anesthesia than intravenous administration, but the recovery is usually longer and can be accompanied by more dysphoria. Recovery from ketamine appears to be due to redistribution and metabolism similar to the thiobarbiturates. Hepatic biotransformation to norketamine (metabolite I) and dehydronorketamine (metabolite II) is the major route of metabolism in most species studied. It was thought ketamine was excreted unchanged in the urine of cats, but this originated from one paper published in 1978 by Gaskell et al. and since that time it has been shown by Waterman that biotransformation is an important route of elimination in domestic cats (Waterman 1983). Norketamine is about one-third to one-fifth as potent as the parent compound but may contribute to the prolonged analgesic effects of ketamine (Kohrs & Durieux 1998).

Ketamine produces a form of anesthesia that is different from other hypnotic drugs. In general terms, ketamine induces anesthesia and amnesia by functional disruption (dissociation) of the CNS through marked CNS stimulation resulting in catalepsy, immobility, amnesia, and marked analgesia. Electroencephalographic analysis indicates that depression of the thalamoneocortical system occurs in conjunction with activation of the limbic system. Awakening from ketamine anesthesia in people is frequently characterized by disagreeable dreams and hallucinations. Sometimes these unpleasant occurrences may recur days or weeks later. Almost half of adults over the age of 30 exhibit delirium or excitement, or experience visual disturbances. The occurrence of adverse psychological experiences is much lower in children. The incidence of adverse psychological experiences in animals is unknown, but a significant number of animals transiently vocalize and have motor disturbances during recovery.

Ketamine's neuropharmacology is complex. The compound interacts with NMDA and non-NMDA glutamate receptors, nicotinic, muscarinic cholinergic, monoaminergic, and opioid receptors. In addition there are interactions with voltage-dependent ion channels such as Na^+ and L-type Ca^{2+} channels. It is believed that the NMDA receptor antagonism accounts for most of the analgesic, amnestic, psychomimetic, and neuroprotective effects of the compound, but the exact mechanism of its anesthetic action is not known. NMDA receptor activation is believed to play a role in the "memory" of the CNS, which is involved in the "wind-up," hyperalgesia, and allodynia seen in certain pain syndromes (Kohrs & Durieux 1998).

Ketamine can increase the $CMRO_2$ due to increased metabolic activity associated with increased activity in certain

areas of the brain. Intracranial pressure (ICP) also increases, possibly because of two mechanisms: (1) ketamine can increase mean arterial blood pressure so CBF can increase and ICP can passively increase in patients with altered autoregulation, and (2) ketamine can depress respiration, increasing the arterial partial pressure of carbon dioxide $PaCO_2$. The brain responds to elevations in $PaCO_2$ by increasing CBF, which will increase ICP. Ventilation may reduce the increase in CBF. Current clinical dogma dictates avoiding ketamine in patients with suspected head trauma.

Ketamine causes a characteristic breathing pattern termed *apneustic breathing*, characterized by prolonged inspiratory duration and relatively short expiratory time. When ketamine is administered by itself, it typically causes minimal respiratory depression that is short-lived. Hypoxic and hypercapnic respiratory regulation appears to remain intact, but ketamine is seldom given alone. It is often combined with benzodiazepines, acepromazine, opioids, or alpha-2 adrenergic agonists. The combined effect of these drugs is usually decreased minute ventilation, increased $PaCO_2$, and mild respiratory acidosis.

Ketamine, when given to animals with functioning sympathetic nervous systems, generally increases heart rate and arterial blood pressure. Cardiac output will usually stay the same or slightly increase. Ketamine is seldom given alone to healthy animals. The use of adjunctive drugs, such as benzodiazepines, acepromazine, or alpha-2 adrenergic agonists, tends to blunt the sympathomimetic effect of ketamine and will tend to decrease cardiac function and decrease arterial blood pressure.

Tiletamine/Zolazepam

Tiletamine/zolazepam combinations are available in a fixed ratio. Telazol® is a non-narcotic, nonbarbiturate, injectable anesthetic agent. Chemically, Telazol® is a combination of equal parts by weight of tiletamine hydrochloride (2-[ethylamino]-2-[2-thienyl]-cyclohexanone hydrochloride), an arylaminocycloalkanone dissociative anesthetic, and zolazepam hydrochloride (4-[o-fluorophenyl]-6,8-dihydro-1,3,8-trimethylpyazolo[3,4-e][1,4]diazepin-7[1H]-1-hydrochloride), a benzodiazepine having minor tranquilizing properties. The product is supplied sterile in vials, each containing a total of 500 mg of active drug as free base equivalents and 288.5 mg of mannitol. The addition of 5 mL of diluent produces a solution containing the equivalent of 50 mg of tiletamine base, 50 mg of zolazepam base and 57.7 mg of mannitol per milliliter. The resulting solution has a pH of 2–3.5. Zoletil® is available in many countries outside North America and is commonly marketed as a mixture containing 25 mg/mL each of zolazepam and tiletamine (Zoletil 50®) or 50 mg/mL each (Zoletil 100®).

Duration of effect is dependent on the route of administration and amount of drug given. When used intravenously it lasts approximately 15–20 minutes. When given intramuscularly it may last 30–45 minutes. It is commonly used in place of ketamine and its duration is typically longer.

Tiletamine induces dissociative anesthesia similar to ketamine. It has the potential to cause seizure activity, but when combined with zolazepam the incidence of seizures is greatly reduced. Its effects on CBF and ICP are similar to those of ketamine. Nephrotoxicity in New Zealand white rabbits has been reported following Telazol® administration (Doerning et al. 1992). Anecdotally, tigers do not appear to recover well after tiletamine/zolazepam therefore its use is generally contraindicated. Tiletamine/zolazepam can be combined with other drugs to improve its analgesic and recovery characteristics.

Miscellaneous Anesthetics

Etomidate

Etomidate has been used extensively as a hypnotic agent for the induction of anesthesia in humans, but less commonly in other species. Etomidate is a rapidly acting, ultrashort acting imidazole derivative. The duration of effect following intravenous bolus administration is typically 5–10 minutes. Etomidate causes dose-dependent CNS depression leading to sedation, hypnosis, and finally an isoelectric electroencephalogram.

Etomidate, in contrast to almost all other induction agents, does not seem to cause significant depression of cardiac contractility and has minimal effects on heart rate, cardiac output, and arterial blood pressure. Elimination of etomidate occurs by ester-hydrolysis in plasma and in the liver at approximately equal rates. Metabolism of etomidate in the liver is a capacity-limited Michaelis–Menten process. Hepatic hydrolysis results in the corresponding inactive carboxylic acid. Etomidate will temporarily reduce steroidogenesis (Boidin 1985; Moon 1997). Steroid synthesis usually increases with the stress of anesthesia so the net effect may be little or no change (Dodam et al. 1990). It is not a clinical contraindication except for animals with hypoadrenocorticism (Addison's disease). Intravenous administration of etomidate may induce excitement, myoclonus, pain on injection, vomiting, and apnea during induction of anesthesia. Some animals may have purposeless myoclonic muscle movements during recovery from anesthesia. The frequency and severity of the side effects can be attenuated or eliminated by the administration of adjunctive drugs such as diazepam, acepromazine, or opioids prior to etomidate administration. A constant rate infusion of etomidate may result in hemolysis (Van de Wiele et al. 1995; Moon 1994). This is thought to be due to

the propylene glycol carrier and the very high osmolality of available products (Doenicke et al. 1997).

Alfaxalone

Alfaxan®

Alfaxalone is a synthetic neurosteroid anesthetic with a relatively wide margin of safety and little cardiovascular or respiratory depression. Due to its poor water solubility, earlier formulations (Saffan®) were a mixture of alfaxalone and alfadolone combined with cremophor EL® as a solubilizing agent. Adverse effects, including histamine release and anaphylactic reactions associated with Cremophor, led to the withdrawal of that product from the market. A novel formulation of alfaxalone, Alfaxan-CD®, was released in Australia in 2001, in the United Kindgom in 2007, in Europe in 2008, in Canada in 2011, and in the United States in 2012. It is a 1% aqueous solution with a pH of 6.5–7.0 containing a non-cremophor vehicle (2-hydroxypropyl-β-cyclodextrin) which does not cause histamine release. The drug is approved for induction and maintenance of general anesthesia in dogs and cats via intravenous administration and has also been approved for intramuscular administration in some countries. Until recently, Alfaxan® was exclusively supplied as a 10-mL vial without added antimicrobial preservatives. This resulted in a shelf-life of only 6 hours and a label recommendation to discard unused drug within this timeframe (Berry 2015). A newer multidose formulation containing the preservatives ethanol, chlorocresol, and benzethonium chloride has recently been approved and appears to have the same efficacy and safety as the preservative-free formulation but offers the advantage of a 28-day shelf-life.

Like other injectable anesthetics, alfaxalone produces its clinical effects via potentiation of GABA at $GABA_A$ receptors in the CNS, resulting in modulation of chloride transport and neuronal hyperpolarization (Berry 2015). After intravenous administration, it produces rapid onset of action and satisfactory muscle relaxation but has no significant analgesic effects. In dogs and cats, it undergoes rapid hepatic metabolism, has a relatively short half-life, and does not accumulate after repeated dosing (Ambros et al. 2008; Ferre et al. 2006; Whittem et al. 2008).

Depending on the species and country-specific labelling, alfaxalone can be used for intramuscular sedation or premedication, for intravenous induction of anesthesia prior to transfer to an inhaled agent, or for intravenous maintenance of anesthesia via intermittent boluses for short procedures or via continuous rate infusion (CRI) for longer procedures. Other off-label routes of administration have been reported, including subcutaneous injection in various domestic and exotic species, intraperitoneal injection in laboratory animals, and immersion/irrigation in fish and amphibians.

Premedication or coadministration with a sedative and/or analgesic is recommended to reduce the dose of alfaxalone required, provide analgesia, and smooth recovery, which can otherwise be rough. Paddling, vocalization, rigidity, myoclonus, and trembling have been reported in dogs and cats recovering from alfaxalone that did not receive other drugs concurrently (Berry 2015). Also, with intramuscular administration, the relatively large volume of alfaxalone required can be a limiting factor and coadministration of more potent sedative and/or analgesic agents may help overcome this.

Alfaxalone produces dose-dependent respiratory depression and apnea is common after rapid intravenous injection of clinically relevant doses (Muir et al. 2008, 2009). Slow injection over 60 seconds is recommended and the anesthetist should be prepared to intubate, provide supplemental oxygen, and support ventilation when administering alfaxalone. Cardiac output and arterial blood pressure remain generally stable after administration of clinically appropriate doses in healthy patients, although caution should be exercised when administering alfaxalone to patients with limited cardiac reserve capacity or hemodynamic instability.

In addition to dogs and cats, off-label alfaxalone use has been reported in many other domestic species and exotic pets, including horses, sheep, swine, rabbits, ferrets, rodents (excluding mice, rats, guinea pigs, chinchillas), birds (excluding budgerigars and finches), reptiles (excluding lizards, turtles, tortoises, and snakes), and amphibians (excluding frogs, toads, and axolotls). It has also been used in a diverse range of captive zoo species (excluding civet cats, macaques, sea lions, crocodiles, pythons, flamingos, parrots, blue crabs, carp, and tarantulas); as well as in free-ranging wildlife (excluding deer, bighorn sheep, seals, koalas, wallabies, and river turtles).

Opioids

All drugs classified as opioids are chemically related to a group of compounds which have been purified from the juice of a particular species of poppy, *Papaverum somniferum*. The unrefined extract from the poppy is called opium and contains approximately 20 naturally occurring pharmacologically active compounds, including morphine and codeine. In addition, numerous semisynthetic and synthetic analogs of these natural compounds have been developed for clinical use. The word "opioid" is typically used to encompass all chemical derivatives of the compounds purified from opium and will be the term used to describe this class of analgesics throughout this section.

The opioids are a versatile group of drugs with extensive applications related to the management of pain in companion animal veterinary medicine. In the past, their use in wild and exotic species has been largely limited to the ultra-potent agents utilized in remote capture techniques. However, with the rapid evolution of zoo animal medicine and surgery, the opioids are being used increasingly as analgesics for the management of surgical pain in a wide variety of species. Although there are few pharmacokinetic or pharmacodynamic studies involving opioids in wild and exotic animals, a general discussion of opioid pharmacology is relevant and may facilitate extrapolation from companion animal species.

Opioid Receptors

It is well known that exogenously administered opioids such as morphine or heroin exert their effects by interacting with specific opioid receptors and mimicking naturally occurring molecules known as endogenous opioid peptides. It is now accepted that there are three well-defined types of opioid receptors, most commonly known by their Greek letter designations as μ (mu), δ (delta), and κ (kappa) (Harrison et al. 1998; Kieffer 1999; Janecka et al. 2004; Inturrisi 2002). This classic system of nomenclature has been under reconsideration for a number of years and during this time several alternative naming systems have been proposed, leading to considerable confusion. In addition, a fourth type of opioid receptor, the nociceptin receptor (also known as the orphanin FQ receptor), has been characterized (Moran et al. 2000; Smith et al. 2001). According to the most recent recommendations of the International Union of Basic and Clinical Pharmacology Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR), variations based on the Greek letters remain acceptable. Thus, mu, μ, or MOP (for "mu opioid peptide"); delta, δ or DOP (for "delta opioid peptide"); kappa, κ or KOP (for "kappa opioid peptide"); and NOP (for "nociceptin opioid peptide") are considered interchangeable abbreviations. Distinct cDNA sequences have been cloned for all four opioid receptor types, and each type appears to have a unique distribution in the brain, spinal cord, and periphery (Smith & Lee 2003).

The diversity of opioid receptors is further extended by the existence of several subtypes of μ, δ, and κ receptors. Based on pharmacologic studies, there are thought to be at least three μ receptor subtypes, μ_1, μ_2, and μ_3; two δ receptor subtypes, δ_1, and δ_2; and perhaps as many as four κ receptor subtypes, κ_{1a}, κ_{1b}, κ_2, and κ_3 (Smith & Lee 2003) The discovery of opioid receptor subtypes generated great enthusiasm among researchers and introduced the possibility of developing subtype-specific therapeutic agents with favorable side-effect profiles. At this point, however, the functional significance of these receptor subtypes remains unclear and distinct cDNA sequences corresponding to these subtypes have not yet been identified (Smith & Lee 2003).

In general, it appears that the μ receptor mediates most of the clinically relevant analgesic effects, as well as most of the adverse side effects associated with opioid administration (Kieffer 1999). Drugs acting at the δ receptor tend to be poor analgesics but may modify μ receptor-mediated antinociception under certain circumstances and mediate opioid receptor "cross-talk". The κ receptor mediates analgesia in several specific locations in the CNS and the periphery, but distinguishing μ- and κ-mediated analgesic effects has proven to be difficult (Kieffer 1999; Smith & Lee 2003). In contrast to the classic opioid receptors, the nociceptin receptor does not mediate typical opioid analgesia, but instead produces anti-opioid (pro-nociceptive) effects (Janecka et al. 2004; Moran et al. 2000; Smith et al. 2001). Due to the considerable structural homology between the three classically described opioid receptors, it is likely that there are significant interactions between these receptors in different tissues, and the loosely defined physiologic roles ascribed to each receptor type still require further clarification.

Endogenous Opioid Receptor Ligands

The opioid receptors discussed above are part of an extensive opioid system that includes a large number of endogenous opioid peptide ligands. Endogenous opioid peptides are small molecules that are naturally produced in the CNS and in various glands throughout the body, such as the pituitary and the adrenal (Janecka et al. 2004). Three classical families of endogenous opioid peptides have been identified: the enkephalins, the dynorphins, and β-endorphin. Each of these is derived from a distinct precursor polypeptide, pro-enkephalin, pro-dynorphin, and pro-opiomelanocortin, respectively (Janecka et al. 2004). These classical endogenous opioid peptides are expressed throughout the CNS and their presence has more recently been confirmed in peripheral tissues as well (Janecka et al. 2004). There are considerable structural similarities between these three groups of peptides, and each family demonstrates variable affinities for μ, δ, and κ receptors. None of them bind exclusively to a single opioid receptor and none of them have any significant affinity for the nociceptin receptor. The physiologic roles of these peptides are not completely understood at this time. They appear to function as neurotransmitters, neuromodulators and, in some cases, as neurohormones. They mediate some forms

of stress-induced analgesia and play a role in analgesia induced by electrical stimulation of discrete regions in the brain, such as the periaqueductal gray of the mesencephalon (Inturrisi 2002).

Nociceptin (also known as orphanin FQ) is the endogenous ligand for the more recently discovered nociception receptor. Nociceptin is derived from pro-nociceptin, and its amino acid sequence is closely related to that of the classical endogenous opioid peptides discussed above (Janecka et al. 2004; Moran et al. 2000). Despite this homology, nociception binding is specific for the nociception receptor and the peptide does not appear to interact with μ, δ, or κ receptors. Furthermore, the physiologic effects of nociceptin are in direct contrast to the actions of the classical endogenous opioid peptides, with nociception producing a distinctly pro-nociceptive effect (Janecka et al. 2004; Moran et al. 2000; Smith 2001). The functional significance of nociception and its receptor remains to be elucidated, but additional insight into this novel opioid peptide may have substantial implications in future therapeutic drug development.

In addition to the enkephalins, dynorphins, β-endorphin, and nociception, there are now two other discovered endogenous opioid peptides called endomorphin-1 and endomorphin-2 (Zadina et al. 1990). These peptides are putative products of an, as yet, unidentified precursor and have been proposed to be the highly selective endogenous ligands for the μ receptor (Janecka et al. 2004; Zadina et al. 1990). The endomorphins are small tetrapeptides that are structurally unrelated to the classical endogenous opioid peptides (Zadina et al. 1990). Their identification has heralded a new era in research of the μ opioid system which may contribute to our understanding of the neurobiology of opioids, and provide new avenues for therapeutic interventions.

Another endogenous opioid receptor agonist, dermorphin, was discovered in the early 1980s in the skin of a South American frog species belonging to the genus Phyllomedusa. Dermorphins are full μ receptor agonists with approximately 30–40 times the potency of morphine. Shortly after the discovery of amphibian dermorphin, another endogenous opioid, deltorphin, was isolated and shown to act as an agonist at δ receptors. These natural opioid peptides appear to be unique to amphibians and, although their functional role is not entirely clear, it has been speculated that they may be involved in protection from predators and/or hibernation (Mosely & Mosely 2015). While the discovery of the dermorphins generated initial interest as potential clinical analgesic agents, little work has been done in recent years. Dermorphin has been used illegally in horse racing as a performance-enhancing drug (Robinson et al. 2015).

Opioid Receptor Signaling and Mechanisms of Analgesia

Binding of an opioid agonist to a neuronal opioid receptor, regardless of whether the agonist is endogenous or exogenous, typically leads to several events that serve to inhibit the activation of the neuron. Opioid receptors are part of a large superfamily of membrane-bound receptors that are coupled to G-proteins (Smith & Lee 2003). As such, they are structurally and functionally related to receptors for many neurotransmitters and other neuropeptides which act to modulate the activity of nerve cells. Opioid receptor binding, via activation of various types of G-proteins, may lead to inhibition of adenylyl cyclase (cAMP) activity, activation of receptor-operated K^+ currents, and suppression of voltage-gated Ca^{2+} currents (Inturrisi 2002).

At the pre-synaptic level, decreased Ca^{2+} influx will result in reduced release of transmitter substances, such as substance P, from primary afferent fibers in the spinal cord dorsal horn, thereby inhibiting synaptic transmission of nociceptive input (Inturrisi 2002). Post-synaptically, enhanced K^+ efflux will result in neuronal hyperpolarization of spinal cord projection neurons and inhibition of ascending nociceptive pathways. A third potential mode of opioid action involves upregulation of supraspinal descending antinociceptive pathways in the periaqueductal gray. It is now known that this system is subject to tonic inhibition mediated by GABAergic neurons, and opioid receptor activation has been shown to suppress this inhibitory influence and augment descending antinociceptive transmission (Inturrisi 2002; Christie et al. 2000). The proposed cellular basis for this involves μ receptors present on pre-synaptic GABAergic nerve terminals which activate voltage-dependent K^+ currents and thereby inhibit GABA release into the synaptic cleft (Christie et al. 2000). It is important to note that while our collective understanding of opioid receptor-mediated signaling has increased dramatically in recent years, the relationship of such subcellular events to clinical analgesia at the level of the organism requires further clarification.

Opioid Receptor Distribution and Therapeutic Implications

While cellular and molecular studies of opioid receptors and ligands are invaluable in understanding their function, it is critical to place them in their anatomical and physiologic context to fully appreciate the opioid system and its relevance to pain management. It has long been a principle tenet of opioid analgesia that these agents are centrally acting, and this understanding has shaped the way we use opioid analgesics clinically. It has been well

established that the analgesic effects of opioids arise from their ability to directly inhibit the ascending transmission of nociceptive information from the spinal cord dorsal horn, and to activate pain control circuits that descend from the midbrain via the rostral ventromedial medulla to the spinal cord. Within the CNS, evidence of μ, δ, and κ opioid receptor mRNA and/or opioid peptide binding has been demonstrated in supraspinal sites, including the mesencephalic periaqueductal gray, the mesencephalic reticular formation, various nuclei of the rostral ventromedial medulla, forebrain regions including the nucleus accumbens, as well as spinally within the dorsal horn (Gutstein & Akil 2001; Yaksh et al. 1998). The interactions between groups of opioid receptors at various spinal and supraspinal locations, as well as interactions between different receptor types within a given location, are complex and incompletely understood at this time.

Systemic administration of opioid analgesics via intravenous, intramuscular, or subcutaneous injection will result in a relatively rapid onset of action via interaction with these CNS receptors. Oral, transdermal, rectal, or buccal mucosal administration of opioids will result in variable systemic absorption, depending on the characteristics of the particular agent, with analgesic effects being mediated largely by the same receptors within the CNS. In addition, neuraxial administration, into either the subarachnoid or epidural space, is a particularly efficacious route of administration. Small doses of opioids introduced via these routes readily penetrate the spinal cord and interact with spinal and/or supraspinal opioid receptors to produce profound and potentially long-lasting analgesia, the characteristics of which will depend on the particular drug utilized.

Despite the fact that opioids have long been considered the prototype of centrally acting analgesics, a body of evidence has emerged over the past decade which clearly indicates that opioids can produce potent and clinically measurable analgesia by activation of opioid receptors in the peripheral nervous system (Stein et al. 2001). Opioid receptors of all three major types have been identified on the processes of sensory neurons, and they respond to peripherally applied opioids and locally released endogenous opioid peptides when upregulated during inflammatory pain states (Stein 1993; Stein et al. 1993, 2001, 2003; Fields et al. 1980). Furthermore, sympathetic neurons and immune cells have also been shown to express opioid receptors, but their functional role remains unclear (Stein et al. 2003). While the binding characteristics of peripheral and central opioid receptors are similar, the molecular mass of peripheral and central μ opioid receptors appears to be different, suggesting that selective ligands for these peripheral receptors could be developed which would produce opioid analgesia without the potential to induce centrally mediated adverse side effects (Stein 1995, Stein & Yassouridis 1997; Stein et al. 1996, 2001, 2003).

Adverse Effects of Clinically Used Opioids

While opioids are used clinically primarily for their pain-relieving properties, they also produce a host of other effects on a variety of body systems. This is not surprising in light of the wide distribution of endogenous opioid peptides and their receptors in supraspinal, spinal, and peripheral locations. Since information regarding opioid side effects in most wild and exotic animals is lacking, reference is made to common domestic species where appropriate.

Central Nervous System

Level of Arousal

There are considerable species differences in the CNS response to opioid analgesics that cannot be attributed to pharmacokinetic variations alone. CNS depression (i.e., sedation) is typically seen in the dog, monkey, and human, while CNS stimulation (i.e., excitement and/or spontaneous locomotor activity) may be elicited in the cat, horse, goat, sheep, pig, and cow following systemic administration of various opioids, most notably morphine (Branson et al. 2001). The reasons for these different responses are not entirely clear at this time, but are presumably related to differing concentrations and distributions of μ, δ and κ receptors in various regions of the brain in these species (Hellyer et al. 2003). Details regarding the CNS responses of specific wild and exotic species to opioids are not yet known. Regardless of the species, however, there are numerous factors which may play a role, including the temperament or condition of the animal, the presence or absence of pain in the animal, the dose, route and timing of drug administration, and the specific opioid administered.

Thermoregulatory Center

The hypothalamic thermoregulatory system is also affected by opioid administration. Hypothermia tends to be the most common response, particularly when opioids are used during the perioperative period in the presence of other CNS depressant drugs (Gutstein & Akil 2001; Branson et al. 2001). Under some clinical circumstances, however, hyperthermia is observed in cats, horses, swine, and ruminants following opioid administration (Niedfeldt & Robertson 2006; Posner et al. 2007, 2010). Part of this increase in body temperature may be attributed to an increase in muscle activity associated with CNS excitation in these species, but a specific central hypothalamic mechanism has also been implicated, although it remains poorly understood (Branson et al. 2001).

Emetic Center

Nausea and vomiting associated with opioid administration are a result of direct stimulation of the chemoreceptor trigger zone for emesis located in the area postrema of the medulla (Gutstein & Akil 2001; Stoelting 1999). As with the other centrally mediated side effects, species plays a role in determining an individual's tendency to vomit after an opioid is administered. Horses, rabbits, ruminants, and swine do not vomit with opioid administration. Cats may vomit, but usually at doses that are greater than those which stimulate vomiting in dogs. Dogs will commonly vomit following opioid administration, especially with morphine.

Cough Center

Opioids have variable efficacy in depressing the cough reflex, at least in part, by a direct effect on a cough center located in the medulla (Gutstein & Akil 2001). Certain opioids are more effective antitussives than others, including drugs like codeine, hydrocodone, and butorphanol.

Pupillary Diameter

As a general rule, opioids tend to produce mydriasis in those species that exhibit CNS excitation, and miosis in those that become sedated following opioid administration (Branson et al. 2001; Stephan et al. 2003; Lee & Wang 1975; Wallenstein & Wang 1979). Miosis is due to an excitatory action of opioids on neuronal firing in the oculomotor nucleus (Stoelting 1999; Lee & Wang 1975; Wallenstein & Wang 1979). In the cat, and presumably in other species that exhibit mydriasis, this increase in activity in the oculomotor nuclear complex still occurs but the miotic effect is masked by increased release of catecholamines, which results in mydriasis (Wallenstein & Wang 1979).

Respiratory System

Opioids produce dose-dependent depression of ventilation, primarily mediated by μ_2 receptors leading to a direct depressant effect on brainstem respiratory centers (Gutstein & Akil 2001; Stoelting 1999). This effect is characterized by decreased responsiveness of these centers to carbon dioxide and is reflected in an increased resting $PaCO_2$ and displacement of the carbon dioxide response curve to the right. This effect is compounded by the coadministration of sedative and/or anesthetic agents, meaning that significant respiratory depression and hypercapnia are much more likely to occur in anesthetized patients who receive opioids versus those who are conscious. It should be noted that, in general, humans tend to be more sensitive to the respiratory depressant effects of opioids when compared to most veterinary species. However, respiratory support and/or specific opioid antagonists should be immediately available anytime very high doses, or very potent opioids are used.

Cardiovascular System

Most opioids have minimal effects on cardiac output, cardiac rhythm, and arterial blood pressure when clinically relevant analgesic doses are administered. Bradycardia may occur as a result of opioid-induced medullary vagal stimulation and will respond readily to anticholinergic treatment if warranted. Particular opioids (morphine and merperidine) can cause release of histamine, especially after rapid intravenous administration, which may lead to vasodilation and hypotension (Branson et al. 2001; Smith et al. 2001). Due to their relatively benign effects on cardiovascular function, opioids commonly form the basis of anesthetic protocols for human patients or animals with preexisting cardiovascular disease.

Gastrointestinal System

The gastrointestinal effects of the opioids are mediated by μ and δ receptors located in the myenteric plexus of the gastrointestinal tract (Gutstein & Akil 2001; Branson et al. 2001). Opioid administration may stimulate defecation in certain species. Following this initial response, spasm of gastrointestinal smooth muscle predisposes to ileus and constipation. Horses and ruminants in particular may be predisposed to gastrointestinal complications associated with opioid administration such as colic and ruminal tympany, respectively. Chronic opioid use may predispose to gastrointestinal stasis in other species.

In human patients, opioids (most notably fentanyl and morphine) have been shown to increase bile duct pressure through constriction of the sphincter of Oddi (Radnay et al. 1984). The incidence of this side effect in humans is, however, quite low (Jones et al. 1981). The incidence of increased bile duct pressure secondary to opioid administration in various animal species, and its potential clinical significance, is unknown at this time.

Genitourinary System

Opioids, particularly when administered neuraxially, may cause urinary retention through dose-dependent suppression of detrusor contractility and decreased sensation of urge (Kuipers et al. 2004; el Bindary & Abu el-Nasr 2001). Urine volume may also be affected by opioids and the mechanism of this effect appears to be multifactorial. μ agonists tend to produce oliguria in the clinical setting and this is in part a result of increased antidiuretic hormone release leading to altered renal tubular function (Stoelting 1999; Mercadante & Arcuri 2004). Elevations in circulating plasma atrial natriuretic peptide may also play a role in morphine-induced antidiuresis (Mercadante & Arcuri 2004). Conversely, κ agonists tend to produce a diuretic effect, possibly through inhibition of antidiuretic hormone secretion (Stoelting 1999; Mercadante & Arcuri 2004).

Other peripheral mechanisms involving stimulation of renal alpha-2 adrenergic receptors may also contribute to this κ agonist effect (Mercadante & Arcuri 2004).

Opioid-Induced Hyperalgesia

There is a growing body of evidence from both human and rodent studies supporting the existence of a condition called opioid-induced hyperalgesia (Lee et al. 2011; Gomez et al. 2009; Yu et al. 2016; Colvin et al. 2019). This phenomenon is characterized by a paradoxical increase in pain associated with opioid administration and can contribute to poorly controlled pain and dose escalation. In humans, it has been observed with acute and chronic exposure, high and low doses, and with different types of opioids and routes of administration. The mechanisms underlying opioid-induced hyperalgesia are not well understood but both μ opioid receptors on transient receptor potential vanilloid-1 (TRPV1)-expressing dorsal root ganglion neurons and NMDA receptors in the spinal cord dorsal horn appear to be involved (Deng et al. 2019). At this time, animal studies involving opioid-induced hyperalgesia are largely confined to experimental pain models in rodents, however, awareness in veterinary medicine is increasing and publications involving dogs and cats are beginning to emerge (Ruíz-López et al. 2020; Borland & Garcia 2019; White et al. 2017).

Opioid Agonists

Almost all clinically useful opioids exert their analgesic and immobilizing effects by acting as agonists at μ receptors. While there are a few opioids which act as κ agonists, these drugs also tend to have antagonist or partial agonist effects at μ and/or δ receptors and are thus not classified as *pure* agonists. Pure or full opioid agonists are capable of eliciting maximal activation of the receptor when they bind it and the subsequent downstream processes result in a maximal analgesic effect (Fig. 1.1). Clinically, the full μ agonists are superior analgesics and they are the drugs of choice for pain of moderate to severe intensity in many veterinary species. The following section contains brief descriptions of full μ agonists currently used in veterinary medicine. Specific details regarding μ agonist clinical pharmacology in various wild and exotic species are lacking.

Morphine (Morphine Sulfate)

Morphine is the prototypical opioid analgesic and acts as a full agonist not only at μ receptors, but also at δ and κ receptors (Gutstein & Akil 2001). Despite the development of numerous synthetic opioids, many of which are more potent than morphine and may have other characteristics that make them desirable alternatives to morphine in certain

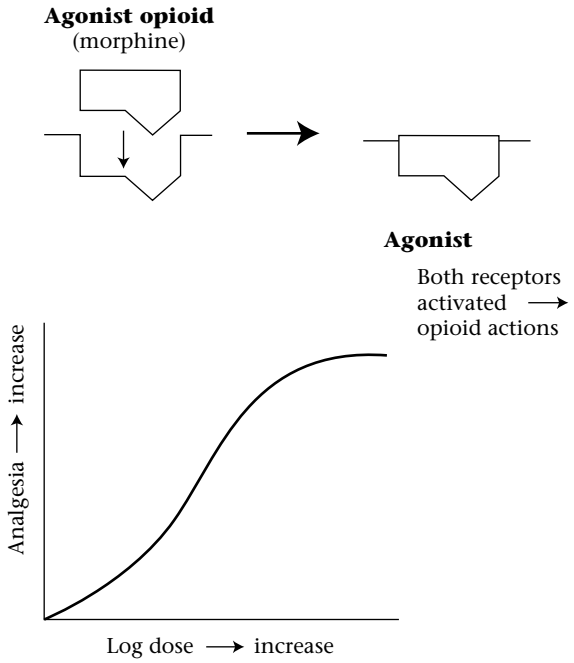


Figure 1.1 Effects of opioid agonists.

circumstances, it is worth noting that no other drug has been shown to be more efficacious than morphine at relieving pain in humans. Compared to the synthetic opioid agonists, morphine is relatively hydrophilic in nature and crosses the blood–brain barrier more slowly than fentanyl or oxymorphone, thereby delaying the peak effect somewhat even after intravenous administration (Gutstein & Akil 2001; Stoelting 1999). Clinically, this lag is not likely to be significant under most circumstances, with the onset of analgesia occurring reasonably promptly after a single dose of morphine and typically lasting 3–4 hours (Barnhart et al. 2000; Taylor et al. 2001). Morphine's poor lipid solubility means that it can produce long-lasting analgesia when administered into the epidural or subarachnoid space, with effects persisting for 12–24 hours. The first-pass effect is significant after oral administration and the bioavailability of oral morphine preparations is at best only in the range of 0–25%.

In most species, the primary metabolic pathway for morphine involves conjugation with glucuronic acid leading to the formation of two major metabolites, morphine-6-glucuronide and morphine-3-glucuronide (Gutstein & Akil 2001; Faura et al. 1998). Despite the low levels of glucuronyl transferase in the cat, the pharmacokinetics of morphine in this species seem to be broadly comparable to the dog and human, though clearance rates may be marginally slower (Barnhart et al. 2000; Taylor et al. 2001; Faura et al. 1998). This suggests that morphine must undergo a different type of conjugation reaction in this species. Morphine-6-glucuronide

has pharmacological activities that are indistinguishable from those of morphine in animal models and in human beings, while morphine-3-glucuronide appears to have little affinity for opioid receptors, but may contribute to the excitatory effects of morphine in some situations (Gutstein & Akil 2001; Smith 2000). With chronic morphine administration, it is likely that the active metabolite, morphine-6-glucuronide, contributes significantly to clinical analgesia.

Very little morphine is excreted unchanged in the urine. The major metabolites, morphine-3-glucuronide and, to a lesser extent, morphine-6-glucuronide, are eliminated almost entirely via glomerular filtration. In human patients, renal failure may lead to accumulation of morphine-6-glucuronide and persistent clinical effects, while liver dysfunction seems to have minimal impact on morphine clearance (Gutstein & Akil 2001; Stoelting 1999).

The side effects associated with morphine administration are typical of most opioid agonists and have been discussed previously in this chapter. In particular, the increased incidence of vomiting after morphine administration as well as its potential to cause histamine release after intravenous administration distinguish morphine from other full opioid agonists.

Hydromorphone

Hydromorphone is a synthetic opioid that acts as a full agonist at μ receptors and is used in both human and veterinary medicine. Clinically, hydromorphone and oxymorphone have similar efficacy, potency, duration of analgesic action, and side-effect profiles, but hydromorphone remains significantly less expensive. Like oxymorphone, hydromorphone is not associated with histamine release so bolus intravenous administration is considered safe (Smith et al. 2001).

Meperidine

Meperidine is a synthetic opioid that exerts its analgesic effects through agonism at μ receptors. Interestingly, it also appears able to bind other types of receptors, which may contribute to some of its clinical effects other than analgesia. Meperidine is capable of blocking sodium channels and inhibiting activity in dorsal horn neurons in a manner analogous to local anesthetics (Wagner et al. 1999; Wolff et al. 2004). It has also recently been shown that meperidine exerts agonist activity at alpha-2 receptors, specifically the alpha-2B subtype, suggesting that it may possess some alpha-2 agonist-like properties (Takada et al. 1999, 2002).

Meperidine has a considerably shorter duration of analgesic action compared to morphine, oxymorphone or hydromorphone, typically not extending beyond 1 hour (Branson et al. 2001). Metabolic pathways vary among different species but, in general, most of the drug is demethylated to normeperidine in the liver and then undergoes further hydrolysis and ultimately renal excretion (Branson et al. 2001; Taylor et al. 2001; Yeh et al. 1981). Normeperidine is an active metabolite and possesses approximately one half of the analgesic efficacy of meperidine (Gutstein & Akil 2001; Branson et al. 2001). Normeperidine has produced toxic neurologic side effects in human patients receiving meperidine for prolonged periods of time, especially in the presence of impaired renal function (Stoelting 1999; Stone et al. 1993).

Unlike most of the other opioids in clinical use, meperidine has been shown to produce significant negative inotropic effects when administered alone to conscious dogs (Priano & Vatner 1981). In addition, due to its modest atropine-like effects, meperidine tends to increase heart rate rather than predispose to bradycardia as is often seen with other opioids (Branson et al. 2001; Stoelting 1999). The clinical significance of these cardiovascular effects in the peri-anesthetic period has never been clearly ascertained. Like morphine, meperidine also causes histamine release when administered intravenously (Branson et al. 2001).

A rare but life-threatening drug interaction has been reported in human patients receiving meperidine that may have relevance in veterinary medicine. The combination of meperidine (and perhaps other opioids) with a monoamine oxidase inhibitor may lead to "serotonin syndrome" which is characterized by a constellation of symptoms including confusion, fever, shivering, diaphoresis, ataxia, hyperreflexia, myoclonus, and diarrhea (Sporer 1995; Bowdle 1998; Heinonen & Myllyla 1998; Tissot 2003). A monoamine oxidase inhibitor, selegiline (Deprenyl®), has been used in dogs to treat pituitary-dependent hyperadrenocorticism or to modify behaviour in patients with canine cognitive dysfunction. Though there have not, to date, been any reports of adverse meperidine-selegiline interactions in dogs, the veterinarian must be aware of the potential for complications if analgesia is required in patients receiving monoamine oxidase inhibitors. A recent study has evaluated the effects of other opioids (oxymorphone and butorphanol) in selegiline-treated dogs and did not identify any specific adverse drug interactions in these animals (Dodam et al. 2004).

Fentanyl

Fentanyl is a highly lipid-soluble, short-acting synthetic μ opioid agonist. A single dose of fentanyl administered intravenously has a more rapid onset and a shorter duration of action than morphine. Peak analgesic effects occur in about 5 minutes and last approximately 30 minutes (Gutstein & Akil 2001; Stoelting 1999). Rapid redistribution of the drug to inactive tissue sites, such as fat and skeletal

muscle, leads to a decrease in plasma concentration and is responsible for the prompt termination of clinical effects. In most veterinary species the elimination half-time after a single bolus or a brief infusion is in the range of 2–3 hours (Carroll et al. 1999; Lee et al. 2000; Maxwell et al. 2003). Administration of very large doses or prolonged infusions may result in saturation of inactive tissues with termination of clinical effects becoming dependent on hepatic metabolism and renal excretion (Gutstein & Akil 2001; Stoelting 1999). Thus, the context-sensitive half-time of fentanyl increases significantly with the duration of the infusion, and clinical effects may persist for an extended period following termination of a long-term intravenous infusion.

Side effects associated with fentanyl administration are similar to those of the other full μ agonist opioids. In general, cardiovascular stability is excellent with fentanyl and intravenous administration is not associated with histamine release (Gutstein & Akil 2001; Stoelting 1999). Bradycardia may be significant with bolus doses but readily responds to anticholinergics if treatment is warranted (Gutstein & Akil 2001; Branson et al. 2001). In human patients muscle rigidity, especially of the chest wall, has been noted after administration of fentanyl or one of its congeners. The potential significance of this adverse effect in animal patients is not clear at this time, and the risk is considered minimal if large rapid bolus administrations are avoided.

Clinically, fentanyl is used most frequently in dogs and cats but it is also a potentially useful analgesic in other species, including the horse, cow, sheep, goat, and pig. Historically, fentanyl was available in combination with the butyrophenone tranquilizer droperidol in a product called Innovar-Vet, which was typically administered in the preanesthetic period to provide sedation and analgesia. This product is no longer available and systemic administration of fentanyl today is usually via the intravenous route.

The development of novel less-invasive routes of opioid administration for use in human patients led to the marketing of transdermal fentanyl patches (Duragesic®). The patches are designed to release a constant amount of fentanyl per hour which is then absorbed across the skin and taken up systemically. Fentanyl patches are designed for human skin and body temperature; however, their use has been evaluated in a number of domestic veterinary species (Carroll et al. 1999; Maxwell et al. 2003; Gilberto et al. 2003; Franks et al. 2000; Wilkinson et al. 2001; Egger et al. 1998, 2003; Gellasch et al. 2002; Robinson et al. 1999). Substantial variations in plasma drug concentrations have been documented and significant lag times after patch placement are common prior to onset of analgesia (Carroll et al. 1999; Lee et al. 2000; Egger et al. 1998, 2003). Furthermore, changes in body temperature have been shown to significantly affect fentanyl absorption in anesthetized cats, and it is likely that other factors associated with skin preparation and patch placement have the potential to substantially alter plasma fentanyl levels and analgesic efficacy (Pettifer & Hosgood 2003). Fentanyl patch safety and efficacy in most species is unknown at this time.

Alfentanil, Sufentanil, and Remifentanil

Alfentanil, sufentanil, and remifentanil are all structural analogues of fentanyl that were developed for use in humans in an effort to create analgesics with a more rapid onset of action and predictable termination of opioid effects. All three are similar with regard to onset and all have context-sensitive half-times that are shorter than that of fentanyl after prolonged infusions (Stoelting 1999) Remifentanil is unique among opioids because it is metabolized by nonspecific plasma esterases to inactive metabolites (Chism & Rickert 1996; Hoke et al. 1997). Thus, hepatic or renal dysfunction will have little impact on drug clearance and this, in combination with the robust nature of the esterase metabolic system, contributes to the predictability associated with infusion of remifentanil (Gutstein & Akil 2001; Stoelting 1999).

All three of these drugs are used during general anesthesia for procedures requiring intense analgesia and/or blunting of the sympathetic nervous system response to noxious stimulation. These agents, specifically remifentanil, are the opioids most frequently associated with opioid-induced hyperalgesia in humans (Santonocito et al. 2018). As yet, they have limited applications for postoperative or chronic pain management. Like fentanyl, they can be administered at relatively low infusion rates as adjuncts to general anesthetic protocols based on volatile inhalant or other injectable agents, or they can be administered at higher rates as the primary agent for total intravenous anesthesia. The minimum alveolar anesthetic concentration-sparing properties of these agents have been demonstrated in both the dog and cat (Hoke et al. 1997; Michelsen et al. 1996; Mendes & Selmi 2004; Ilkiw et al. 1997; Pascoe et al. 1997). In the horse, systemic infusions of alfentanil did not have significant effects on minimum alveolar concentrations of inhalant anesthetics and when administered to conscious horses were associated with increases in locomotor activity (Pascoe et al. 1991, 1993; Pascoe & Taylor 2003). There is little evidence to suggest that any of the fentanyl analogues offer advantages over morphine when administered into the epidural space for analgesia (Natalini & Robinson 2000).

Methadone

Methadone is a synthetic μ opioid agonist with pharmacologic properties qualitatively similar to those of morphine, but possessing additional affinity for NMDA receptors (Gorman et al. 1997; Ripamonti & Dickerson 2001). Methadone's unique clinical characteristics include excellent absorption following oral administration, no known active metabolites, high potency, and an extended duration of action (Gutstein & Akil 2001; Branson et al. 2001; Ripamonti & Dickerson 2001). In human patients, the drug has been used primarily in the treatment of opioid abstinence syndromes but it is being used increasingly for the management of chronic pain. In contrast to humans, methadone has low bioavailability in most veterinary species and consequently has limited efficacy when administered orally. A racemic injectable formulation of methadone hydrochloride (Comfortan®) is approved for use in dogs and cats for analgesia and premedication prior to general anesthesia in Europe and the United Kingdom. Numerous publications involving intramuscular, intravenous, and subcutaneous methadone in these and other domestic species have emerged in recent years as the drug gains popularity in clinical veterinary practice (Bini et al. 2018; Bitti et al. 2017; Hunt et al. 2013; Slingsby et al. 2015; Shah et al. 2018; Trimble et al. 2018; Warne et al. 2013; Gozalo-Marcilla et al. 2019).

Codeine

Codeine is the result of substitution of a methyl group onto morphine which acts to limit first-pass hepatic metabolism and accounts for codeine's high oral bioavailability (Gutstein & Akil 2001; Stoelting 1999). Codeine is well known for its excellent antitussive properties and is often combined in an oral formulation with a nonopioid analgesic, such as acetaminophen (Tylenol 3®), for the management of mild to moderate pain in human patients.

Oxycodone and Hydrocodone

Oxycodone and hydrocodone are opioids that are typically administered orally for the treatment of pain in human patients. Though oxycodone is available as a single drug continuous-release formulation (Oxycontin®), these drugs are most often prepared in combination with nonopioid analgesics such as aspirin and acetaminophen (Percocet®, Percodan®, Lorcet®, Vicodan®, etc.). In light of the epidemic of opioid addiction in humans and the potential for drug diversion, veterinarians are advised to prescribe alternative analgesics and avoid off-label use of opioids such as oxycodone and hydrocodone due to their extremely high abuse potential.

Etorphine and Carfentanil (M-99® and Wildnil®, Respectively)

These two opioids are discussed together because they are both used exclusively for the restraint and capture of wild animals, rather than as analgesic agents. They are extremely potent opioids and the immediate availability of a suitable antagonist is mandatory before these drugs are to be used, not only to reverse drug effects in animal patients, but also as a safety precaution in the event of accidental human injection. Though etorphine and carfentanil are most often injected intramuscularly (usually using a remote drug delivery technique) recent studies suggest that carfentanil is useful when administered orally in a variety of species, including the brown bear, the Brazilian tapir, and the chimpanzee (Mortenson & Bechert 2001; Pollock & Ramsay 2003; Kearns et al. 2000; Mama et al. 2000). A number of different drugs have been used in combination with etorphine or carfentanil to enhance muscle relaxation, including acepromazine, xylazine, and medetomidine (Caulkett et al. 2000; Miller et al. 2003; Ramdohr et al. 2001; Roffe et al. 2001).

Thiafentanil

Thiafentanil is an opioid agonist that has been utilized to facilitate the capture of many species of mammals, mainly ungulates, as well as large birds. It is pharmacologically classified as a synthetic opioid that has a relatively short duration of action. The shorter duration of action in combination with its reversibility with the opioid antagonist naltrexone make it an attractive agent when long periods of narcotization are not desirable.

Opioid Agonist-Antagonists and Partial Agonists

This group includes drugs that have varying opioid receptor binding profiles, but which have one thing in common: they all occupy μ opioid receptors, but do not initiate a maximal clinical response. Drugs such as butorphanol and nalbuphine are classified as agonist-antagonists. They are competitive μ receptor antagonists, but exert their analgesic actions by acting as agonists at κ receptors (Fig. 1.2). Buprenorphine, on the other hand, is classified as a partial agonist and binds μ receptors but produces only a limited clinical effect (Fig. 1.3). These mixed agonist-antagonist drugs were developed for the human market in an attempt to create analgesics with less respiratory depression and addictive potential. Due to their opioid receptor binding affinities, the side effects associated with these drugs demonstrate a so-called "ceiling effect" whereby increasing doses do not produce additional adverse responses. Unfortunately, the benefits of this ceiling effect on ventilatory depression come at the expense of limited analgesic efficacy and only a modest ability to decrease anesthetic requirements.

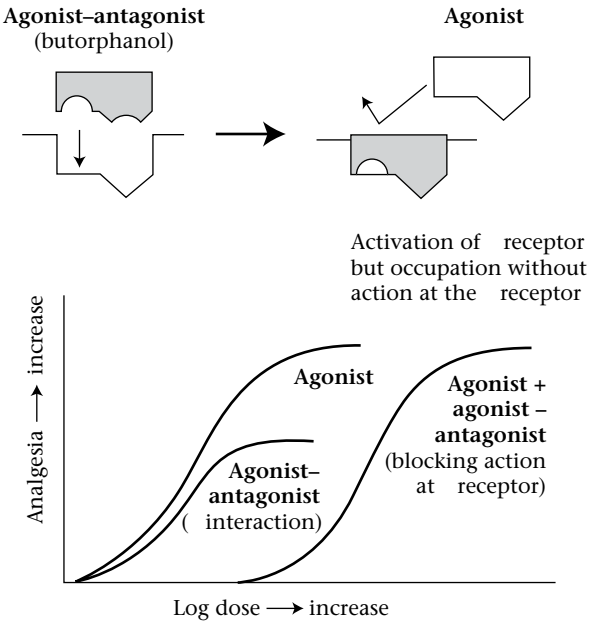


Figure 1.2 Activation of κ receptor, but occupation without action at the μ receptor.

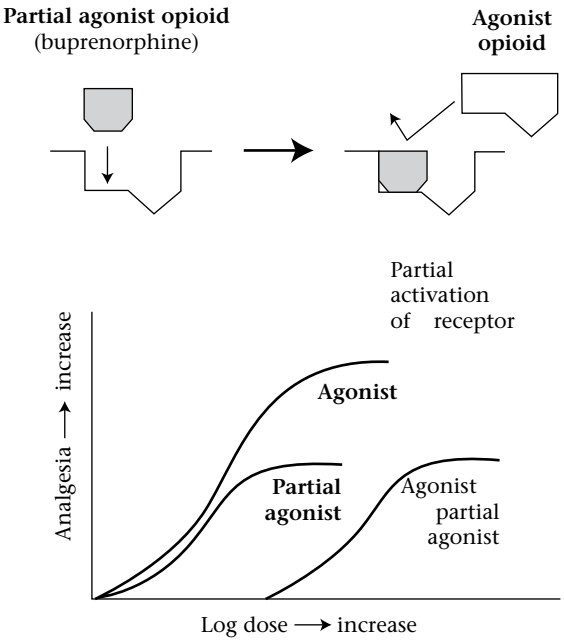


Figure 1.3 Partial activation of μ receptor.

The coadministration of opioids with differing receptor binding profiles is currently an active area of research that deserves further attention. The interactions in this setting are complex and it appears that opioid coadministration has the potential to produce additive, synergistic, or antagonistic analgesic effects depending on the particular species, dosage, drugs, and pain model being evaluated. The following section contains brief descriptions of opioid agonist-antagonists and partial agonists that are currently used in veterinary medicine.

Butorphanol

Butorphanol is a synthetic agonist-antagonist opioid and has been used extensively in a wide variety of veterinary species. The drug was originally labelled as an antitussive agent in dogs and, even now, is approved as an analgesic in the cat and horse only (Branson et al. 2001). Butorphanol exerts its relevant clinical effects through its interactions at κ receptors and acts as an antagonist at μ receptors. The duration of butorphanol's analgesic effects remains somewhat debatable and likely varies with species, type and intensity of pain, dosage, and route of administration (Sawyer et al. 1991; Robertson et al. 2003a; Sellon et al. 2001). In general, its effects are shorter-lived than those of morphine and are probably in the range of one to three hours. Butorphanol does not induce histamine release when administered intravenously and has minimal effects on cardiopulmonary function. There is conflicting evidence regarding the effects of butorphanol on inhalant anesthetic requirements in the dog, cat, and horse. Earlier studies failed to demonstrate a significant sparing effect on minimum alveolar concentration when butorphanol was coadministered with halothane in dogs and ponies (Quandt et al. 1994; Doherty et al. 1997; Matthews & Lindsay 1990). More recently, isoflurane MAC reductions have been documented after administration of clinically relevant doses of butorphanol in both dogs and cats (Ilkiw et al. 2002; Ko et al. 2000). The reasons for these discrepancies are probably related to differences in study techniques and, in the dog and cat specifically, it seems that butorphanol is capable of inducing at least modest reductions in inhalant anesthetic requirements.

Traditionally, it was thought that the simultaneous or sequential administration of butorphanol with a pure μ opioid agonist such as morphine or hydromorphone would be counterproductive from an analgesic standpoint because butorphanol's ability to antagonize μ receptors could inhibit or even reverse the effects of the agonist drug. Certainly, it has been clearly demonstrated that excessive sedation associated with a pure μ agonist can be partially reversed by the administration of low doses of butorphanol, and it was presumed that butorphanol would similarly reverse the μ-mediated analgesic effects as well. It would now appear that the potential interactions between butorphanol and full μ-opioid agonists are more complex than originally believed. One study demonstrated that coadministration of butorphanol and oxymorphone to cats subjected to a visceral noxious stimulus resulted in enhanced analgesic effects (Briggs et al. 1998). A more recent feline study, however, evaluated the combination of butorphanol

and hydromorphone in a thermal threshold pain model and failed to demonstrate enhanced analgesia and suggested that butorphanol did, in fact, inhibit hydromorphone's analgesic effects (Lascelles & Robertson 2004). These contradictory findings illustrate that we still have much to learn about coadministration of opioid agents with differing receptor binding profiles and the clinical effects produced by such coadministration likely depend on many factors, including species, type of pain, dose, and the specific drugs involved.

Nalbuphine and Pentazocine

Nalbuphine and pentazocine are classified as agonist-antagonist opioids and are clinically similar to butorphanol. They induce mild analgesia accompanied by minimal sedation, respiratory depression, or adverse cardiovascular effects. Like butorphanol, nalbuphine is occasionally used to partially reverse the effects of a full μ agonist opioid while maintaining some residual analgesia.

Buprenorphine

Buprenorphine is a semisynthetic, highly lipophilic opioid derived from thebaine. Unlike other opioids in this category, buprenorphine is considered to be a partial agonist at μ opioid receptors. The drug binds avidly to and dissociates slowly from μ receptors, but is not capable of eliciting a maximal clinical response. Due to its receptor binding characteristics, buprenorphine has a delayed onset of action and takes at least 60 minutes to attain peak effect after intramuscular administration. It also has a relatively long duration of action with clinical analgesic effects persisting for 6–12 hours in most species. Also, its high affinity for the μ receptor means that it may be difficult to antagonize its effects with a drug such as naloxone. Buprenorphine has most often been administered intravenously or intramuscularly, however, due to the long lag time before clinical effects are achieved after intramuscular administration, the intravenous route is preferred. Comparable plasma drug levels and analgesic efficacy with oral transmucosal administration versus intravenous administration has been demonstrated in cats (Robertson et al. 2003). Compounded versions of buprenorphine are widely available and include higher concentrations for convienent dosing to larger animals and sustained release formulations for increased duration of action. Reports describing use of the compounded sustained-release buprenorphine formulation by ZooPharm are available in a wide range of zoo and wildlife species. If sustained release preparations are used, there should be a plan for supportive care should significant adverse effects occur since complete reversal of buprenorphine with conventional antagonists is often unsuccessful. In addition, a commercially available highly concentrated formulation (1.8 mg/mL) called Simbadol® has been approved for perioperative analgesia in domestic cats with a label dose of 0.24 mg/kg administered subcutaneously every 24 hours for up to 3 days. Extralable intravenous and intramuscular administration has been used at lower doses and dosing intervals comparable to tradidional buprenorphine doses. The duration of action of Simbadol is not due to any specific formulation characterists. Rather it is a function of administration into adipose tissue which results in a gradual release into the circulation. A recent report describes the pharmacokinetics of highly concentrated buprenorphine/Simbadol® in Rhesus macaques (Mackiewicz et al. 2019).

Opioid Antagonists

These drugs have high affinities for the opioid receptors and are able to displace opioid agonists from μ and κ receptors. After this displacement, the pure antagonists bind to and occupy opioid receptors, but do not activate them (Fig. 1.4). Under ordinary circumstances, in patients that have not received exogenous agonist opioids, the opioid antagonists have few clinical effects when administered at clinically relevant dosages (Gutstein & Akil 2001). It is important to recognize that these drugs will rapidly reverse all opioid-induced clinical effects, including analgesia.

Naloxone

This pure opioid antagonist is capable of reversing all opioid agonist effects, producing increased alertness, responsiveness, coordination, and, potentially, increased perception of pain. Naloxone's duration of action is shorter than many

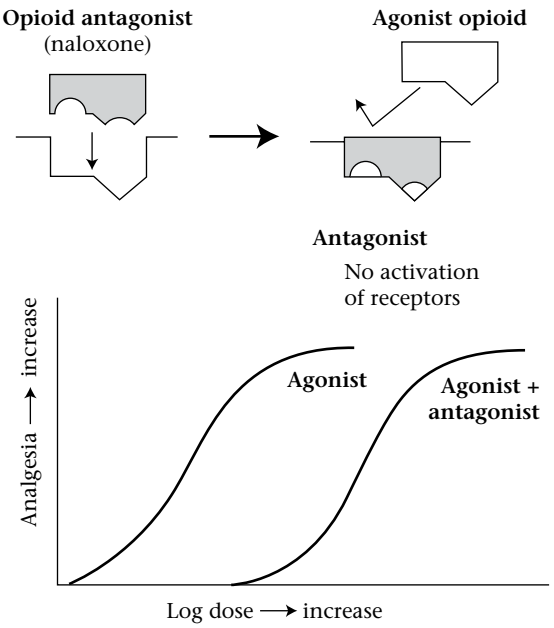


Figure 1.4 No activation of receptors.

of the opioid agonists with recommended intravenous doses lasting between 30 and 60 minutes. Consequently, animals need to be closely monitored for renarcotization after a dose of naloxone. Occasionally, excitement or anxiety may be seen after naloxone reversal of an opioid agonist. Premature ventricular contractions have also been documented after reversal, but are not a common occurrence and seem to be more likely if there are high levels of circulating catecholamines. This drug is sometimes administered sublingually to neonatal patients exhibiting respiratory depression that have been delivered by Caesarean section after maternal administration of an opioid agonist.

Nalmefene and Naltrexone

Both of these drugs are pure opioid antagonists with clinical effects that last approximately twice as long as naloxone (Veng-Pedersen et al. 1995). Though little is published about the use of these drugs in veterinary patients, they may be advantageous in preventing renarcotization when used to antagonize the effects of a long-acting opioid.

Nonsteroidal Anti-inflammatories

The nonsteroidal anti-inflammatory analgesics (NSAIDs) relieve mild to moderately severe pain and have been used extensively in a wide variety of domestic animals for many years. While pharmacokinetic and pharmacodynamic studies involving NSAIDs in wild and exotic animals are lacking, their use in such species continues to increase. This class of drugs dates back thousands of years, with the salicylates being among the oldest and still most commonly used analgesics (Vane & Botting 2003). Salicylate is a naturally occurring substance found in willow bark and was used for centuries to manage pain associated with rheumatism prior to production of the synthetic compound. In 1878, Felix Hoffman working at the Bayer company in Germany made the acetylated form of salicylic acid which has come to be known as aspirin (Vane & Botting 2003). While aspirin (acetylsalicylic acid [ASA]) has been found to be effective in the management of acute and chronic mild discomfort, the newer injectable NSAIDs appear to have comparable efficacy to the pure μ agonist opioids in controlling moderate to severe soft tissue and orthopedic pain. The NSAIDs appear to confer synergism when used in combination with opioids and may demonstrate an opioid-sparing effect should lower dosages of opioid be required. Their extended duration of action, in addition to their analgesic efficacy, make the NSAIDs ideal for treating acute and chronic pain in veterinary species. Careful patient and drug selection is critical, however, due to their potential for harmful side effects.

Cyclooxygenases and Prostaglandin Synthesis

In 1971, Vane discovered the mechanism by which aspirin exerts its anti-inflammatory, analgesic, and antipyretic actions. He proved that aspirin and other NSAIDs inhibited the activity of a cyclooxygenase (COX) enzyme which produced prostaglandins (PGs) involved in the pathogenesis of inflammation, swelling, pain, and fever (Vane 1971). Twenty years later, the discovery of a second COX enzyme was made and more recently COX-3 (Botting 2000, 2003; Chandrasekharan et al. 2002). Cyclooxygenase (previously termed prostaglandin synthase) oxidizes arachidonic acid (previously termed eicosatetraenoic acid) to various eicosanoids (including PGs and other related compounds) (Fig. 1.5) (Livingston 2000). Oxidation of arachidonic acid by 5-lipoxygenase (5-LOX), the most biologically important of the mammalian oxygenases, results in the series of eicosanoids termed leukotrienes (Fig. 1.5). The release of arachidonic acid from membrane phospholipid is catalyzed by the enzyme phospholipase A_2 and is the rate-limiting step in PG and leukotriene synthesis. Prostaglandin G_2 is the initial prostanoid formed, followed by prostaglandin H_2 which serves as a substrate for prostaglandin E-synthetase, prostaglandin D-isomerase, prostaglandin F-reductase, prostacyclin synthetase, and thromboxane synthetase for conversion to a variety of other prostenoids ubiquitous throughout cells and tissues in the body (Livingston 2000). These include the PGs PGE_2, PGD_2, PGF_2, and PGI_2 (prostacyclin), and the thromboxanes TXA_2 and TXB_2, all with diverse functions (Vane & Botting 1995). The PGs are not stored but are synthesized at a constant rate. They have short half-lives of 4–6 minutes at 37°C, and act locally at the site of production.

The PGs produced by both COX-1 and COX-2 are ubiquitous throughout the body and serve to facilitate many normal physiologic functions during both health and illness. Consequently, the clinical use of NSAIDs has the potential to disrupt these functions with the possibility of significant organ dysfunction. Thus, in addition to their role as analgesics, the effects of NSAIDs on the constitutive functions of the PGs must always be considered. There are several key points to note: (i) COX-1 generates PGs that are responsible for "mucosal defence" (i.e., secretion of bicarbonate and mucus, mucosal blood vessel attenuation of constriction, and mucosal epithelial regeneration), as well as thromboxane A_2, which is necessary for platelet function; (ii) COX-2 produces PGs which function in the prevention and promotion of healing of mucosal erosions, exert anti-inflammatory effects by inhibiting leukocyte adherence, aand play a role in renal protection and maturation; and (iii) COX-3 produces PGs which exert a protective function by initiating fever (Vane & Botting 1995; Botting 2003).

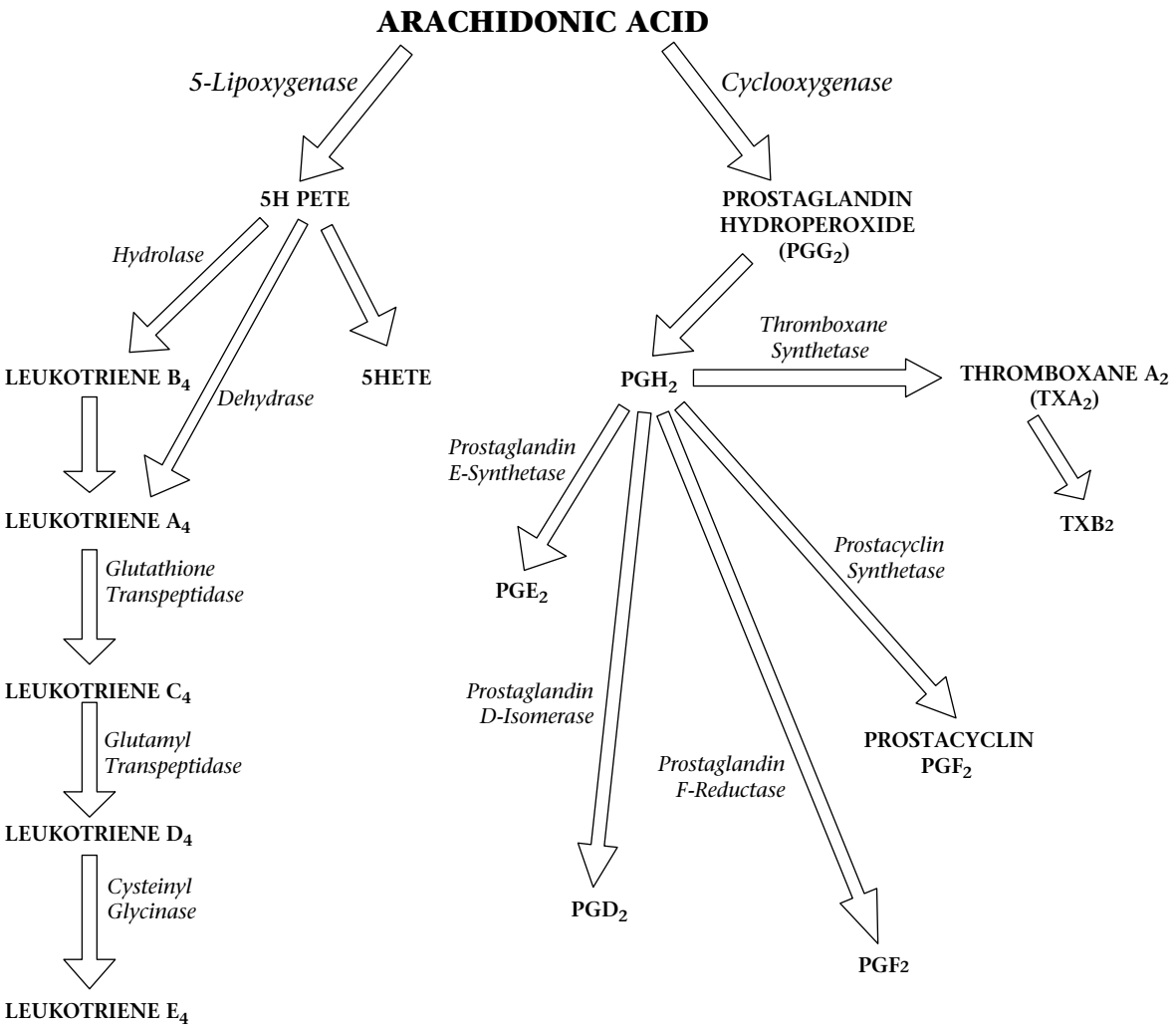


Figure 1.5 Eicosanoid synthesis.

Thus, depending on the NSAID selected, primary plug formation of platelets, modulation of vascular tone in the kidney and gastric mucosa, cytoprotective functions within the gastric mucosa, smooth muscle contraction, and regulation of body temperature will all be affected (Vane & Botting 1995). However, in this regard not all NSAIDs are created equal. As noted above, the COX-1, COX-2 and COX-3 enzymes make variable contributions to these functions, and individual NSAIDs inhibit each of these enzymes differently. Some NSAIDs inhibit both COX-1 and COX-2 (i.e., aspirin, phenylbutazone, ketoprofen/Anafen®, ketorolac/Toradol®, flunixin meglumine/Banamine®), while other NSAIDs preferentially inhibit COX-2 with only weak inhibition of COX-1 (i.e., meloxicam/Metacam®, carprofen/Rimadyl®, etodolac/Etogesic®, vedaprofen/Quadrisol-5®, tolfenamic acid/Tolfedine®). Yet others inhibit COX-2 exclusively (i.e., deracoxib/Deramax®, firacoxib/Previcox®, Robenacoxib/Onsior®, mavicoxib/Trocoxcil®), while still another drug, acetaminophen, only weakly inhibits both COX-1 and COX-2, but is able to inhibit COX-3 activity preferentially (Botting 2000).

Several in vitro studies investigating NSAID selective inhibition of the COX-1 and COX-2 isoenzymes have been published, but these are very difficult to interpret due to inconsistencies in the assays used (Kay-Mugford et al. 2000). Clinically, this information is confusing as it does not consider the pharmacokinetics of particular drugs and their concentrations in various tissues (Bertolini et al. 2001). Most NSAIDs that inhibit COX have been shown to result in diversion of arachidonate to the 5-LOX pathway. 5-LOX is principally found in polymorphonuclear cells, mast cells, monocytes, basophils, and B lymphocytes that are recruited during inflammatory and immune reactions (Bertolini et al. 2001). This enzyme catalyzes the initial step in leukotriene biosynthesis, which subsequently produces various eicosanoids, with LTB_4 being the most notable potent mediator of inflammation. The excessive production of leukotrienes has been implicated in the

creation of NSAID-induced ulcers (Hudson et al. 1993; Rainsford 1992). As always, however, the biological system is not clear-cut. While the LOX pathway is pro-inflammatory, there is also an anti-inflammatory pathway, which is discussed in more detail later (Serhan & Chiang 2004).

The contribution of the leukotrienes to the inflammatory process would seem to suggest that inhibition of both the COX and 5-LOX pathways by a therapeutic agent would result in an enhanced safety profile and may confer even greater analgesic efficacy due to broader anti-inflammatory and antinociceptive effects (Kirchner et al. 1997a). Data available show that dual-acting compounds are effective in arthritic models, where they also retain antithrombotic activity, produce little or no gastrointestinal damage, and do not adversely affect the asthmatic state (Bertolini et al. 2001).

A dual COX/5-LOX inhibitor called tepoxalin/Zubrin® underwent clinical trials and was approved for veterinary use in dogs (Kirchner et al. 1997b; Argentieri et al. 1994). Tepoxalin demonstrated gastrointestinal anti-inflammatory activity in mice, which supported the theory that 5-LOX inhibition may play a vital role in the prevention of NSAID-induced gastric inflammation (Kirchner et al. 1997b). Despite its approval in the United States, the manufacturer has voluntarily withdrawn the product from the market and it is no longer available.

Prostaglandin Receptor Antagonism

Instead of limiting prostaglandin production through COX inhibition, a novel and more targeted therapeutic approach involves a class of drugs known as piprants, which are prostaglandin receptor antagonists (PRAs). Prostaglandin E_2 has been identified as a key mediator of the classic signs of inflammation including swelling, erythema, and pain through PGE_2-mediated sensitization of peripheral neurons, as well as vasodilation and increased vascular permeability (Ricciotti & FitzGerald 2011). While PGE_2 exerts its effects via four different G protein-coupled receptors (EP1, EP2, EP3, and EP4), the EP4 receptor has been shown to play a dominant role in inflammation and pain, and may mediate central sensitization in chronic pain states. A specific EP4 receptor antagonist, grapiprant/Galliprant®, has been demonstrated to provide relief from arthritic pain in canine clinical patients and appears to act without affecting the synthesis and widespread activity of PGE_2 and other prostanoids (Kirkby Shaw et al. 2015).

Analgesic and Anti-inflammatory Effects of NSAIDs

There is overwhelming evidence indicating that decreased PG synthesis due to COX inhibition and/or antagonism of PG activity at the EP4 receptor mediates NSAID-induced analgesic and anti-inflammatory effects. Traditionally, NSAIDS have been considered peripheral-acting drugs that penetrate inflamed tissues, decrease PG-induced vasodilation and extravasation of protein exudates, and attenuate nociceptor sensitization. These local effects make them excellent analgesic choices for injuries with associated inflammation, as well as conditions such as synovitis, arthritis, cystitis, dermatitis, etc. (Chopra et al. 2000).

In addition to their peripheral effects, central analgesic effects have also been documented in several animal models of pain where NSAIDs have been shown to disrupt prostaglandin-mediated effects at both spinal and supraspinal levels (Chopra et al. 2000; Malmberg & Yaksh 1992; McCormack 1994; Yaksh et al. 1998). This central effect may account for the overall well-being and improved appetite that is often observed in patients receiving parenterally administered NSAIDs for relief of acute pain.

The relationship between COX inhibition and clinical relief of pain and inflammation in the intact animal is complex. Nociceptive pathways may involve either the COX-1 or COX-2 gene, and these genes are expressed in different locations and under different circumstances.

NSAIDs and Fever

Just as the relationship between pain and the various activities of the COX system is complex, so too is the association between fever and the COX isoenzymes. The mechanisms leading to the generation of fever vary depending on the inciting factor, which may be peripheral (i.e., endotoxin) or central (i.e., endogenous pyrogens, such as IL-1). Interspecies variation is also substantial and the definitive role of the COXs in pyresis remains to be clearly elucidated. Evidence suggests that COX-2 plays a role in endotoxin pyrexia while, based on the antipyretic effects of acetaminophen and aspirin, COX-1 and COX-3 appear to function in endogenous pyrexia (Botting 2000, 2003; Chandrasekharan et al. 2002).

Other Pharmacologic Considerations for NSAID Use

Because of their high protein binding NSAIDs can displace other drugs from their plasma protein binding sites and potentially increase their plasma concentration. This is rarely a concern unless administered to animals with organ dysfunction or in those receiving other highly protein-bound medications with a narrow therapeutic index. Interference with the metabolism and excretion of certain coadministered drugs may occur, therefore verifying the safety of combination therapy is always mandatory.

Some NSAIDs may induce the syndrome of inappropriate secretion of ADH. Renal water reabsorption depends

on the action of ADH mediated by cyclic adenosine monophosphate (cAMP). As PGs exert a controlled negative feedback action on cAMP production, inhibition of PG synthesis results in above normal levels of cAMP with potential for enhanced ADH activity. In addition, the administration of a COX-2 selective NSAID may enhance sodium and water reabsorption. Clinically, both mechanisms may result in high specific gravity urine with dilutional hyponatremia. Urine volume may be decreased through this mechanism but without renal injury (Petersson et al. 1987; Dunn & Buckley 1986).

Contraindications for NSAIDs

Nonsteroidal anti-inflammatory analgesics should not be administered to animals with acute renal insufficiency, hepatic insufficiency, dehydration, hypotension, conditions associated with low effective circulating volume (i.e., congestive heart failure, ascites), coagulopathies (i.e., factor deficiencies, thrombocytopenia, von Willebrand's disease), or evidence of gastric ulceration (i.e., vomiting with or without the presence of "coffee ground material", melena). Administration of NSAIDs following gastrointestinal surgery must be determined by the health of this organ at the time of surgery. As the COX-2 isoenzyme is important for healing, intuitively NSAIDs would be contraindicated where a compromised bowel is noted. Concurrent use of other NSAIDs (i.e., aspirin) or corticosteroids is not recommended. The COX-1 preferential NSAIDs are contraindicated in animals with spinal injury (including herniated intervertebral disc) due to the potential for hemorrhage and neurologic deterioration, and due to excessive bleeding at the surgical site should surgical treatment be pursued. The NSAIDs should never be administered to animals in shock, trauma cases at the time of presentation, or animals with evidence of hemorrhage (i.e., epistaxis, hemangiosarcoma, head trauma). Animals with severe or poorly controlled asthma, or other types of moderate to severe pulmonary disease, may deteriorate with NSAID administration. Aspirin has been documented to exacerbate asthma in human patients, but COX-2-specific NSAIDs did not result in worsening of clinical signs (West & Fernandez 2003). It is not known whether animals may be affected in this way. Although administration of NSAIDs in head trauma, pulmonary diseases, or thrombocytopenia is generally contraindicated, COX-2 preferential NSAIDs (i.e., meloxicam, etodolac, carprofen, tolfenamic acid, and deracoxib) may prove to be safe with further study. Due to inhibition of PG activity, the NSAIDs may be detrimental to reproductive function. Indomethacin may block PG activity in pregnant women, resulting in cessation of labour, premature closure of the ductus arteriosus in the fetus, and disruption of fetal circulation (DuBois et al. 1998). These effects may occur in animals, therefore NSAIDs should not be administered during pregnancy. As COX-2 induction is necessary for ovulation and subsequent implantation of the embryo (DuBois et al. 1998), NSAIDs should also be avoided in breeding females during this stage of the reproductive cycle. As previously mentioned, the COX-2 isoenzyme is required for maturation of the embryological kidney so administration to lactating mothers should be avoided.

NSAIDs Used in Veterinary Medicine

There are few data regarding clinical pharmacology of NSAIDs in exotic species, thus care must be taken when extrapolating from common domestic species.

Meloxicam

Meloxicam is a COX-2 preferential NSAID approved for use in dogs in Australasia, Europe, and North America. The parenteral formulation is approved for cats in the United States and Australasia. Its use in cats in Canada is under investigation, with completed studies indicating safety and efficacy. Its use in horses is also under investigation, with pharmacokinetic studies indicating that the half-life is shorter and clearance greater than in the dog, suggesting that dosing more than once a day may be necessary (Sinclair et al. 2003).

Studies indicate no renal or hepatic abnormalities with acute administration and minimal to no antithromboxane activity, suggesting hemostasis in normal animals may not be a problem (Mathews et al. 1999; Poulsen & Justus 1999). Few adverse reactions have been documented and most involve the gastrointestinal tract. A recent study showed no difference in gastric erosions over saline placebo when meloxicam was administered at 0.1 mg/kg for 3 days post electrical stimulation (i.e., surgical simulation) under anesthesia. However, corticosteroids plus meloxicam in this study resulted in significant gastric erosions (Boston et al. 2003). A case report of combination aspirin and meloxicam in a dog resulted in duodenal perforation (Reed 2002). This case illustrates the importance of COX-2 in intestinal protection when aspirin is coadministered, and reinforces that different NSAIDs should not be administered concurrently. Analgesia is excellent when meloxicam is combined with an opioid.

In recent years, meloxicam has become the most widely used NSAID in exotic and zoo animals, including reptiles, birds, and numerous mammalian species. Drug use remains off-label, with doses largely extrapolated from domestic animal pharmacokinetic and pharmacodynamic studies. Species-specific studies are beginning to appear in

the literature and should be consulted wherever possible prior to prescribing meloxicam or any NSAID.

Carprofen

Although classified as a NSAID, carprofen administration to beagle dogs did not inhibit PGE_2, 12-hydroxyeicosatetrenoic acid, or thromboxane B_2 synthesis in an experimental study utilizing subcutaneous tissue cage fluids (McKellar et al. 1994b). It was concluded that the principle mode of action of carprofen must be by mechanisms other than cyclooxygenase or 12-lipoxygenase inhibition. However, more recent studies indicate that it is a COX-2 preferential NSAID (Kay-Mugford et al. 2000; Ricketts et al. 1998). Carprofen is approved for perioperative and chronic pain management in dogs in Australasia, Europe, and North America. Carprofen is approved for single dose, perioperative use in cats in Europe, and is licensed for use in horses in the United Kingdom. In sheep, carprofen (0.7 mg/kg IV) resulted in plasma concentrations of 1.5 μg/mL, similar to those required to confer analgesia in horses, for up to 48 hours (Welsh et al. 1992). However, analgesia was not assessed in this sheep study (Welsh et al. 1992). Antithromboxane activity is minimal, suggesting that induced coagulopathy may not be a problem in animals with intact hemostatic mechanisms (Poulsen & Justus 1999; McKellar et al. 1990).

Ketoprofen

Ketoprofen is approved for postoperative and chronic pain in both dogs and cats in Europe and Canada. Ketoprofen is also approved for use in horses and ruminants. As ketoprofen is an inhibitor of both COX-1 and COX-2, adverse effects are a potential problem requiring careful patient selection. Although several studies using ketoprofen preoperatively indicate its effectiveness in controlling postoperative pain, a general consensus among veterinarians has restricted its use primarily to the postoperative period to reduce the potential for hemorrhage (Mathews et al. 1999; Lobetti & Joubert 2000; Pibarot et al. 1997). Ketoprofen should not be administered to patients with risk factors for hemorrhage. It is often administered to animals immediately after orthopedic procedures (i.e., fracture repair, cruciate repair, onychectomy).

Deracoxib

Deracoxib is a COX-2 specific inhibitor. It is approved in the United States and Canada for control of postoperative pain and inflammation associated with orthopedic surgery in dogs. The incidence of vomiting and diarrhea were similar in dogs receiving deracoxib compared to dogs receiving placebo in a perioperative field trial, and overall the drug was well tolerated and effective (Novartis Animal Health USA 2004). It was also shown to be effective in attenuating lameness in dogs with urate crystal-induced synovitis after prophylactic and therapeutic administration (McCann et al. 2004; Millis et al. 2002). This group of NSAIDs appeared to be gastroprotective in human patients when compared to the less COX-2 specific NSAIDs, when used for 8 days to 3 months (Silverstein et al. 2000). However, more recent studies in humans indicate these NSAIDs cannot guarantee gastroprotection with chronic use. Furthermore, in a canine study comparing the gastrointestinal safety profile of licofelone (a dual inhibitor) to rofecoxib (another specific COX-2 inhibitor), rofecoxib was found to induce significant gastric and gastroduodenal lesions (Moreau et al. 2005).

Diclofenac

Diclofenac is available worldwide as several different human and veterinary formulations. It is a useful anti-inflamatory and analgesic drug, and has been studied for antimicrobial activity (Dutta eta l. 2007). Diclofenac has been observed to cause severe hepatic and nephrotoxicity in many species of birds and its use, or accidental ingestion from carcasses, should be avoided (Jayakumar et al. 2010; Jain et al. 2009; Naidoo et al. 2009; Hussain et al. 2008; Taggart et al. 2007; Oaks et al. 2004).

Firocoxib

Firocoxib is available as an oral paste and injectable for horses and as an oral formulation for dogs. The efficacy and adverse events appear similar to other coxib-class NSAIDs (US Food and Drug Administration 2011). There are few reports of firocoxib use in birds, reptiles, or exotic mammals in the literature.

Robenacoxib

Robenacoxib is available as an oral and injectable formulation for treatment of pain and inflammation in both dogs and cats. Specific label indications and doses vary by country. The efficacy and adverse events appear similar to other coxib-class NSAIDs.

Mavicoxib

Mavicoxib is a long-acting NSAID approved outside the United States for use in dogs. The dosing interval is usually 2 weeks between doses 1 and 2, then 4 weeks between subsequent doses. The elimination half-life in healthy dogs is approximately 2 weeks (range 7.9–38.8 days) (Cox et al. 2010). Significant individual and breed-associated differences have been observed but effects on drug safety and effectiveness have yet to be determined (Cox et al. 2011).

Tolfenamic Acid

Tolfenamic acid is approved for use in cats and dogs in Europe and Canada for controlling acute postoperative and chronic pain. The dosing schedule is 3 days on and 4 days off, which must be strictly adhered to. Reported adverse effects are diarrhea and occasional vomiting. Tolfenamic acid has significant anti-inflammatory and antithromboxane activity, therefore post-traumatic and surgical hemostasis may be compromised during active bleeding after administration of this NSAID (McKellar et al. 1994b).

Flunixin Meglumine

Flunixin meglumine is a COX-1 and COX-2 inhibitor that is approved for use in dogs in Europe but not North America. It is also approved for use in ruminants and horses, and is commonly used for equine colic pain.

Phenylbutazone

Phenylbutazone is approved for use in horses, cattle, and dogs in North America. Since safer NSAIDs are approved for dogs, phenylbutazone is not recommended for this species. In horses, there is high risk of gastric ulceration and nephrotoxicity, where signs of toxicity may progress from inappetence and depression to colic, gastrointestinal ulceration, and weight loss (MacAllister et al. 1993; Collins & Tyler 1984; Snow et al. 1981). Phenylbutazone has a prolonged elimination half-live in cattle, ranging from 30 to 82 hours (DeBacker et al. 1980; Arifah & Lees 2002).

Aspirin

Aspirin is primarily a COX-1 inhibitor. It has been most commonly used as an analgesic for osteoarthritic pain in dogs. It is also available in proprietary combinations with various opioids (aspirin plus codeine or aspirin plus oxycodone) to achieve a synergistic effect for the treatment of moderate pain. It is also used as an antipyretic and anticoagulant in dogs and cats. Aspirin has also been recommended in cattle (Gingerich et al. 1975).

Grapiprant

Grapiprant is a non-COX-inhibiting NSAID that acts as an EP4 PG receptor antagonist downstream of traditional NSAIDs in the arachidonic acid cascade. It is approved for treatment of pain and inflammation associated with osteoarthritis in dogs and is supplied in 20-, 60-, and 100-mg flavored tablets. In a clinical trial submitted as part of the regulatory approval process in the United States, grapiprant was found to be effective compared to placebo, although there was no positive control. In the same study, grapiprant was generally well tolerated by dogs, with intermittent diarrhea, vomiting, and anorexia the most commonly reported adverse effects (Rausch-Derra e al. 2016). More studies are needed to demonstrate grapiprant's analgesic efficacy in osteoarthritis and other types of pain and inflammation in dogs and to compare its safety to other approved COX-2 inhibiting NSAIDs.

NSAIDs Not Approved for Use in Veterinary Medicine (Off-label Use)

Ketorolac

Ketorolac is a COX-1 and COX-2 inhibitor that is included for the benefit of those working in the research setting associated with human hospitals where the availability of ketorolac is more likely than other NSAIDs. Adverse gastrointestinal effects are common.

Acetaminophen

Acetaminophen is a COX-3 inhibitor with minimal COX-1 and COX-2 effects. It should not be administered to feline species due to deficient glucuronidation of acetaminophen in these species (Court & Greenblatt 1997). Reptiles are known to be particularly sensitive to the toxic effects of acetaminophen and this has been exploited to combat the invasive brown treesnake on the island of Guam by lacing dead mice with 80 mg of acetaminophen and baiting snake habitats. A recent study has confirmed that the standard 80-mg dose used operationally to kill brown treesnakes produced acute methemoglobinemia, with severe hypoxia and respiratory failure cited as the probable cause of death (Mathies & Mauldin 2020). Based on these findings, acetaminophen should not be administered to any reptile at any dose.

Dipyrone

Dipyrone is a COX-3 inhibitor and is approved for use in cats and dogs in Europe and Canada. Dipyrone should be given intravenously to avoid the irritation experienced when given intramuscularly. The analgesia produced is not usually adequate for moderate to severe postoperative pain, and dipyrone is reserved for use as an antipyretic in cases where other NSAIDs are contraindicated. Dipyrone induces blood dyscrasias in humans, but this has not been reported in animals.

Alpha-2 Adrenergic Receptor Agonists and Antagonists

Introduction

The use of alpha-2 adrenergic agonists in veterinary medicine began following the synthesis of xyalazine in 1962. Early reports of the sedative and anesthetic sparing qualities of xylazine predated the elucidation of its mechanism

of action in 1981. Alpha-2 adrenoreceptors have been identified in the CNS, cardiovascular, respiratory, renal, endocrine, gastrointestinal, and hemotologic systems, resulting in widespread drug effects (Aantaa et al. 1995). Most FDA-CVM approved alpha-2 agonists carry label indications as sedatives and analgesics.

Alpha-2 adrenoceptors are linked to Gi-protein second messengers (Aantaa et al. 1995). These are similar to those used by many opioid receptor subtypes and in fact opioid and alpha-2 agonists usually have additive or synergistic effects (Maze & Tranquilli 1991). Alpha-2 adrenoreceptors are classically described as being located presynaptically at noradrenergic neurons, exerting an inhibitory feed-back role on the release of subsequent norepinephrine (Maze & Tranquilli 1991). This results in decreased sympathetic nervous system efferent activity and is probably related to the decreased vigilance, decreased anesthetic requirements, and decreased heart rate and blood pressure observed following administration of these drugs to most species. Alpha-2 adrenoreceptors are also found in the vascular smooth muscle (a non-presynaptic site) and when activated result in vasoconstriction. This results in increased vascular resistance and will result in increased baroreceptor-mediated vagal tone. The result is slowing of heart rate and decreasing cardiac output, but blood pressure remains within physiologic normal values. Confusion often exists about the clinical effect of alpha-2 agonist administration (e.g., hypertension [post-synaptic[vs. hypotension [pre-synaptic[) expected in a patient. The net clinical result will vary with route of administration, dose, species, and the duration of time following the administration.

Alpha-2 agonist doses vary at least 10-fold across species. Pigs tend to have the highest requirements, followed by cats, dogs, horses, and finally ruminants. Breed and sex differences also exist within cattle that should be appreciated.

Alpha-2 Adrenergic Agonist Effects

Central Nervous System

Alpha-2 adrenergic agonists exert many of their inhibitory effects on CNS function through inhibiting norepinephrine release from sympathetic neurons (Maze & Tranquilli 1991). Inhibition of intraneuronal transmission is also responsible for muscle relaxation observed following alpha-2 adrenergic agonist administration. Analgesia is mediated by spinal and supraspinal alpha-2 adrenergic receptors. Agonist binding modulates afferent activity at a spinal level and increases the diffuse noxious inhibitory control system activity. The net result is sedation, reduced anesthetic requirements, reduced stress responses, and analgesia. It should be noted that alpha-2 agonists, like all sedatives and tranquilizers, are not anesthetics. Although animals can appear in a sleep-like state, they may become aroused by noxious stimulation and may become defensive. Additionally, on rare occasions, paradoxical behavior (aggression rather than sedation) may be noted. Accidental intracarotid injection of alpha-2 adrenergic agonists will induce seizure-like activity and must be avoided.

Emetic Center

Alpha-2 agonists are predictable emetics in cats and dogs, especially at high doses. This is due to activation of the chemoreceptor trigger zone of the area postrema (Hikasa et al. 1992). Dopaminergic blocking agents do not prevent alpha-2 induced emesis.

Thermoregulation

Alpha-2 agonists will often cause changes in thermoregulation. The effect is usually a decrease; however, increases can be seen when animals are placed in warm environments. This is especially a concern when alpha-2 agonists are used for capture of cattle or other hoof-stock. If possible, body temperature should be monitored for 12–24 hours following sedation or administration of an alpha-2 adrenergic antagonist should be considered. In smaller animals, hypothermia is more common and may be due to decreased metabolic activity accompanying sedation as well as decreased thermoregulatory control. It is usually not a life-threatening problem if managed appropriately.

Eyes

Alpha-2 agonists generally cause mild miosis to little change in pupil diameter and a mild decrease in intraocular pressure (IOP) (Verbruggen et al. 2000). This class of drugs is relatively contraindicated, with increases in IOP or corneal lacerations because of the probability of inducing vomiting (which causes further increases in IOP) in those species that can vomit.

Respiratory System

Most alpha-2 adrenergic receptor agonists can cause decreased responsiveness to CO_2, especially in higher doses. This effect is compounded by the coadministration of opioids or anesthetic agents and is of concern during anesthesia. In some species alpha-2 agonists do not normally depress respiration to the point of creating hypoxia and cyanosis. In fact, arterial blood gas values for PaO_2 are usually normal. The bluish color of the mucous membranes that may be noticed on occasion is usually due to slowed venous blood flow accompanying vasoconstriction. As the capillary transit time increase, oxygen extraction increases and notable hemoglobin desaturation will appear as a blue(ish) color. Oxygen therapy will often resolve this

condition. However, in sheep and possibly some other species, xylazine administration has been shown to result in central hypoxemia related to pulmonary changes (Celly et al. 1997, 1999).

Cardiovascular System

Intravenous administration of alpha-2 adrenergic agonists typically results in rapid and pronounced vasoconstriction (Pypendop & Verstegen 1998). If heart rate and cardiac output do not decrease (as can be seen with atropine administration), blood pressure would increase impressively (Alibhai et al. 1996; Short 1991). However, normal baroreceptor reflexes attempt to maintain blood pressure within physiologic limits by increasing vagal tone and slowing heart rate. Heart rate may decrease by 50–75% in some individuals. The cardiac rhythm is often a slow sinus rhythm characterized by two or three sequential beats followed by a long sinus pause. Occasionally, second degree atrioventricular blockade will be seen. Both rhythms are often responsive to antimuscarinic administration (block the vagal reflex) and high heart rates (and blood pressures) will result. Intramuscular or oral administration tends to decrease the incidence of profound bradycardia.

After the initial direct vasoconstriction occurs, vasodilation and reduction in blood pressure may be seen. This is more prominent in primate species. The alpha-2 adrenergic receptor agonists decrease sympathetic nervous system efferent activity, which results in decreased vasomotor tone and heart rate. Alpha-2 adrenergic agonists have historically been used in humans as antihypertensive agents because they reduce vasomotor tone and block the reflex increase in heart rate that can accompany alpha-1 antagonists.

Most of the contraindications to alpha-2 adrenergic receptor agonist administration are related to their cardiovascular side effects. As a general rule, this class of drugs should not be administered to animals that do not have normal healthy cardiovascular systems and/or are exercise intolerant. There are some exceptions, but a thorough understanding of the underlying disease is required and appropriate monitoring is necessary.

Urinary Tract

Alpha-2 adrenergic receptor agonists increase urine output by increasing production of dilute urine (Saleh et al. 2005; Grimm et al. 2001). This is primarily related to inhibition of ADH release and/or synthesis as well as changes in renal hemodynamics (Saleh et al. 2005).

Gastrointestinal Tract

Animals may have complications associated with decreased propulsive activity, including colic and bloat, although this is unusual in most species (Thompson et al. 1991). Longer-acting drugs are more likely to result in a problem. Patients should be observed following alpha-2 adrenergic receptor agonist administration for signs of abdominal distension.

Endocrine

A classic neroendocrine response is hyperglycemia following alpha-2 agonist administration (Abdel el Motal & Sharp 1985; Osman & Nicholson 1991). This is due to a decrease in insulin release. It is usually transient and not clinically significant, although alpha-2 agonists should not be used to sedate animals for glucose curves.

Since alpha-2 agonists reduce sympathetic activity and inhibit the stress response, neuroendocrine markers of the stress response should be affected. Cortisol levels are usually decreased following alpha-2 agonist administration and may not be reliable as indicators of stress or pain (Brearley et al. 1990; Sanhouri et al. 1992).

Specific Drugs

Several alpha-2 adrenergic receptor agonists are approved for veterinary use. Generally, their pharmacologic actions will be similar, but the duration of action and species compatibility will vary. All alpha-2 agonists are potent and potentially dangerous following accidental human ingestion or injection. Care should be taken when handling syringes loaded with these drugs and medical help should be sought immediately if exposure occurs.

Xylazine

Xylazine is the prototypical veterinary alpha-2 adrenergic receptor agonist. Another alpha-2 agonist, clonidine, has been used in humans as an antihypertensive agent and is often used as the prototypical drug in research applications. Xylazine has been administered to many different species, both domestic and exotic. It is readily available and relatively inexpensive.

Xylazine has a shorter duration of action than many of the other drugs. Typical doses will result in muscle relaxation and sedation of horses for 45–60 minutes. This can be advantageous when performing field anesthesia/sedation when a rapid recovery is desired. Xylazine is often combined with opioids such as butorphanol to enhance sedative and analgesic qualities.

Detomidine

Detomidine is a longer-acting alpha-2 agonist approved for use in horses as a sedative. It is commonly administered when profound, long-lasting sedation is needed. When used in high doses as a preanesthetic, low respiratory rates may accompany induction. Detomidine is not used in small

animals but there are a number of reports evaluating its use in combination with other agents in large exotic species, including rhinoceros and zebras.

Medetomidine

Medetomidine is formulated as a racemic mixture that was originally approved as a sedative/analgesic in dogs. Though it is no longer widely available except as formulations prepared for wildlife capture and restraint, it has been extensively evaluated in all domestic species and many exotic and zoological species. It is extremely selective for the alpha-2 receptor and binds it avidly. Atipamezole was developed as the specific antagonist for medetomidine for this reason.

Romifidine

Romifidine is an alpha-2 adrenergic receptor agonist that is approved for use in horses. It has been evaluated in other species and appears to be relatively safe but offers few advantages over other approved products. Some equine clinicians believe is it is a good sedative without causing excessive ataxia.

Dexmedetomidine

Dexmedetomidine contains only the pure dextrorotatory enantiomer of racemic medetomidine, which appears to be responsible for all of the clinically relevant properties of the drug. Due to the absence of the inactive levorotatory enantiomer, dexmedetomidine is twice as potent as medetomidine. It is currently marketed as a solution with half the strength of medetomidine, meaning that equivalent doses of dexmedetomidine and medetomidine have the same volume. The sedative, analgesic, and anesthetic-sparing effects of both drugs appear to be similar when administered at equivalent doses in dogs and cats (Ansah et al. 1998; Granholm et al. 2006, 2007; Kuusela et al. 2000). Hemodynamic side effects and reversal characteristics with administration of the specific antagonist atipamezole also appear similar. Dexmedetomidine has been evaluated in combination with a variety of other injectable agents, including benzodiazepines, dissociatives, opioids, and alfaxalone, in many zoo, exotic, and wildlife species.

Alpha-2 Adrenergic Receptor Antagonists

One big advantage alpha-2 adrenoreceptor agonists have over other sedative/tranquilizers such as acepromazine is reversibility. It is possible to administer an antagonist and within minutes animals will regain function and be able to be released. Antagonist administration will usually result in opposite hemodynamic effects (e.g., acute vasodilation and tachycardia) and they should not be administered in a cavalier fashion. Many of the difficulties (including some deaths) occur with reversal. Also, alpha-2 agonist mediated analgesia is reversed, necessitating administration of other analgesic classes to painful animals. Some species (e.g., domestic horses) are not routinely reversed because of the potential for uncontrollable activity and possible self-trauma.

Yohimbine

Yohimbine is a plant-derived compound that has been used by humans for centuries because of its performance enhancing properties. It is relatively effective for reversing xylazine in horses, dogs, and cats, but is less effective in ruminants. Additionally, yohimbine has some stimulant actions that may result in excitation on recovery. Yohimbine has not been effective at reversing newer agents, such as medetomidine.

Tolazoline

Tolazoline was originally used as a therapy for human infants suffering from pulmonary hypertension. It is a relatively nonselective alpha-receptor blocker and is useful for reducing pulmonary vascular resistance. It is also effective at antagonizing xylazine sedation. It is most commonly used for equine and ruminant species. It appears more effective in ruminant species than yohimbine.

Atipamezole

Atipamezole is the marketed antagonist for medetomidine and dexmedetomidine. It is effective at reversing all available alpha-2 adrenoreceptor agonists and its use is limited only by cost. It is relatively selective for alpha-2 adrenergic receptors and usually does not cause excessive stimulation, although excitation may occur. Atipamezole is approved for use in dogs, but it is used in other species commonly. Under most circumstances, it is best given by the intramuscular route except in emergency situations.

Phenothiazines and Butyrophenones

Introduction

The phenothiazines and butyrophenones produce an array of behavioral, autonomic, and endocrine effects and have been used clinically in numerous domestic and wild species. Their tranquilizing effects are mediated by antagonism of dopamine receptors (primarily the D2 subtype) located in the cerebral cortex, basal ganglia, and limbic system. In addition, other antidopamine effects are noted in the hypothalamus (increased prolactin secretion and impaired thermoregulation), brainstem (impaired vasomotor reflexes), and chemoreceptor trigger zone of the

medulla (antiemesis). Both drug classes also have varying antagonistic effects at adrenergic (alpha-1 and alpha-2), serotonergic (5-hydroxytryptamine receptors), muscarinic (M1), and histaminergic (H1) receptor systems. It is important to note that they do not possess any inherent analgesic properties and their effects are not reversible.

Acepromazine

Acepromazine is the most widely used phenothiazine tranquilizer in veterinary medicine. In dogs and cats it is commonly combined with an opioid to produce a state historically referred to as "neuroleptanalgesia". Such combinations are suitable to provide chemical restraint for short, noninvasive procedures or as preanesthetic medication prior to induction of general anesthesia. Acepromazine administration in the preanesthetic period will cause dose-dependent reductions in both injectable and inhalant anesthetic requirements in these species. In horses and cattle, the drug is used primarily for its anti-anxiety effects. In susceptible pigs, acepromazine has been shown to prevent or reduce the onset of halothane-induced malignant hyperthermia. In certain wild and exotic species, the combination of acepromazine and the potent opioid etorphine (Large Animal Immobilon) has been used for immobilization and anesthesia.

The cardiovascular effects of acepromazine include decreases in mean arterial blood pressure in the range of 20–30% accompanied by dose-dependent reductions in stroke volume and cardiac output. Isoflurane, due to its potent vasodilatory effects, appears to potentiate acepromazine-induced hypotension. At clinically relevant doses, heart rate may not change appreciably or may increase slightly. At very high doses, bradycardia and sinoatrial block may occur. Acepromazine has also been shown to reduce the arrhythmogenic effects of epinephrine and halothane.

In general, effects on pulmonary function (i.e., oxygenation and ventilation) tend to be minimal in conscious animals, although respiratory rate may decrease somewhat. Acepromazine has been shown to dose-dependently decrease hematocrit by as much as 20–50% in dogs and horses due to splenic sequestration. This effect occurs within 30 minutes and appears to persist for at least 2 hours. The drug also decreases platelet aggregation but the clinical hemostatic significance of this appears minimal.

Regarding the gastrointestinal system, acepromazine has been shown to have antiemetic effects when administered 15 minutes prior to morphine, hydromorphone, or oxymorphone. Lower esophageal sphincter tone is reduced, which may lead to an increased risk of gastric reflux, though this has not been proven. Decreased gastrointestinal motility and delayed gastric emptying have been demonstrated in horses.

Renal blood flow and glomerular filtration rate appear to be well-maintained in dogs receiving acepromazine and isoflurane. In cats under halothane anesthesia, urethral pressure has been shown to decrease by 20% with acepromazine administration. There are anecdotal reports of penile prolapse/priapism in stallions. The magnitude and duration of the protrusion appear to be dose-dependent and this side effect appears to be mediated by alpha-adrenergic antagonism. Also, because of its antihistaminergic effects, acepromazine is not suitable for allergic skin-testing.

Azaperone

Azaperone is classified as a butyrophenone and its only approved indication is for control of aggression associated with mixing or re-grouping of swine. It is also used as a preanesthetic agent in pigs and has clinical properties and side effects similar to acepromazine. In various wild and exotic species azaperone is used in combination with potent opioids such as etorphine or carfentanil to produce immobilization or anesthesia.

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2

Analgesia

Douglas P. Whiteside and Kurt K. Sladky

"Pain is inevitable, suffering is optional." Buddhist proverb

Introduction

Over the past decade, pain management has emerged as an important discipline in veterinary medicine, with significant growth of scientific knowledge in neuroanatomy and neurophysiology across the vertebrate taxa. Pain is often now referred to as the fifth vital sign. Optimal management of pain, and the development of future analgesic strategies, requires a lucid understanding of the pathophysiology of pain across taxa, and of the basic pharmacology of the analgesic drugs used to treat it. While pain can be a protective mechanism against acute injury, it also can be a chronic, nonrelenting, and crippling sensory experience that leads to severe stress, with profound changes in normal behaviour and in neuroendocrine, metabolic, and immune responses (Kehlet 1997; Kehlet & Wilmore 2002; Lemke & Creighton 2010; Sneddon et al. 2014; Sneddon 2019).

Many myths have been associated with pain management in zoological, aquatic, and free-living wildlife species and this has led to poor analgesia use in the past. New understandings and techniques have allowed us to develop improved strategies for analgesia and to promote education in their use. Adequate pain relief is not only humane but improves recovery. Understanding that pain is a continuum across species allows for more effective treatment.

Clinicians working with wildlife under human care or in a free-living setting face a number of unknown variables compared to their companion animal counterparts due to the tremendous diversity of species they are presented with, marked differences in physiology across the vertebrate taxa, lack of diagnostic techniques and pain scoring systems to adequately evaluate pain, and the paucity of pharmacokinetic (PK) or clinical studies for free-living and captive wildlife species. However, the physiological, behavioural, and ethical consequences of inadequate pain management behoove us as responsible clinicians to make every effort possible to prevent or control pain in the animals under our care (Hess 2010; Sneddon et al. 2014; Chinnadurai et al. 2016; Balko & Chinnadurai 2017; Mather 2019).

Numerous barriers exist to appropriately managing pain in wildlife species, including lack of familiarity with current therapeutic modalities and techniques, concerns regarding drug-induced adverse effects or toxicity, inadequate species-specific PK and clinical efficacy data, economic considerations, poor assessment of pain, and personal views on pain perception. However, studies of behaviour demonstrate that animals not only experience pain but remember the experience and try to avoid it in the future. No longer should the question be asked "Does the animal experience pain?", but rather "What kind of pain can the animal experience?" Species variability in the expression of pain can occur due to a failure to recognize species-specific pain behaviours, difference in pain sensitivity, and the conscious response of a species. Pain does not always lend itself to objective measures, so the art of medicine should not be overlooked in favour of the science (Nolen 2001; Paul-Murphy et al. 2004b; Hawkins 2006; Chinnadurai et al. 2016; Balko & Chinnadurai 2017; Sneddon 2019).

This chapter is an overview of analgesia across vertebrates and invertebrates, and readers are encouraged to refer to other chapters for references on pharmacology and for more species-specific information.

Physiology of Pain

Pain is a complex sensation that requires integration of nociceptive and other sensory input at the cortical level, while nociception is the neural response to a noxious

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stimulus. The International Association for the Study of Pain (1979) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. The inability to communicate pain, and the lack of understanding of whether the vast number of species that are worked with actually experience the emotional experience of pain, does not negate the fact that all potential or actual tissue damages in animals should be considered painful. In addition, it must be recognized that neonates are capable of experiencing pain; in mammals the pain pathways necessary for pain perception are well developed in late gestation, and in humans the spinal cord sensory nerve cells are more excitable in infants with an amplified, prolonged response and larger receptive field to pain. As a result, painful experiences in early life may produce long-term alterations in sensory processing and pain sensitivity (Anand & Hickey 1987; Fitzgerald & McIntosh 1989; Walker 2008; Babos et al. 2013; Anwar 2016).

Our understanding of pain is still based primarily on mammalian studies, although the recognition of pain and its treatment is receiving much more attention now in non-mammalian species. An understanding of the pathophysiology of pain is important to enable more effective management and target future research. Pain can be classified anatomically as somatic or visceral pain, or temporally as acute or chronic. While a significant amount of research has been carried out with acute pain, there is still a paucity of information regarding chronic pain. Pain also is commonly categorized as physiologic or clinical (inflammatory or neuropathic in origin). Physiological pain is protective in nature, well localized, proportionate to the peripheral stimulus, and subsides once the inflammatory process resolves. Clinical pain occurs with significant tissue trauma and inflammation, and is pathological or debilitating in nature. It is diffuse, disproportionate to the peripheral stimulus, and can continue beyond the resolution of the inflammatory process. Clinical pain can take on a disease character in pathological states such as inflammation, neuropathy, cancer, viral infections, chemotherapy, and diabetes. This state is manifest as an increased sensitivity to painful stimuli (hyperalgesia) or withdrawal behavioural responses to innocuous stimuli (tactile allodynia). Furthermore, individuals with chronic pain often show maladaptive, disease-induced, therapy-resistant deviations from normal tactile sensation, such as paraethesias and dysesthesias (Truini & Cruccu 2006; Kuner 2010; Lemke & Creighton 2010; Babos et al. 2013; Anwar 2016).

Ascending Nociceptive Pathways

Most tissues are rich in afferent nociceptors, the free nerve ending receptors that are responsible for the detection of thermal, mechanical, or chemical noxious stimuli. The majority of these receptors are nonselective cation channels that are gated by temperature (e.g., transient receptor potential channels), chemical ligands (e.g., acid sensing ion channels), or mechanical shearing forces. Activation of these channels increases inward conduction of sodium and calcium ions, which ultimately depolarizes the membrane and generates a burst of action potentials. Tissue trauma leads to the release of inflammatory mediators from damaged cells (H^+, K^+, prostaglandins), plasma (bradykinin), platelets (serotonin), mast cells (histamine), and macrophages (cytokines). Some of these inflammatory mediators activate nociceptors directly (bradykinin), whereas others sensitize nociceptors (prostaglandins). Release of neuropeptides such as substance P leads to vasodilation and edema, resulting in further activation and sensitization of nociceptors. Ultimately, tissue trauma and inflammation produce a "sensitizing soup" of chemical mediators that convert high-threshold nociceptors to low-threshold nociceptors. This is known as peripheral sensitization (Muir & Woolf 2001; Lemke & Creighton 2010; Babos et al. 2013; Anwar 2016; Sneddon 2019).

Somatic tissues have a higher density of nociceptive nerve fibers and smaller receptive fields, whereas visceral tissues have a lower density of nociceptive nerve fibers and larger receptive fields. These anatomical differences may account for some of the qualitative differences between somatic (discrete) and visceral (diffuse) pain. The stimuli are converted to an electrical signal (transduction), which is then transferred via myelinated A β and Aδ fibers (sharp or pricking pain, rapid transmission) or unmyelinated C fibers (dull burning pain, slow transmission) to the spinal cord dorsal horn cells (nerve conduction) where they synapse with second-order neurons. Visceral pain, in contrast to somatic pain, lacks the fast and slow components (Julius & Basbaum 2001; Woolf & Ma 2007; Yaksh 2009; Babos et al. 2013; Anwar 2016; Sneddon 2019). Polymodal C fibers can adapt to a variety of physiologic changes with responses to hypoxia, hypercapnea, hyperthermia, hypothermia, hypoglycemia, hyperosmolarity, hypoosmolarity, and lactic acidosis (Riddell & Craig 2003; Sneddon 2019).

Second-order projection neurons in the spinal cord are responsible for transmission of signals (projection) to the thalamus, hypothalamus, medulla, pons, and midbrain. Spinal inhibitory and excitatory interneurons are responsible for gating and modulating nociceptive input from the periphery. The spinothalamic tract is the major ascending nociceptive pathway. Additionally, propriospinal neurons that project across several dermatomes are present in the dorsal horn and are responsible for segmental reflexes associated with nociception. Glutamate is the primary excitatory neurotransmitter in the dorsal horn of the spinal

cord. Nociceptive as well as non-nociceptive fibers co-release glutamate and neuropeptides such as substance P and neurokinin A. Activation of a specific type of glutamate receptor, the N-methyl-D-aspartate (NMDA) receptor, plays a key role in the development of central sensitization, known as "wind up" (Woolf & Chong 1993; Muir & Woolf 2001; Lemke & Creighton 2010; Babos et al. 2013; Anwar 2016).

Third-order supraspinal neurons integrate the input from spinal neurons, thalamus, hypothalamus, medulla, pons, and midbrain and project to the somatosensory and insular (interoceptive) cortex where the pain is perceived (perception) and there are linkages with the autonomic nervous system. Projection from neurons in the lateral thalamus to neurons in the insular and secondary somatosensory cortex appears to be responsible for the sensory-discriminative aspects of pain. Projection from neurons in the medial thalamus to neurons in the anterior cingulate cortex appears to be responsible for the motivational-affective (emotional) aspects of pain. Projection from neurons in the motor thalamus to neurons in the primary somatosensory cortex appears to be responsible for sensory and motor integration. Once received by the conscious brain, the brain interprets and gives cognition to nociceptive signals, giving rise to a state of pain-induced distress (Kuner 2010; Lemke & Creighton 2010; Babos et al. 2013; Anwar 2016).

Antinociceptive Descending Pathways

Modulation or inhibition of nociceptive input at the spinal and supraspinal levels is the basis for descending antinociceptive pathways. This modulation leads to hyposensibility or a lack of pain in spite of inputs coming in from the periphery. The antinociceptive pathways begin at the supraspinal level (thalamus, hypothalamus, midbrain, medulla, and pons) with indirect input from the insular cortex and the anterior cingulate cortex. Release of norepinephrine, endogenous opioids (endorphins, enkephalins, dynorphins), and gamma-aminobutyric acid (GABA) inhibits synaptic transmission between primary afferent neurons and projection neurons by inhibiting neurotransmitter release and hyperpolarizing the postsynaptic membrane, which effectively shuts down the key synapse in the dorsal horn. This has evolutionary value because these mechanisms can enable the organism to ignore pain in critical situations, such as flight or fight, and may contribute to analgesia produced by a variety of nonpharmacological pain control approaches, such as transcutaneous electrical nerve stimulation and acupuncture (Muir & Woolf 2001; Kuner 2010; Lemke & Creighton 2010; Babos et al. 2013; Sneddon et al. 2014; Anwar 2016).

Principles of Pain Management

Effective analgesic therapy blunts the neuroendocrine response, reduces major complications, produces discernible changes in posture and behavior, and improves outcome (Carli & Schricker 2009; Wu & Liu 2009; Mosley 2011; Sneddon et al. 2014). The World Health Organization outlines a three-step analgesic ladder for the control of cancer pain in people, which has been well received and adapted by the veterinary community for managing pain (World Health Organization 2018). Nonopioids, generally nonsteroidal anti-inflammatory drugs (NSAIDs), are used for mild pain. If the pain persists, or is of moderate intensity, it is treated with the combination of a nonopioid and a 'weak' opioid. More severe pain dictates that a "strong" opioid replace the 'weak" opioid, often at higher doses or titrated to the degree of pain. At any of these levels, adjunctive analgesia (e.g., local anesthetics, alpha-2 agonists, NMDA antagonists, tricyclic antidepressants, anticonvulsants, corticosteroids, bisphosphonates, nutraceuticals), can be used to augment analgesia, taking into consideration the potential interactions and side effects (Babos et al. 2013).

Pain management should not just revolve around drugs, and whenever possible a more holistic, multimodal approach should be taken. Environmental conditions should be optimized for the species. Weight loss and adjunctive therapies such as chondroprotectants, physical therapy and rehabilitation, acupuncture and laser therapy, dietary manipulations, and even surgery also play an important role in the multimodal approach to pain (Truini & Cruccu 2006; Whiteside et al. 2006; Koski 2011; Rychel et al. 2011; Dadone & Harrison 2017). Atraumatic surgical technique is always the most effective method to prevent peripheral and central sensitization and the development of postoperative pain (Lemke & Creighton 2010).

There are five major classes of analgesic drugs, and each class blocks or modulates nociceptive input at one or more sites of action (Fig. 2.1). Alpha-2 agonists and opioids alter the central perception of pain. Activation of supraspinal and spinal alpha-2 receptors and opioid receptors also inhibits synaptic transmission in the dorsal horn of the spinal cord. Peripheral and central neural blockade with local anesthetics inhibits the development of central sensitization, as does administration of dissociative anesthetics such as ketamine which block NMDA receptors on projection neurons. Cyclooxygenase (COX) inhibitors such as NSAIDs reduce the synthesis of prostaglandins, which reduces inflammation and limits the development of both peripheral and central sensitization (Lamont & Grimm 2014; Lemke & Creighton 2010; Babos et al. 2013).

Trauma and inflammation sensitize the peripheral nervous system, and the subsequent barrage of nociceptive input

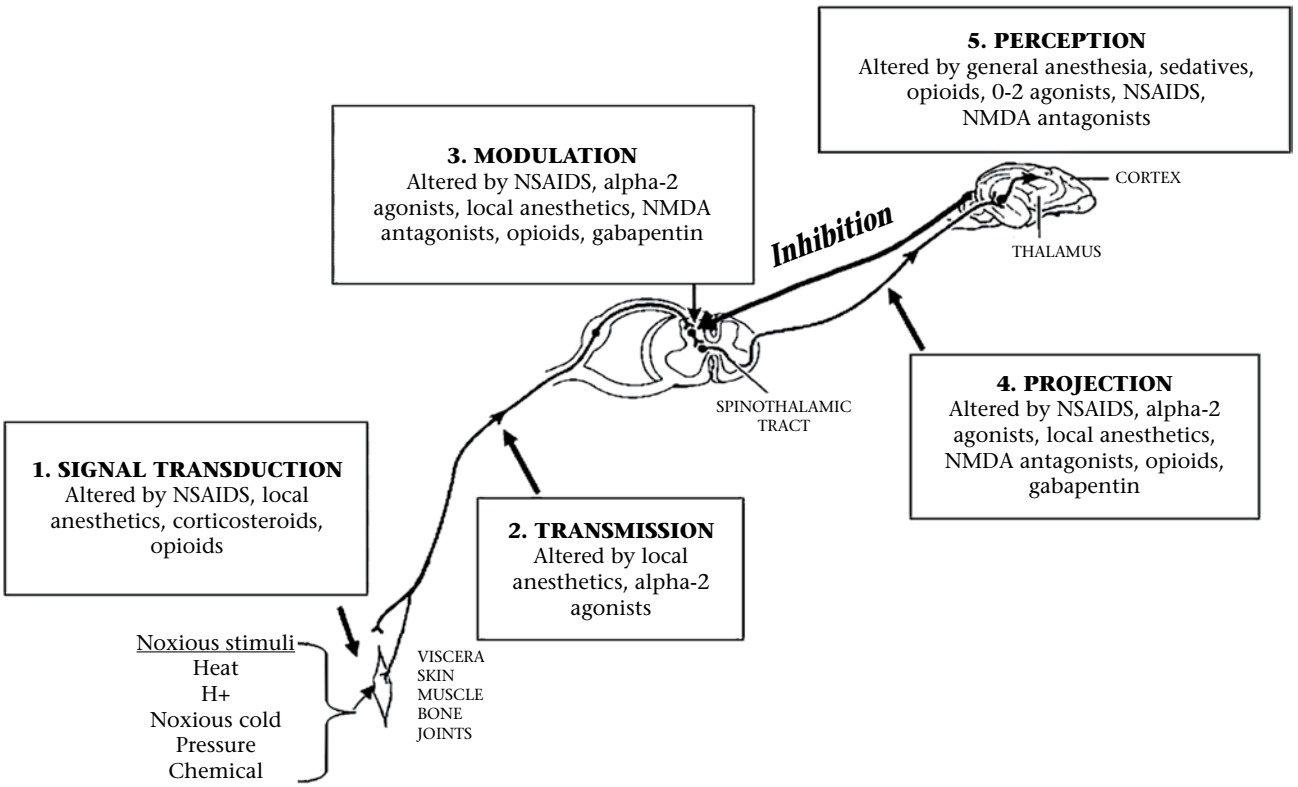


Figure 2.1 The pain pathway. Alpha-2 agonists, NMDA, N-methly-D-aspartate; NSIADs, nonsteroidal anti-inflammatory drugs.

produces sensitization of neurons in the dorsal horn of the spinal cord. Peripheral and central sensitization of nociceptive pathways plays a central role in the development of pathological pain (Woolf & Chang 1993; Babos et al. 2013). Blockade or attenuation of ascending nociceptive pathways or activation of descending antinociceptive pathways by different classes of analgesic drugs usually provides better analgesia with fewer side effects than unimodal therapy with a single class of analgesic drugs. Because peripheral and central neural blockade with local anesthetics are the only analgesic techniques that can produce complete blockade of peripheral nociceptive input, these techniques are the most effective way to attenuate sensitization of the central nervous system and the development of pathological pain (Lemke & Dawson 2000; Carli & Schricker 2009; Siddall & Cousins 1998; Lemke & Creighton 2010; Babos et al. 2013).

Behavioural responses are one of the first observable signs that an animal is reacting to a stimulus. Whenever possible, species-specific pain scores should be developed that incorporate established normal behaviours and alterations associated with pain (Hampshire & Robertson 2015; Dunbar et al. 2016; Klune et al. 2019; MacRae et al. 2018; McLennan et al. 2019). However, using a consistent generic scale (e.g., 1–10 scale) can also be of great value to evaluate pain and response to therapy (Paul-Murphy & Hawkins 2012).

Pain and its Management in Vertebrate Species

Historically, it was a commonly held belief that mammals had a higher neurological capacity to experience pain compared to nonmammalian species, and that this capacity was directly related to the phylogenetic hierarchy. However, biochemical, anatomical, and physiological studies convincingly show the transmission, mediation, and central processing and modulation of painful stimuli in the lower vertebrates is analogous to that of mammals (Chandroo et al. 2004; Sneddon et al. 2014; Sneddon 2019). Neuroanatomy is largely conserved among vertebrate animals within the peripheral nervous system and central nervous system (Brenner et al. 1994; Chandroo et al. 2004; Butler & Hodos 2005; Sneddon et al. 2014; Sneddon 2019). While mammals, birds, and reptiles have more highly developed specialized sensory cortical regions of thickened grey matter covering the telencephalon known as the neopallium or neocortex, the relative lack of pallial development in amphibians and fish, unfortunately, has formed the basis for biases that the latter do not experience pain but rather only nociception (Striedter 1997). However, fundamental features have been conserved throughout pallial evolution. The less-evolved pallium still can execute similar

physiological functions in fish and amphibians as in higher vertebrates because the neural basis for consciousness involves widespread integration of differentiated neurons in the pallial and subpallial regions of the brain (Echteler & Saidel 1981; Northcutt 1981; Davis & Kassel 1983; Saidel et al. 2001; Wullimann & Rink 2002; Chandroo et al. 2004; Sneddon et al. 2014). Summaries of commonly used analgesics in nonmammalian vertebrates and in mammals are provided in Tables 2.1 and 2.2, respectively.

Fish

Fish nociceptors are physiologically identical to higher vertebrates, responding to mechanical pressure, heat, and noxious chemical stimuli (Sneddon 2004, 2009; Ashley et al. 2007). Of the three major classes of fish, Osteichthyes (bony fishes) have both types of polymodal fibers (Aδ and C fibers), with Aδ fibers being the predominant type (Sneddon et al. 2003a; Chandroo et al. 2004; Ashley et al. 2007; Webber 2011). In Chondrichthyes (elasmobranchs), only Aδ fibers have been identified (Coggeshall et al. 1978; Chandroo et al. 2004) while the Agnatha (hagfishes and lamprey) primarily have C-type fibers (Matthews & Wickelgren 1978).

Fish also show similar organization of their major spinal pathways (spinothalamic tract and trigeminal tract) as in other tetrapods and exhibit analogous biochemical mediation of nociception (Ronan & Northcutt 1990; Sneddon 2011, 2019; Webber 2011). In teleosts, several peptides may transmit and modulate nociceptive signals (e.g., substance P), and the behavioural and autonomic nervous system responses to noxious stimuli are specifically indicative of detection (Ostlund & Von Euler 1956; Weld & Maler 1992; Ide & Hoffmann 2002; Chandroo et al. 2004). Electrical activity during noxious stimulation has been recorded in the forebrain and midbrain of rainbow trout, goldfish, and Atlantic salmon (Dunlop & Laming 2005; Nordgreen et al. 2007), and this electrical activity differed according to stimulus type (e.g., simple touch vs. noxious, potentially painful stimuli). In addition, rainbow trout and carp exposed to noxious stimuli experienced global gene expression changes to their brains, particularly the forebrains, which mirrors the importance of the forebrain in mammalian pain processing (Reilly et al. 2008; Sneddon 2009).

Opioid receptors and endogenous substances (e.g., enkephalin-like) are present in the brain and spinal cord of those fish species studied, and frequently demonstrated a similar distribution pattern to that of higher vertebrates (Buatti & Pasternak 1981; Rosenblum & Callard 1988; Li et al. 1996; Porteros et al. 1999; Alvarez et al. 2006; Sneddon 2009, 2019). Administration of morphine can blunt physiological and behavioural changes associated with noxious stimuli in fish species (Ehrensing et al. 1982; Sneddon 2003, 2019; Nordgreen et al. 2009). COX enzymes have also been identified in a zebrafish (Grosser et al. 2002; Teraoka et al. 2009).

Recognition of Pain in Fish

Current behavioral studies of pain in fish are restricted to a few species (zebrafish, rainbow trout, common carp, koi, and silver catfish) and include three experimental models and one surgical model of pain. Experimental models include subcutaneous (SC) injection of noxious substances such as acetic acid and bee venom, thermonociception, and, more recently, electrical nociception. One study evaluated a surgical model of pain in koi, in which an ethogram was developed for measuring pain-related behaviours (Baker et al. 2013). As fish are one of the most diverse vertebrate groups, there is a definite need for future research to include a wider range of species, different pain measures, and different models of pain. However, these studies have provided further proof that fish have the capacity to detect, conceptualize, and subsequently respond to nociceptive stimuli. There is growing scientific evidence to support the case for fish perceiving and experiencing some of the negative affective aspects of pain. It is clear that a painful stimulus does result in adverse changes in behaviour and physiology which may impair the welfare and well-being of fish (Sneddon 2003; Chandroo et al. 2004; Reilly et al. 2008; Sneddon et al. 2003b; Roques et al. 2010; Correia et al. 2011; Sneddon 2011, 2019; Webber 2011).

The paucity of comprehensive clinical baseline data for the majority of fish species complicates the identification of pain and or distress in fish. Depending on the environment, it may be difficult to observe behavioural changes, especially with secretive species. Most behavioral changes in fish after noxious stimulation occur in the period immediately after the treatment for up to 6 hours, often peaking between 1 and 1.5 hours. Goldfish and trout demonstrate learned avoidance behaviour after exposure to a noxious stimulus (Overmier & Hollis 1990; Ehrenshing et al. 1992; Sneddon et al. 2003b). Clinical signs ascribed to pain in fish are anomalous behaviors such as rubbing the affected area, rocking from side to side with the pectoral fins, decreased activity or swimming behaviour, increased gill ventilation (opercular) rates, decreased feeding behaviour, colour changes, changed postural positions in the water column, increased cortisol levels, and exocytosis of mucous from gill cells. In rainbow trout, the administration of morphine significantly reduced all of the behavioral and physiological changes described above, further demonstrating that they were specifically due to pain (Sneddon et al. 2003b; Chandroo et al. 2004; Reilly et al. 2008; Ashley et al. 2009; Sneddon 2011; Webber 2011).

Table 2.1 Commonly used analgesics in nonmammalian vertebrates.

Analgesic	Avian	Reptiles	Amphibians	Fish
Opioids				
Buprenorphine	0.1 mg/kg IM q6h (American kestrel) (Cuelmans et al. 2014; Gustavsen et al. 2014) 0.25–0.5 mg/kg IM q2–5h (pigeon) (Gaggermeier et al. 2003) 1.8 mg/kg IM q24–48h sustained release formulation (American kestrel, red tailed hawk) (Mazor-Tomas et al. 2014; Gleeson et al. 2018; Sanchez-Migallon Guzman et al. 2017a, 2018a) No evidence of analgesic efficacy in studied psittacines or chickens (Paul-Murphy et al. 2004a; Sanchez-Migallon Guzman et al. 2018)	No evidence of analgesic efficacy	46–100 mg/kg SC, ICe q24h (Stevens 2004; Koeller 2009)	0.1 µg/mL (zebrafish larvae) (Steenbergen et al. 2018) No evidence of analgesic efficacy; prolonged bradypnea and bradycardia (trout) (Mettam et al. 2011; Grans et al. 2014)
Butorphanol	1.0–5.0 mg/kg IM Frequent dosing needed due to short half-life (Paul-Murphy et al. 1999; Hawkins 2006; Klaphake et al. 2006; Sladky et al. 2006; Hawkins & Paul-Murphy 2011; Sanchez-Migallon Guzman et al. 2011; Singh et al. 2018)	1.5–8.0 mg/kg SC, IM UID-BID (Greenacre 2008) Questionable efficacy in some studied species Respiratory depression and profound sedation at >10 mg/kg	25–33 mg/kg SC q8–12 h (Stevens et al. 2011) 0.5 mg/L continuous bath q24h (Koeller 2009)	0.25–0.5 mg/kg IM q24h (Harms et al. 2005; Davis et al. 2006) No clear efficacy after gonadectomy (koi) (Baker et al. 2010) Equivocal data using MS-222 MAC (goldfish) (Ward et al. 2012) No efficacy in studied elasmobranch (dogfish)
Fentanyl	0.02 mg/kg IV (raptors) (Pavez et al. 2011) Fentanyl patch (7.3–11.3 µg/kg/h) (chicken) (Delaski et al. 2016) 5 mg/kg transdermal (helmeted guineafowl) (Waugh et al. 2016)	12 µg/h patch q72h (skinks) (Gamble 2009) 12 µg/h patch (snakes) PK (Kharbush et al. 2017) 0.05 mg/kg SC (slider turtles) (Kaminishi et al. 2019)	0.8 mg/kg SC q24h (Stevens 2004, 2011) 0.5 mg/kg SC (bullfrog) (Van Bonn 2009)	6 µM bath (larval zebrafish) (Curtright et al. 2015)
Hydromorphone	0.1–0.6 mg/kg IM q3–6h (American kestrel) (Sanchez-Migallon Guzman et al. 2013b, 2014) No evidence of analgesic efficacy in studied psittacines (Houck et al. 2018)	0.1–1.0 mg/kg SC, IM q24h (Mans et al. 2011) 0.5–1.0 mg/kg SC q24h (RES, BD) (Hawkins et al. 2019) Watch for sedation and respiratory depression >0.5 mg/kg	No data available	0.25–0.5 mg/kg IM
Morphine	Not recommended	Saurians, Chelonians: 1–5 mg/kg SC, IM, IT q24h (Mauk et al. 1981; Hawkins 2006; Mans et al. 2011) Crocodilians: 0.3 mg/kg q24h (Kanui & Hole 1992) 0.5 mg/kg + lidocaine (4 mg/kg) IT (bearded dragons) (Fink et al. 2022)	114 mg/kg SC q12h (Stevens 2004, 2011) 40–100 mg/kg SC (leopard frogs) (Stevens 2011) 10 mg/kg ICe (Xenopus and leopard frogs) (Coble et al. 2011; Moorea & Jessop 2003)	5–40 mg/kg IM, IP q24–48h (Nordgreen et al. 2009; Newby et al. 2009; Baker et al. 2012) 3–6 mg/kg IM (zebrafish) (Correia 2011) 48 mg/L bath (zebrafish) (Lopez-Luna et al. 2017a,b) Decreased MS-222 MAC (goldfish) (Ward et al. 2014)

Nalbuphine	12.5 mg/kg IM Frequent dosing needed due to short half-life (Sanchez-Migallon Guzman et al. 2011b)	No data available	No data available	No data available
Remifentanil	No data available	No data available	2.8 mg/kg SQ (Mohan & Stevens 2006)	No data available
Tramadol	5 mg/kg IV, 5–30 mg/kg PO (Souza et al. 2009, 2010; Black et al. 2010; Geelan et al. 2013; Kilburn et al. 2014; Bailey et al. 2019; Raisi et al. 2019)	5.0–25 mg/kg PO q48–72h (Greenacre 2008; Baker et al. 2011; Norton et al. 2015)	25 mg/kg PO q24–48h	0.26–2.6 mg/kg IM (Chervova & Lapshin 2000)
NSAIDS				
Aspirin				2.5 mg/L bath (larval zebrafish) (Lopez-Luna et al. 2017a,b)
Carprofen	2.0–4.0 mg/kg SC, IM q12h (Paul-Murphy et al. 2009; Oakes & Meteyer 2012)	2.0–4.0 mg/kg IM q24h (Greenacre 2008)	2.0–4.0 mg/kg IM q24h	2–3 mg/kg IM (Mettam et al. 2010)
Flunixin	3.0–5.5 mg/kg IM Watch for renal lesions and muscle necrosis (Machin et al. 2001; Baert & De Backer 2003)	0.1–2.0 mg/kg SQ, IM q24–48h (Mosely 2011)	25 mg/kg SC q24h (Terril-Robb et al. 1996; Coble et al. 2011)	2–8 mg/L bath (zebrafish) (Deakin et al. 2019) 2.2 mg/kg IM (Nile tilapia) PK (Martin 2021)
Ketoprofen	2.0–5.0 mg/kg IM, PO q8–12h (Graham et al. 2005; Machin et al. 2001; Oaks & Meteyer 2012)	2.0 mg/kg SC, IM >q31h (Greenacre 2008; Tuttle et al. 2006) 2.0 mg/kg IM/IV (PK, loggerhead sea turtles) (Thompson et al. 2018; Harms et al. 2021)	No data available	No evidence of analgesic efficacy
Meloxicam	1–2 mg/kg SC, IM q12–24h 0.5–2 mg/kg PO q12–24h (Baert & De Backer 2003; Wilson et al. 2005; Lacasse et al. 2013; Molter et al. 2013; Lindemann et al. 2016; Zordan et al. 2016; Boonstra et al. 2017; Dhondt et al. 2017; Montesinos et al. 2017; Morrison et al. 2018; Miller et al. 2019; Sartini et al. 2019) Sustained release formulation: 3 mg/kg (Guzman et al. 2017; Sim & Cox 2018)	0.1–0.5 mg/kg SC, IM, PO q24–48h (Greenacre 2008; Divers et al. 2010; Lai et al. 2015) 1.0 mg/kg SC q24h and 2.0 mg/kd SC q48h (PK, sea turtles) (Norton et al. 2021a,b)	0.2–0.3 mg/kg SC, IM q24h (Coble et al. 2011; Minter et al. 2011)	0.2–0.3 mg/kg SC, IM q24–48h
Piroxicam	0.5–0.8 mg/kg PO q12h (Paul-Murphy 2010)	No data available	No data available	No data available
Robenacoxib				2 mg/kg IM (rainbow trout) (Raulic et al. 2021)

(*Continued*)

Table 2.1 (Continued)

Analgesic	Avian	Reptiles	Amphibians	Fish
Local anesthetics				
Bupivicaine	1–5 mg/kg SC, IM	1.0–<2.0 mg/kg SC, IM, IT (Mans et al. 2011) 2.0 mg/kg IT (bearded dragons) (Ferreira et al. 2021)	0.5–2.0 mg/kg SQ, TO	1.0 mg/kg SC, IM
Lidocaine	1–5 mg/kg SC, IM, ED, PN (d'Ovidio et al. 2015; Kazemi-Darabadi et al. 2019)	1–4 mg/kg SC, IM, IT (Mans et al. 2011; Mosley 2011)	1–5 mg/kg SC, TO 50 mg/kg SC (Williams et al. 2017)	1–16 mg/kg SC, IM (Mettam et al. 2011) 5 mg/L bath (zebrafish) (Deakin et al. 2019; Lopez-Luna et al. 2017a,b)
Mepivicaine	No data available	1.0 mg/kg SC (Wellehan et al. 2006)	No data available	No data available
Alpha-2 agonists/other analgesics				
(Dex) Medetomidine	No data available	0.05–0.15 mg/kg SC, IM (Mosley 2011) 0.1 mg/kg SC (ball pythons) (Bunke et al. 2018)	0.6 mg/kg SQ, IM (Stevens 2011) 0.3 mg/100 mL bath (Brenner et al. 1994)	No data available
Gabapentin	11–25 mg/kg PO q8–12h (Donely 2007; Siperstein 2007; Shaver et al. 2009; Yaw et al. 2015; Browning et al. 2018)	No data available	No data available	No data available

Source: Adapted from the literature and the authors' experience.
BD, bearded dragon; ED, epidural; ICe, intracoelomic; IM, intramuscular; IP, intraperitoneal; IT, intrathecal; IV, intravenous; PK, Pharmacokinetic study; PN, perineuronal; PO, per os; RES, red-eared slider turtles; SC, subcutaneous; TO, topical; UID-BID, Once daily-twice daily.

Table 2.2 Commonly used analgesics in mammals.

Analgesic	Carnivores	Primates	Elephants/ Perissodactylids	Artiodactylids	Rodents/Lagomorphs	Marine Mammals	Other Mammals
Opioids							
Buprenorphine	0.01–0.02 mg/kg q6–12h IV, IM, SC (all), PO (felids, viverrids) 0.04 mg/kg SC, IM q4–6h (ferrets) (Kolata 2002; Velguth et al. 2009; Katzenbach et al. 2018)	0.005–0.03 mg/kg IV, IM, SQ q8–12h 0.24–0.72 mg/kg SR SC q48–72h (macaques) (Allison et al. 2007; Nunamaker et al. 2013; Williams & Junge 2014; Mackiewtz et al. 2019)	No data available	0.01–0.03 mg/kg IV, IM q12h (Minter et al. 2010)	0.01–0.05 mg/kg SC, IM, IV, IP q6–12h (rabbits) 0.05 mg/kg SC, q6–12h (guinea pigs) 0.05–0.1 mg/kg SC, IV q4–8h (rodents) 1.2–1.5 mg/kg SR SC q48–72h (rodents) (Wenger 2012; Heard 2014a,b; Balko & Chinnadurai 2017; Flecknell 2019)	1–2 µg/kg (walrus) 9–10 µg/kg (California sea lion) 3–20 µg/kg (northern fur seal) IM, PO q12–24h (Moore et al. 2010)	0.028–0.042 mg/kg SC (sugar gliders) 0.01–0.05 mg/kg IM (edentates, marsupials) (Morges et al. 2009; Holz 2014)
Butorphanol	0.1–0.4 mg/kg IV, IM, SC q2–4h 0.4–1.5 mg/kg q8h PO (Kolata 2002; Velguth et al. 2009; Katzenbach et al. 2018)	0.02–0.15 mg/kg IV, IM, SC q6–12h 0.1–0.4 mg/kg IV, IM, SQ q3–4h (prosimians) (Williams & Junge 2014)	0.015–0.027 mg/kg IV, IM q12–24h (Asian elephants) 0.02–0.05 mg/kg IV, IM (equids) 0.05–0.1 mg/kg PO q12h (rhinoceros) (Abou-Madi et al. 2004; Tana et al. 2010; Kottwitz et al. 2016)	0.1–0.2 mg/kg IM, SC q6–12h 0.02 mg/kg PO q24h (hippopotamus) (Carroll et al. 2001; Howard & Richardson 2005; MacLean et al. 2006; Boothe et al. 2016)	0.1–0.5 mg/kg SC, IM, IV q2h (rabbits) 1–5 mg/kg SC q2h (rodents) (Wenger 2012; Heard 2014a,b; Flecknell 2019)	0.05–0.2 mg/kg PO, IM, IV q6h pinnipeds (Haulena 2014)	0.2–0.5 mg/kg IM, IV (marsupials) 0.2–0.4 mg/kg IM (bats) 0.4 mg/kg q12h (hedgehog) (Wellehan et al. 2001; Lafortune et al. 2004; Done et al. 2007; Clarke & DeVoe 2011; Holz. 2014)
Fentanyl	2–4 µg/kg IV (Spriggs et al. 2007) 2–4 µg/kg/h patch q72h (McNulty et al. 2000) 5–15 µg/kg/h CRI (Spriggs et al. 2007; Schroeder et al. 2010)	5–10 µg/kg/h IV CRI 2–5 µg/kg/h fentanyl patch TO q72h 1.3 mg/kg TO q7d transdermal fentanyl solution (macaques) (Carlson et al. 2016; Salyards et al. 2017)	No data available	1.5–2 µg/kg/h patch q72h (Grubb et al. 2005; Howard & Richardson 2005)	2–4 µg/kg/h patch q72h (rabbits, rodents) (Wenger 2012)	No data available	5 µg/kg IV (koalas) (Holz 2014)

(*Continued*)

Table 2.2 (Continued)

Analgesic	Carnivores	Primates	Elephants/ Perissodactylids	Artiodactylids	Rodents/Lagomorphs	Marine Mammals	Other Mammals
Hydromorphone	0.04–0.2 mg/kg IM, IV, SC q6–12h 0.1 mg/kg IM, SC q1–2h (ferrets) (Spriggs et al. 2007; Katzenbach et al. 2018)	0.02–0.05 mg/kg IM	0.05–0.1 mg/kg IM	0.025–0.1 mg/kg IM	0.05–0.2 mg/kg SC, IM, q8–12h (rodents)	No data available	0.05–0.1 mg/kg IM (bats, marsupials)
Morphine	0.05–0.5 mg/kg IV, IM, ED (McNulty et al. 2000; Mylniczenko et al. 2005)	0.1–2.0 mg/kg IV, IM, SC, ED (Pollock et al. 2008)	No data available	0.24–0.5 mg/kg IV, IM q8–12h (Uhrig et al. 2007; Minter et al. 2010)	2–5 mg/kg IM, SC q3–4h (rabbits) 2–5 mg/kg SC, IM q4h (rodents) (Wenger 2012; Heard 2014a,b; Flecknell 2019)	No data available	No data available
Tramadol	1–5 mg/kg PO, IM q8–24h (Spriggs et al. 2007; McCain et al. 2009)	1–5 mg/kg PO, IM q12–24h (Williams & Junge 2014)	1–3 mg/kg PO q12h (elephants) 0.8–3.0 mg/kg PO q12h (rhinoceros) Poor oral absorption in equids (Kottwitz et al. 2016)	0.48–3 mg/kg PO q1224h (giraffe, hippopotamus) (Boothe et al. 2016)	5 mg/kg q12–24h PO, IM, SC (rodents) 10–20 mg/kg SC (rabbits) (Wenger 2012; Balko & Chinnadurai 2017; Flecknell 2019)	0.8 mg/kg PO (dolphin) 0.5–3.6 mg/kg PO q12–24h (pinnipeds) (Schmitt & Sur 2012; Moore et al. 2010)	4 mg/kg SC (koalas) (Kimble et al. 2021)
NSAIDS							
Carprofen	2–4 mg/kg PO, IM q12–24h Avoid use in felids	2–4 mg/kg PO, SC q12–24h (Allison et al. 2007; Okeson et al. 2010)	Not recommended in elephants 0.78–2 mg/kg PO q24h (rhinoceros) (Kottwitz et al. 2016)	1.9–2.2 mg/kg PO q24h (Dutton et al. 2002; Boothe et al. 2016)	1.5–4 mg/kg PO, SC, IV q12h (rabbits) 4–5 mg/kg SC, IM q6–12h (rodents) (Wenger 2012; Heard 2014a,b; Flecknell 2019)	2.0–4.4 mg/kg PO q24h (pinnipeds) (Walker et al. 2011; Haulena 2014)	1.5–2.0 mg/kg SC, PO q24h (edentates, marsupials) (Holz 2014)
Firocoxib	5 mg/kg PO q24h (canids)	No data available	0.088–0.1 mg/kg PO q24h (elephants, equids, rhinoceros) (Kottwitz et al. 2016)	0.045–0.3 mg/kg PO q24h (giraffe) 0.09–0.11 mg/kg PO q24h (hippopotamus, ruminants) (Boothe et al. 2016)	No data available	No data available	No data available

Flunixin meglumine	0.5–1.5 mg/kg PO, IM, SC q12–24h Avoid use in felids	0.3–2.0 mg/kg IM, SC q12–24h	1.0 mg/kg PO q24h (Asian elephants) 1.2 mg/kg PO q24h (African elephants) (Bechert et al. 2021) 0.5–1.1 mg/kg IV, IM q24h 0.2–1.6 mg/kg PO q24–48h (rhinoceros) 0.2–1.1 mg/kg IM, IV, PO q12–24h (Kottwitz et al. 2016)	0.25–2.2 mg/kg IV, IM, PO q12–24h (ruminants) 0.3–1.3 mg/kg IM, PO q24–48h (hippopotamus) 1.1 mg/kg IM q12–24h (camel) Oukessou 1994; (James et al. 2000; Howard & Richardson 2005; Gyimesi et al. 2008; Borkowski et al. 2009; Minter et al. 2010; Gyimesi et al. 2011)	1–2 mg/kg SC, IM q12h (rabbits) 0.5–2.5 mg/kg SC, IM q12h (rodents) (Wenger 2012; Heard 2014a,b)	1 mg/kg IM q24h (Haulena 2014)	0.25–1.0 mg/kg SC, IM, q12–24h (Holz 2014)
Ibuprofen	Not recommended in carnivores	2–10 mg/kg PO q6–12h (Wellehan et al. 2004; Bronson et al. 2005; Williams & Junge 2014)	6 mg/kg PO q12h (Asian elephants) 7 mg/kg PO q12h (African elephants) 1–1.8 mg/kg PO q12h (rhinoceros) (Bertelsen et al. 2004; Bechert & Christensen 2007; Kottwitz et al. 2016)	4 mg/kg PO q24h (giraffe) (Boothe et al, 2016)	No data available	No data available	No data available
Ketoprofen	0.5–2.2 mg/kg IM, SC, PO q24h (Mylniczenko et al. 2005; Pye et al. 2010)	1–5 mg/kg PO, IM, SC q24h 1–2 mg/kg IV, IM, SQ, PO q24h (prosimians) (Wellehan et al. 2004; Bronson et al. 2005; Williams & Junge 2014)	1–2 mg/kg IV, IM, PO q24h (elephants, equids) 0.5 mg/kg IV, PO q12–24h (rhinoceros) (Wack et al. 2010; Kottwitz et al. 2016)	0.5–3 mg/kg IV, IM, PO q24h (giraffe) 0.8–2.17 mg/kg IM, PO q24h (hippopotamus) 1–4 mg/kg IM, SC q24h (ruminants) (Dutton et al. 2002; Howard & Richardson 2005; Gyimesi et al. 2008, 2011; Boothe et al. 2016)	2–3 mg/kg SC, IM q12h (rabbits) 1–3 mg/kg SC, IM q12h (rodents) (Heard 2014a,b)	1–1.2 mg/kg IM, PO q24h (pinnipeds) (Dennison et al. 2007; Rush et al. 2012; Haulena 2014)	1.0 mg/kg IM (macropods)

(*Continued*)

Table 2.2 (Continued)

Analgesic	Carnivores	Primates	Elephants/ Perissodactylids	Artiodactylids	Rodents/Lagomorphs	Marine Mammals	Other Mammals
Meloxicam	0.2 mg/kg loading dose, then 0.1–0.2 mg/kg SC, PO q24h (non-felids) 0.2 mg/kg loading dose then 0.025–0.1 mg/kg q24–48h (felids) (Whiteside & Black 2004; Whiteside et al. 2006; McCain et al. 2009; Pye et al. 2010)	0.1–0.2 mg/kg SC, PO, IV q24h (Pollock et al. 2008; Chai et al. 2009; Okeson et al. 2010; Williams & Junge 2014)	0.2–0.3 mg/kg PO q24h (elephants, rhinoceros) 0.3–0.5 mg/kg SC, IM, PO q24h (equids) (Kottwitz et al. 2016)	0.2–0.6 mg/kg IM, PO (giraffes) 0.1–0.15 mg/kg IM, SC, PO q24h (hippopotamus) 0.25–0.5 mg/kg SC, PO q24h (ruminants) (Boothe et al. 2016)	0.5–2.0 mg/kg q12–24h SC, PO (rodents) 0.4–0.6 mg/kg q24h PO, SC, IM (rabbits) (Carpenter et al. 2009; Wenger 2012; Heard 2014a,b)	0.1 mg/kg PO, SC q24h (pinnepeds) (Rush et al. 2012)	0.1–0.2 mg/kg SC, PO q24h (marsupials, most mammals) 0.2–0.5 mg/kg SC, PO q12–24h (bats) (Whiteside & Black 2006; Pye et al. 2008; Okeson et al. 2009; Clarke & DeVoe 2011; Holz 2014; Goodnight & Cox 2018)
Phenylbutazone	Not recommended	Not recommended	3 mg/kg PO q48h (Asian elephants) 2 mg/kg PO q24h (African elephants) 2.5–310 mg/kg PO q24–48h (rhinoceros) 2.2–4.4 mg/kg PO) q12–24h (equids) (Bechert et al. 2008; Harrison et al. 2011; Kottwitz et al. 2016)	1–6 mg/kg PO q24–48h (Kadir et al. 1997; James et al. 2000; Larsen et al. 2000; Howard & Richardson 2005; Boothe et al. 2016)	No data available	No data available	No data available
Local anesthetics							
Bupivicaine	0.25–2.0 mg/kg SC, IM (Schroeder et al. 2010) Do not exceed 1.5 mg/kg	Do not exceed 1.5 mg/kg	Do not exceed 1.5 mg/kg	Do not exceed 1.5 mg/kg	0.5–1.0 mg/kg SC, IM (Dadone et al. 2011)	Do not exceed 1.5 mg/kg	Do not exceed 1.5 mg/kg
Lidocaine	Do not exceed 4 mg/kg	0.5–2.0 mg/kg SQ	Do not exceed 4 mg/kg	Do not exceed 4 mg/kg	Do not exceed 4 mg/kg	Do not exceed 4 mg/kg	1.8–3.7 mg/kg SC (sugar gliders) (Morges et al. 2009)

Alpha-2 agonists/other analgesics							
Medetomidine	No data available	No data available	0.01–0.02 mg/kg IM (equids)	No data available	No data available	0.01–0.04 mg/kg IM (pinnipeds) (Moore et al. 2010; Haulena 2014)	No data available
Gabapentin	2–5 mg/kg PO q12h (Adkesson 2006)	4–5 mg/kg PO q12h (Adkesson 2006)	0.4–6 mg/kg PO q12–24h (elephants) 2.5–5 mg/kg PO q24h (rhinoceros) 2.5 mg/kg PO q12h (equids) (Bronson et al. 2008; Kottwitz et al. 2016)	0.2–1.6 mg/kg PO q12h (giraffe) 1.5 mg/kg PO q12h (hippopotamus) (Boothe et al. 2016)	5–15 mg/kg PO q12h	1.1 mg/kg PO q12h (walrus) 2.3–7.4 mg/kg PO q12h (California sea lion) 4.3–12.0 mg/kg PO q12h (northern fur seal) 4.5–8.2 mg/kg PO q12h (sea otter) (Moore et al. 2010)	No data available

Source: Adapted from the literature and the authors' experience.
CRI, Constant Rate Infusion; ED, epidural; IM, intramuscular; IP, intraperitoneal; IV, intravenous; PO, per os; TO, topical; SC, subcutaneous; h, hours(s); SR, sustained release.

Analgesia in Fish

Although empirical usage of analgesics in fish has become more widespread in a captive setting, its use in a field setting has been minimal where invasive surgeries such as implantation of intracoelomic electronic transmitters occurs (Harms & Lewbart 2011). The lack of approved analgesics for fish further complicates treatment. There are relatively few studies of analgesic use in fish, and varying results highlight the challenge of extrapolating findings between species.

Sladky et al (2001) demonstrated that red pacu (*Piaractus brachypomus)* anesthetized with eugenol, the active ingredient in clove oil and an effective studied anesthetic in numerous fish species, did not blunt the responses to a noxious stimulus compared to tricaine methanesulfonate (MS-222). In zebrafish injected with acetic acid in the face, low concentrations of eugenol had no effect on pain-associated behavior (Baldisserotto et al. 2018). No other published studies have demonstrated an analgesic effect of eugenol in fish. This is particularly concerning with the worldwide use of isoeugenol for fish anesthesia, including invasive surgical procedures, which likely provides no analgesic properties. Alpha-2 agonists, such as medetomidine, induce sedation in those fish species studied but analgesic activity has not been demonstrated (Neiffer & Stamper 2009). Local anesthetics such as lidocaine and benzocaine have been used for immersion anesthesia and for local effects anecdotally, but have not been well studied in a research setting. Mettam et al. (2011) demonstrated that local infiltration of lidocaine (6.25–16 mg/kg) was the most effective analgesic compared with buprenorphine and carprofen in trout being injected with noxious acetic acid. Using a caudal fin forceps pinch to induce a painful stimulus in adult zebrafish, a combination of lidocaine (100 μg/mL) + propofol (1.25 μg/mL) administered as a bath solution was as effective as MS-222 for reducing a movement response to the pinch (Martins et al. 2018). In larval zebrafish, lidocaine (5 mg/L) administered as a bath decreased behavioral changes induced by acetic acid added to the water of the fish (Lopez-Luna et al. 2017a).

Parenteral morphine, a μ receptor agonist, has been demonstrated to be effective in ameliorating the adverse physiological or behavioural reactions to noxious stimuli in goldfish, winter flounder (*Pseudopleuronectes americanus*), and trout, and to pain from gonadectomy in koi (*Cyprinus carpio*) (Sneddon 2003; Newby et al. 2007, 2009; Baker et al. 2013). Morphine also reduced the minimum inhibitory concentration (MAC) of MS-222 in goldfish that was deemed necessary to attenuate a response to an intramuscular (IM) needle insertion in goldfish, therefore suggesting morphine may have analgesic properties (Ward et al. 2012). In adult zebrafish, morphine administered 30 minutes prior to acetic acid injections into the lips attenuated the decreased activity observed in control fish receiving saline; naloxone eliminated this response (Correia et al. 2011). Morphine (48 mg/L) administered as a bath decreased behavioral changes after exposure to acetic acid and hot water baths in larval zebrafish, but had no effect on the fish when exposed to a cold-water bath (Lopez-Luna et al. 2017a,b). This suggests that the type of experimental model plays a role in how and when fish species will respond to specific noxious stimuli. Conversely, morphine was found to be ineffective at studied doses (40 and 50 mg/kg) in goldfish in thermonociception experiments (Nordgreen et al. 2009), supporting the idea that the type of noxious stimulus may be important in determining the efficacy of an analgesic in fish. Morphine has also been shown to have potential deleterious consequences in fish species. In winter flounder, morphine administration was associated with a marked bradycardia and reduction in cardiac output initially, followed by a significant increase in heart rate for 48 hours compared to controls (Newby et al. 2007). The elimination half-life of morphine in studied fish species is several fold longer that in mammals, ranging from 12.5 to 37 hours, and may be associated with water temperature (Nordgreen et al. 2009). Morphine elimination after IM administration appears to be species-specific, as rainbow trout eliminated morphine faster than winter flounder (Newby et al. 2007). However, morphine administered via the water had extremely slow uptake in goldfish (Newby et al. 2009).

Butorphanol (0.4 mg/kg IM), a κ-opioid receptor agonist, but not ketoprofen (NSAID) was effective at reducing postsurgical pain-related behavioural changes in koi, although ketoprofen reduced postsurgical muscle damage (Harms et al. 2005). At higher doses butorphanol (10 mg/kg) provided antinociceptive activity in koi undergoing gonadectomy but was associated with respiratory depression and abnormal buoyancy (Baker et al. 2013). However even at higher doses, neither drug was effective in an elasmobranch, the chain dogfish (*Scyliorhinus rotifer*), for reducing minimum anesthetic concentrations (Davis et al. 2006). In a (MAC) study using goldfish as subjects, a low dose of butorphanol decreased the MAC of MS-222, but a higher dose increased the MAC of MS-222, making interpretation of analgesic properties unclear (Ward et al. 2012).

Other opioid or opioid-like drugs, buprenorphine (partial μ agonist), and tramadol (μ-opioid properties), also have been studied in fish. IM buprenorphine did not provide evidence of analgesia in rainbow trout subjected to SC acetic acid injections (Mettam et al. 2011). However, in zebrafish larvae, bath-administered buprenorphine prevented stimulus-induced responses to noxious stimuli (e.g., electrical, thermal, and SC acetic acid administration), and

these responses were eliminated when bath naloxone was administered prior to the buprenorphine (Steebergen 2018; Curtright et al. 2015). Buprenorphine administered intramuscularly to rainbow trout caused significant and prolonged bradycardia and bradypnea that lasted 4–5 days post-administration (Grans et al. 2014). Tramadol administered intramuscularly in common carp induced a prolonged (greater than 2 hours) dose-dependent analgesic response to a noxious electrical stimulus, while still maintaining normal swimming and other behaviours (Chervova & Lapshin 2000). However, in a study using zebrafish, tramadol (25 μg/fish IM) caused hyperactivity and tachypnea, and at 50 μg/fish caused 100% mortality (Zhao et al. 2016). These conflicting data may be due to species or dose-response differences.

Fentanyl, a synthetic μ-opioid agonist that is approximately 80–100 times the potency of morphine, attenuated nocifensive behavioral reactions to formalin added to water (6 μM bath) in larval zebrafish, but also caused respiratory depression (Zaig et al. 2021). The μ-opioid antagonist naloxone reversed these behaviors, and so these data corroborate the morphine data that μ-opioid receptor agonists are a logical choice when considering opioid analgesic drugs in fish.

There are very few data in the literature with respect to nonsteroidal analgesic efficacy or anti-inflammatory activity in fish species, primarily because efficacy is difficult to measure. Aspirin (2.5 mg/L) prevented the hypoactivity associated with exposure to 0.1% or higher acetic acid in zebrafish (Lopes-Luna et al. 2017). Ketoprofen was demonstrated to reduce the MAC of MS-222 in goldfish (Ward et al. 2012). Carprofen administered to rainbow trout appeared to normalize behavior (increase activity and decrease respiratory rate) after acetic acid was administered subcutaneously, but decreased activity was observed at a high dose (Mettam et al. 2011). Meloxicam has not been systematically studied as an analgesic in fish species but is eliminated more rapidly in Nile tilapia compared to mammals when administered both intramuscularly and intravenously (Fredholm et al. 2016). Nevertheless, in clinical practice, meloxicam is administered empirically at doses of 0.2–0.3 mg/kg as an analgesic and anti-inflammatory drug. Flunixin meglumine (2.2 mg/kg IM) administered to Nile tilapia achieved relatively high plasma concentrations by 12 hours post drug administration and remained detectable for 96 hours, although concentrations were below clinically relevant plasma concentrations (compared to mammals) by 24 hours post administration (Martin 2021). These data compare favorably to an efficacy study in which the avoidance behavior of female zebrafish subjected to a fin clip was unchanged after exposure to bath flunixin meglumine at multiple concentrations (2, 4, and 8 mg/L) (Deakin et al. 2019). More recently, using a different NSAID, robenacoxib (2 mg/kg IM) was shown to be antinociceptive in rainbow trout after acetic acid lip injections, and the clinically relevant plasma concentrations (compared to mammals) lasted up to 3 days after a single IM dose (Raulic et al. 2021). More NSAID efficacy and PK studies are needed across a variety of fish species, since NSAID use is a staple of clinical veterinary medicine.

A few other classes of drugs have been evaluated as analgesics in zebrafish using a thermal nociceptive model in which fish are exposed to either cold or hot water, with and without the drug, and their behavior measured. Both clonidine (an alpha-2 adrenergic agonist) and amitriptyline (a tricyclic antidepressant and used for neuropathic pain) diminished the behavioral response to thermal noxious stimuli, but gabapentin did not (Curtright et al. 2015). Using an different alpha-2 adrenergic agonist in goldfish, medetomidine (0.025 mg/kg IM), had a minimal effect on decreasing the MAC of MS-222, suggesting a possible, yet negligible, analgesic effect (Ward et al. 2012).

Amphibians

Amphibian nociceptive afferents are analogous to the primary afferents of other vertebrates, including mammals, with both lightly and heavily myelinated (Aβ and Aδ, respectively) and unmyelinated (C) afferent fibers found in mixed-fiber peripheral sensory nerves (Stevens 2004, 2011). The majority of all impulses induced by noxious stimuli such as pinching, pin pricks, and heat are conducted by slowly conducting C fibers, while epidermal application of dilute acetic acid evoked Aδ and C fibers to a relatively equal extent (Maruhashi et al. 1952; Hamamoto & Simone 2003). Sensory afferents terminate in the dorsal horn of the spinal cord and, similar to mammals, pain-signaling neurotransmitters such as substance P, glutamate, and calcitonin have been identified (Inagaki et al. 1981; Lorez & Kemali 1981). Amphibian studies have demonstrated responsiveness to alpha-2 agonists and to local anesthetics. In addition, met-enkepahalin and four types of opioid receptor (μ, κ, δ, and ORL-1) are abundant in the amphibian spinal cord and brain but exhibit less selective binding compared with mammals (Newman et al. 2002; Stevens 2004; Walthers et al. 2005; Bradford et al. 2005). There have only been a few studies that evaluated opioid receptor density in amphibians, with μ receptors being more abundant than κ receptors in leopard frogs (*Lithobates pipiens*), but the reverse was found in marine toads (*Bufo marinus*) (Brooks et al. 1994; Newman et al. 2002). Further research is required to elucidate opioid receptor densities in other amphibian species.

Although the spinal ascending nociceptive pathways in amphibians are not clearly defined, a single study in frogs

identified that electrical stimulation of the sciatic nerve traveled through the spinal ascending pathways and produced evoked potentials in the thalamus and primordial hippocampus (Vesselkin et al. 1971; Munoz et al. 1997). Thalamocortical projections in anurans are more diffuse and less organized than in mammals, but terminate in the nonolfactory telencephalon as with other vertebrates. Similar to fish, there is minimal cerebral or limbic cortical pallial development, but it is likely that other neural pathways have developed for the perception of pain (Stevens 2004, 2011).

Recognition of Pain in Amphibians

The acetic acid test has been used for decades to assess amphibian nociception, with application of varying diluted concentrations to the hind limb and monitoring for a wipe response by the fore limb (Pezalla 1983; Coble et al. 2011; Stevens 2011). The primary problem associated with the acetic acid test is that it causes inflammation, in addition to being a noxious nociceptive chemical, which is a confounding factor in attempts to discriminate only nociception. Based on this test, dermal exposure to other noxious stimuli is likely to elicit a similar response. More recently the Hargreaves test has been validated to evaluate thermonociception, where heat is applied to the inner thigh of the frog in a specialized apparatus and the frog is monitored for withdrawal movement of the hind limb (Coble et al. 2011). Recently, this model was applied to African clawed frogs (*Xenopus laevis*) after surgical laparotomy, but the author concluded that the frog subjects, with or without MS-222 anesthesia, did not consistently respond to the thermal noxious stimulus (Vachon 2014). In a different study, the thermal noxious stimulus withdrawal model was used in comparison with the acetic acid wipe test in *Xenopus laevis*, and the authors found the acetic acid test caused significant skin lesions, while the thermal latency test was useful for testing analgesic and anti-inflammatory drugs (Coble et al. 2011). One of the current author's laboratories (K.K.S.) recently determined that White's tree frogs and leopard frogs consistently respond to a thermal noxious stimulus applied to the hind limb, but there was wide variability in the temporal latency for the responses (Sladky 2019).

Physiologic changes have been used to quantify stress and pain in amphibians (Moorea & Jessop 2003). In a comparative anesthesia/analgesia study using Oriental fire-bellied toads (*Bombina orientalis*), heart and respiratory rates were depressed in toads immersed in alfaxalone-butorphanol, but the same toads immersed in alfaxalone-morphine had normal heart rates and depressed respiratory rates (Adami et al. 2016). In Indian bullfrogs (*Rana tigrina*), the number of eye blinks and the gular respiration rate were used to measure pain associated with intracoelomic administration of concentrated saline (Pathak et al. 2014). Changes in these two behaviors were quantified following administration of NSAIDS to determine analgesic efficacy. Piroxicam, diclofenac sodium, and ketoprofen decreased the number of eye blinks, but there were no statistically significant differences compared with saline controls.

Several behavioural parameters have been clinically associated with pain in amphibians, including decreased activity and feeding behaviour, colour changes, increased reclusive behaviours, and postural changes. Painful amphibians also may spend more time in atypical locations (Duncan 2012). Koeller (2009) demonstrated that Eastern red-spotted newts (*Notophthalmus viridescens*) undergoing bilateral forelimb amputation did not eat for 72 hours post surgery without analgesics, while feeding resumed within 24 hours in those newts receiving intracoelomic buprenorphine or immersion bath butorphanol. In addition, the newts that received no analgesics did not move in response to tapping on the aquarium glass until 72 hours post surgery, while those receiving an analgesic moved at the first postsurgical test point at 24 hours. Finally, abnormal postures in nontreated newts were observed for 72 hours post surgery, while eight out of 10 newts treated with buprenorphine or butorphanol had resumed normal postures within 4 hours and 10 out of 10 by 24 hours post surgery.

Analgesia in Amphibians

Numerous analgesics have been studied in a research setting in amphibians for brief noxious stimuli, but very little data exist for analgesic use in a clinical setting for pain. The most effective studied analgesics to date in amphibians are the opioids followed by the alpha-2 agonists, particularly dexmedetomidine. Although the μ agonist opioids demonstrate more effectiveness compared with κ agonists, owing to the decreased selective binding of the opioid receptors, both appear suitable for use in amphibians. Amphibians require higher doses of opioids compared with mammals, but the analgesic effect of the opioid also lasts longer (Benyhe et al. 1990; Stevens 2004, 2011; Koeller 2009). In Oriental fire-bellied toads, an antinociceptive response was elicited to a noxious mechanical stimulus when toads were sedated with alfaxalone and morphine in an immersion bath (Adami et al. 2016). Using multiple experimental models, including the acetic acid wipe test, the thermal noxious withdrawal stimulus test, and a mechanical noxious stimulus test (von Frey filaments model of nociception), morphine, at very high doses, was antinociceptive in Northern leopard frogs (*Rana pipiens*) across all nociceptive models (Willenbring & Stevens 1996). An analog of oxymorphone, oxymorphazone, a μ-opioid agonist, was demonstrated to be a relatively weak analgesic drug, even

at 200 mg/kg, when subcutaneously administered to edible frogs (*Rana esculenta*, now *Pelophylax esculentus*) and subjected to the acetic acid wipe test, but had an approximately 48-hour duration of effect (Benyhe et al. 1990). In Northern leopard frogs, fentanyl and remifentanil were determined to be antinociceptive in frogs after either SC or intraspinal administration using the acetic acid wipe test (Stevens 2004). Using fentanyl in a clinical situation, Van Bonn (2009) administered a presurgical dose (0.5 mg/kg) into the dorsal lymph sac of an American bullfrog during an extra-articular surgical stifle stabilization, and the frog recovered normally and returned to normal behavior immediately post surgery. Using intracoelomic buprenorphine, Eastern red-spotted newts (*Notophthalmus viridescens*) subjected to limb amputation surgery displayed more normal postoperative behavior (e.g., feeding, body posture, and response to observer) compared to saline controls (Koeller 2009). However, in axolotls, buprenorphine administered either intracoelomically or as an immersion bath did not provide analgesia after animals were subjected to the acetic acid test or a von Frey mechanical noxious stimulus (Llaniguez et al. 2020).

In a single study, the antinociceptive effects of tramadol were studied in White's tree frogs and Northern leopard frogs using a thermal noxious stimulus, but there were no significant differences in hindlimb withdrawal latencies after administration to either species at any of three tramadol doses (15, 25, and 40 mg/kg per os [PO]) (Hausmann et al. 2021). From a clinical perspective, one current author (D.W.) has used tramadol orally in aged marine toads with arthropathies (25 mg/kg PO every 48 hours) with positive clinical results. Further evaluation of tramadol use in amphibians is needed.

Other parenteral anesthetics have been studied in amphibians. Intraspinal dexmedetomidine, an alpha-2 receptor agonist, administered to Northern grass frogs (*Rana pipiens*) caused a dose-dependent increase in pain thresholds using the acetic acid wipe test (Stevens & Brenner 1996). In a similar study using the acetic acid wipe test in Northern grass frogs (*Rana pipiens*), systemic administration of dexmedetomidine was analgesic compared to other alpha-adrenergic agonists (Brenner et al. 1994). Similarly, a thermal noxious withdrawal stimulus test and a mechanical noxious stimulus test applied to Northern leopard frogs (*Lithobates pipiens*) showed that dexmedetomidine was antinociceptive after exposure to the acetic acid and thermal noxious stimuli, but not after exposure to the von Frey filaments (Willenbring & Stevens 1996).

Of the few studied NSAIDs in amphibians, flunixin meglumine (25 mg/kg SC) has been the most effective for decreasing responsiveness to cutaneous noxious stimulation (Terril-Robb et al. 1996; Coble et al. 2011). In African clawed frogs, flunixin meglumine (25 mg/kg) administered in the dorsal lymph sac may have contributed to analgesia-related behavior using the acetic acid test, but exposure to 50 mg/kg caused death in five of 12 frogs (Smith et al. 2018). Minter et al. (2011) demonstrated that the systemic administration of meloxicam at a dosage of 0.1 mg/kg once daily decreases the circulating serum prostaglandin E2 levels in North American bullfrogs (*Rana catesbeiana)* measured 24 hours after the induction of the inflammatory cascade through surgical muscle biopsies. Meloxicam (0.2 mg/kg SC) in African clawed frogs (*Xenopus laevis*) demonstrated a very mild analgesic effect against cutaneous noxious stimuli (Coble et al. 2011). It is quite probable that for analgesic effects, the dose needs to be increased, especially when compared to the flunixin dose, which is approximately 20–25-fold higher than in mammals. One current author (D.W.) has observed anti-inflammatory effects of meloxicam when administered parenterally (0.2–0.3 mg/kg) in frogs with cutaneous ulcers. Further research is needed to assess the clinical efficacy, PKs, and toxicity of NSAID use in amphibians.

Local anesthetics should be used judiciously in amphibians due to potential systemic toxicity associated with dermal absorption, but they can be very effective when local analgesia is required (e.g., microchip implantation, distal digital amputation). Topical applications of lidocaine, benzocaine, or a prilocaine-lidocaine (EMLA®) have all been used anecdotally for their local effects (Fig. 2.2). However, in one study that evaluated benzocaine and prilocaine-lidocaine as potential topical agents to induce anesthesia in leopard frogs, the latter was associated with 41.7% mortality at a dose greater than 5 mg/kg (Guenette & Lair 2006). There is recent evidence in amphibians that lidocaine will

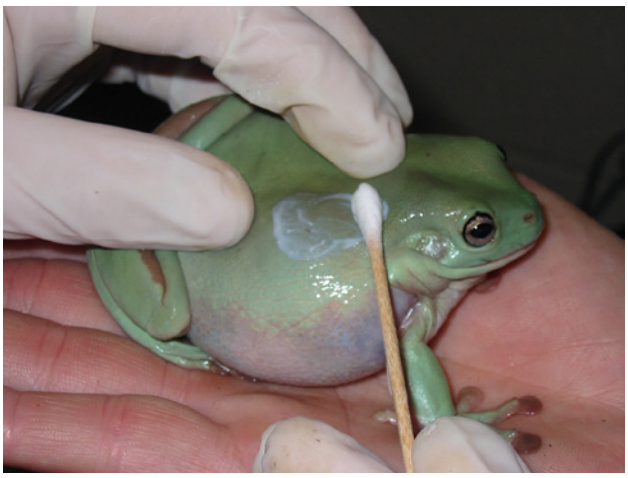


Figure 2.2 Topical application of a local anesthetic cream (lidocaine/prilocaine) in a White's tree frog (*Litoria caerulea*) prior to microchipping.

have systemic effects at very high doses (Williams et al. 2017). In bullfrogs (*Lithobates catesbeianus*), lidocaine (50 mg/kg), administered subcutaneously, caused a significant decrease in respiratory rate, a progressive loss of righting and palpebral reflexes, and contralateral toe pinch withdrawal. However, these systemic effects were not associated with local analgesia and frogs reacted to a forceps pinch at the site of the lidocaine injection at the time of maximal systemic effects (Williams et al. 2017).

Reptiles

Similar to mammals and birds, reptiles possess the appropriate neuroanatomical components for nociception with well-developed antinociceptive mechanisms. Aδ nociceptors have been isolated in the oral mucosa and facial skin of snakes, which are similar to those in primates, and the arrangement of the spinal cord in reptiles is similar to that in mammals. Spinal projections between the brainstem and the superficial layers of the dorsal horn have been identified in Tokay gecko lizards (*Gekko gecko*) and are analogous to those in mammals that promote spinal inhibition. In addition, neurotransmitters responsible for nociceptive modulation in other vertebrates have been identified in reptiles, and nociception can be modulated with analgesics used in other taxa. Opioid receptors are present throughout the central nervous system, although the efficacy of opioid agonists may vary between species. Cyclooxygenase enzymes can be inhibited by the use of NSAIDs in reptiles (Ng et al. 1986; Reiner 1987; ten Donkelaar & de Boer-van 1987; Kanui et al. 1990; Kanui & Hole 1992; Liang & Terashima 1993; Schaefffer & Waters 1996; Seebacher & Franklin 2003; Sladky et al. 2007, 2008, 2009; Mosley 2011; Sladky & Mans 2012).

Recognition of Pain in Reptiles

An objective understanding of the normal behavior of a particular species, and the ability to differentiate the presence of abnormal behavior indicative of discomfort, are critical to the understanding of pain and analgesia. Methods for assessing and measuring pain in reptiles have been described previously (Sladky & Mans 2014). Ideally, a combination of appropriate behavioral and physiologic parameters might best be employed to measure pain and analgesia in reptiles. Clinical experience and research demonstrate that reptiles display a number of behaviours that are consistent with pain in mammalian species, including decreased activity levels and appetite, immobility, guarding of painful limbs or regions, changes to ambulation patterns, exaggerated withdrawal, escape or avoidance responses, attempts to bite, closed eyes, colour changes, abnormal posture, and elevated heart and respiratory rates (Kanui & Hole 1992; Stoskopf 1994; Eatwell 2010; Mosley 2011; Duncan 2012; Sladky & Mans 2014). Tortoises can accurately locate a tactile stimulus applied to the shell and respond by rubbing at the stimulated area with a foot (Stein & Grossman 1980; Rosenberg 1986). However, it is important to realize that some reptiles may suppress some pain-related behaviours when an observer is present (Fleming & Roberston 2006). The development of a species- and context-specific ethogram for each species being evaluated would provide the best method for distinguishing normal versus abnormal (e.g., painful) behaviours, and should be the standard for any clinical study.

Analgesia in Reptiles

In general, the opioids have been the most studied analgesic drugs in reptile species. Morphine sulfate, a μ-opioid agonist, has been shown to be an effective analgesic in reptiles (Sladky & Mans 2014). In the anole lizard (*Anolis carolinensis*), intraperitoneally administered morphine at 5 mg/kg slowed the tail-flick response to a noxious stimulus (Mauk et al. 1981). Green iguanas (*Iguana iguana*) demonstrated significantly reduced tail movement after an electrical stimulation when IM morphine (1 mg/kg) was administered (Hawkins 2006), while crocodiles developed significant latencies in response to painful stimuli with maximal effect at 0.3 mg/kg (Kanui & Hole 1992). Morphine also has clear analgesic effects in red-eared sliders (*Trachemys scripta*) and bearded dragons (*Pogona vitticeps*), but profound long-lasting respiratory depression was observed in the turtles at higher doses. When morphine was administered intrathecally (0.1–0.2 mg/kg) to red-eared slider turtles, it resulted in thermal antinociception of the hind limbs for up to 48 hours (Mans et al. 2011). Morphine at studied doses was not found to be effective in corn snakes (*Elaphe guttata*) (Sladky et al. 2008). Morphine and pethidine, a synthetic, short-acting μ-opioid agonist, provided analgesia in Speke's hinged tortoises (*Kinixys spekii*) exposed to formalin administered into a limb, which was reversible after naloxone administration (Wambugu et al. 2010). The duration of action may vary considerable between species, and the onset of action of morphine may be delayed for 2–8 hours after administration (Sladky et al. 2007, 2008). Related to morphine, hydromorphone is a semisynthetic, μ-opioid receptor agonist, which was demonstrated to be provide analgesia in red-eared sliders using the thermal hindlimb withdrawal nociception model at 0.5 mg/kg SC for up to 24 hours (Mans et al. 2012). Hydromorphone plasma concentrations were considered analgesic for 12–24 hours after bearded dragons and red-eared slider turtles were administered either 0.5 or 1.0 mg/kg (Hawkins et al. 2019). Respiratory depression is a side effect at higher doses.

Fentanyl is a synthetic, μ-opioid receptor agonist, with 75–100 times the potency of morphine, which can be administered either transcutaneously as an impregnated patch, subcutaneously, intramuscularly or intravenously. In reptiles, two separate studies have evaluated the PKs of fentanyl in two reptile species. In ball pythons, fentanyl plasma concentrations reached 1 ng/mL within 4 hours of application of a transdermal fentanyl patch (12.5 μg/h) (Kharbush et al. 2017) and were detectable by 4–6 hours, and for more than 72 hours, in the plasma of prehensile-tailed skinks (fentanyl dose was applied at 10% exposure of a total surface area of a 25 μg/h patch for 72 hours) (Gamble 2009). It remains unclear whether there is any biological significance to these plasma fentanyl concentrations. A recently completed study in one current author's (K.K.S.) laboratory evaluated the efficacy of transdermal fentanyl patch (12.5 μg/h) administration in ball pythons and found no analgesic efficacy, even after repeating the study. At the same time it was confirmed that fentanyl was readily absorbed through the skin of the snakes and remained at very high plasma levels during patch application. Fentanyl patch application decreased respiration in the same snakes, indicating that fentanyl is biologically active in the snakes, even though analgesic efficacy cannot be determined using current laboratory methods (Kharbush et al. 2017). Further evaluation of fentanyl analgesic efficacy using a surgical model in several snake species is underway.

Although butorphanol has been used frequently as an analgesic with variable clinical results, few studies support its analgesic properties in reptiles. In red-eared slider turtles and bearded dragons it did not yield significant antinociceptive effects (Sladky et al. 2007, 2008). However, in snakes at higher doses (20 mg/kg) it did result in thermal antinociception, but the authors suggested using caution (Sladky et al. 2008). Olesen et al. (2008) demonstrated that butorphanol (5 mg/kg IM) did not have analgesic properties in ball pythons (*Python regius)* and had no effect on physiologic parameters compared to salin. In green iguanas, butorphanol (1 mg/kg) did not have an isoflurane sparing effect on minimum alveolar concentrations (Mosley et al. 2003), but analgesia was observed at doses between 1.5 and 8.0 mg/kg in electrostimulation experiments (Greenacre et al. 2006).

Buprenorphine is an effective analgesic in many mammalian species and is used extensively due to its longer duration of action compared to other opioids. However, there is no published evidence that buprenorphine has analgesic activity in studied reptiles (red-eared slider turtles or green iguanas), but does cause profound respiratory depression red-eared slider turtles (Greenacre et al. 2006; Sladky & Mans 2012).

Tramadol has become a widely used analgesic alternative to other opioids in veterinary medicine because it can be administered orally and has a relatively long duration of action. Tramadol and its major active metabolite, O-desmethyl-tramadol (M1), produce analgesia in mammals by activating μ-opioid receptors, but also by inhibiting central serotonin and norepinephrine reuptake. In bearded dragons, a significant analgesic effect was observed in electrostimulation experiments at 11 mg/kg (Greenacre et al. 2008). Long-lasting analgesia (up to 96 hours) was observed after oral and SC tramadol administration (10–25 mg/kg) in red-eared sliders, but a significant decrease in ventilation rates was observed and at the highest dose sedation with flaccid neck and limbs was observed (Baker et al. 2011). Doses of 5 mg/kg did not suppress ventilation and provided analgesia for at least 24 hours (Baker et al. 2011). Recently, tramadol PKs and efficacy were evaluated in yellow-bellied slider turtles (*Trachemys scripta scripta*) after a single IM dose (10 mg/kg) administered in either the hind limb or fore limb (Giorgi et al. 2015a). Using a thermal hindlimb withdrawal latency test, antinociceptive efficacy appeared to last approximately 48 hours regardless of whether the tramadol was administered in the fore limb or hind limb, and tramadol and O-desmethyl-tramadol remained above a high target plasma concentration for approximately 48 hours. In loggerhead turtles (*Caretta caretta*), plasma concentrations of tramadol and O-desmethyl-tramadol remained above the target concentration for analgesia for approximately 48 hours at a dose of 5 mg/kg PO and for 72 hours when tramadol was administered at 10 mg/kg PO Subjectively, appetite, swimming, and general activity level did not change after drug administration (Norton et al. 2015). Tapendatol, similar mechanistically to tramadol, was administered to red-eared and yellow-bellied slider turtles and plasma concentrations were detectable for approximately 24 hours and the duration of antinociceptive efficacy was approximately 10 hours in both turtle species (Giorgi et al. 2014, 2015b). The shorter duration of antinociceptive efficacy, compared to tramadol, may have been due to the lack of an active metabolite.

NSAIDs are the most widely used analgesic in reptiles, with very few clinical studies to evaluate their PKs or clinical efficacy (Read 2004; Greenacre et al. 2008; Olesen et al. 2008; Mosley 2011). Determining the efficacy of NSAIDs in reptiles is very difficult, which is why most studies of reptiles and NSAIDS are PK studies. As such, it is difficult to recommend effective and safe dosing intervals as plasma concentrations of NSAIDS do not always directly correspond with clinical efficacy (Mosley 2011). Meloxicam has been used most frequently by clinicians, with no reports of toxicity in reptiles. Daily IM administration of meloxicam (0.2 mg/kg) or carprofen (2 mg/kg) for 10 days

in green iguanas did not yield any significant alterations to hematological or serum biochemical parameters (Trnková et al. 2007), and high daily oral doses of meloxicam (1 or 5 mg/kg) for 12 days did not induce any histological changes to renal, hepatic, or gastric tissues (Divers et al. 2010). In green iguanas dosed orally or intravenously at 0.2 mg/kg, plasma concentrations associated with analgesia in other species were maintained for 24 hours (Divers et al. 2010). In loggerhead turtles, meloxicam (0.1 mg/kg) administered both intramuscularly and intravenously did not reach plasma concentrations consistent with analgesia in humans, horses, or dogs, and the half-life was short (Lai et al. 2015). In red-eared slider turtles, IM administration of meloxicam (0.5 mg/kg) provided for the most consistent clinical PK behaviour with a terminal half-life of 7.57 hours, while oral bioavailability was only 37% (Rojo-Solís et al. 2009). In a PK study in which meloxicam (0.2 mg/kg IM and IV) was administered to red-eared slider turtles, the IM dose provided a therapeutic (i.e., anti-inflammatory) concentration range equivalent to mammals for approximately 48 hours (Di Salvo et al. 2015). In a different study evaluating the PKs of meloxicam (0.2 mg/kg PO, ICe and IM) in red-eared slider turtles, only the ICe and IM routes, but not the PO route, provided mean blood concentrations of meloxicam that were above those considered effective to induce anti-inflammatory effects in mammals for approximately 8 hours (IM) or 12 hours (ICe) (Uney et al. 2016). Meloxicam has PK patterns that differ species of sea turtles. For example, administration of meloxicam (1 mg/kg SC) in Kemp's ridley (*Lepidochelys kempii*) and green sea turtles (*Chelonia mydas*) resulted in plasma concentrations greater than those considered effective in mammals for 12 and 120 hours, respectively, while the administration of meloxicam (2 mg/kg SC) to loggerhead sea turtles resulted in plasma concentrations greater than those considered effective in mammals for only 4 hours (Norton et al. 2021b). The same authors used a follow-up, multidose PK study to demonstrate that meloxicam (1 mg/kg SC) should be administered to Kemp's ridley sea turtles every 12 hours and in green sea turtles every 48 hours (Norton et al. 2021a). Olesen et al. (2008) found no discernable effects on mitigating changes in physiological parameters in ball pythons undergoing surgery when comparing preoperative meloxicam (0.2 mg/kg IM) to saline. However, meloxicam (0.4 mg/kg IM) was effective in significantly decreasing tail movement responses in bearded dragons to electrostimulation, as was carprofen (2 and 4 mg/kg IM) and ketoprofen (2 mg/kg IM), compared with saline (Greenacre et al. 2008). Ketoprofen bioavailability when administered intramuscularly in green iguanas was 78%, with a longer terminal half-life compared with dogs (Tuttle et al. 2006). The longer half-life of studied NSAIDs necessitates judicious use in compromised reptiles. In loggerhead sea turtles, a ketoprofen dose (2 mg/kg IM or IV q24h) is likely appropriate based on therapeutic plasma concentrations equivalent to mammals (Thompson et al. 2018). Regarding safety, ketoprofen (2 mg/kg IM) administered q24h for up to 5 days in loggerhead sea turtles appeared to be safe with respect to several hematologic parameters (Harms et al. 2021). Recently, the safety of ketoprofen was evaluated in bearded dragons and it was found that there were no significant biochemical or pathologic changes other than muscle necrosis at the administration site (Vigneault et al. 2022). Using a different NSAID, the PKs of a single dose of ketorolac (0.25 mg/kg IM) was evaluated in loggerhead sea turtles, and therapeutic plasma concentrations equivalent to mammals were never achieved, so its use in this species couls not be recommended (Gregory et al. 2021). However, the same dose of ketorolac (0.25 mg/kg IM) administered to eastern box turtles (*Terrapene carolina carolina*) provided plasma concentrations above a therapeutic target level for 24-hour analgesia in mammals (Cerreta et al. 2019).

Local anesthetics are commonly used for surgical procedures in reptiles and can be an effective local analgesic (Bennet 1998; Hawkins 2006). Care must be taken to avoid accidental overdose, especially in small patients. Doses should not exceed 10 mg/kg for lidocaine, 5 mg/kg for bupivacaine, or 25 mg/kg for mepivacaine (Wellehan et al. 2006; Eatwell 2010; Mosley 2011). For smaller patients, less concentrated commercially available solutions (e.g., 1% lidocaine or 0.25% bupivacaine) should be used to minimize the decreased efficacy of local anesthetics when they are diluted (Kanai & Hoka 2006; Kanai et al. 2007). Some clinicians, including one author (D.W.), prefer to combine these two local anesthetics in a 1:1 ratio to enhance effects and duration, and minimize the potential for toxicity (Eatwell 2010). Clinical evaluation of local anesthetic use in reptiles is rare in the veterinary literature. A technique for a mandibular nerve blockade using 2% mepivacaine was described in crocodilians (Wellehan et al. 2006) and more recently intrathecal administration of lidocaine (4 mg/kg) or bupivacaine (1 mg/kg) in red-eared sliders resulted in motor block of the hind limbs for approximately 1 and 2 hours, respectively (Mans et al. 2011). Lidocaine (4 mg/kg, <1 hour duration), bupivacaine (1 mg/kg, 1–2 hours duration) or preservative-free morphine sulfate (0.1–0.2 mg/kg, up to 48 hours duration) can be administered intrathecally between the coccygeal vertebrae of turtles and bearded dragons (Mans et al. 2011; Ferreira et al. 2021). In a clinical setting, bupivacaine (0.1 mL for each 10 cm of carapace) was administered intrathecally to facilitate surgical excision of fibropapillomas from the posterior flippers of a green sea turtle (Futema et al. 2020).

Similarly, lidocaine (1 mL/20–25 kg) was administered intrathecally in hybrid Galapagos tortoises (*Chelonoidis niger*) prior to phallectomy surgery (Rivera et al. 2011). Lidocaine can be combined with morphine for intrathecal administration in bearded dragons, providing analgesia to the caudal half of the body for 12–24 hours (Fink et al. 2022). In desert tortoises (*Gopherus agassizii*) undergoing orchiectomy, lidocaine (2 mg/kg) + morphine (0.1 mg/kg) intrathecal was effective in providing analgesia in the caudal half of the body (Proenca et al. 2014a,b). For topical ocular administration to block corneal sensitivity, the local anesthetic, proparacaine hydrochloride (0.5%), was used clinically in reptiles during eye examinations, especially to measure intraocular pressure (Gornik et al. 2015). Similar proparacaine results were determined in bearded dragons and Yacare caiman (*Caiman yacare*) (Ruiz et al. 2015; Schuster et al. 2015). Further research into local anesthetic use in reptiles is needed.

There are few published data demonstrating analgesic efficacy associated with administration of other anesthetic drugs, such as ketamine, dexmedetomidine, medetomidine, midazolam, or propofol in reptiles. While alpha-2 adrenergic drugs are commonly used, in combination with ketamine or midazolam, for sedation in reptiles, few data exist with respect to the analgesic effects of these drugs. A recently completed study in one current author's (K.K.S.) laboratory demonstrated that dexmedetomidine (0.1 mg/kg) produced antinociception for up to 24 hours in ball pythons (*Python regius*) (Bunke et al. 2018). In tegu lizards (*Salvator merianae*) exposed to a toe pinch, dexmedetomidine (0.2 mg/kg IM) provided antinociception without sedation, while midazolam (1.0 mg/kg IM) provided no antinociception, but caused sedation (Bisetto et al. 2018). While there is interest in the fact that low-dose ketamine provides analgesia in mammals, there are no current data in reptiles to support this.

Complementary therapies such as acupuncture (Fig. 2.3) and cold laser therapy appear to be valuable based on clinical impressions and deserve further study (Koski 2011; Dadone & Harrison 2017; Sladky & Mans 2014).

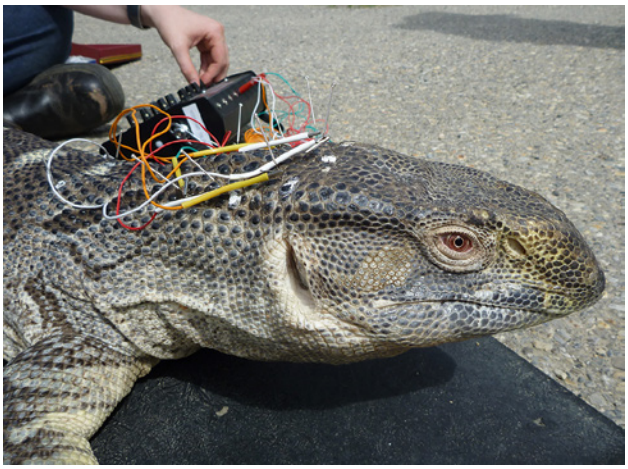


Figure 2.3 Electroacupuncture in a black throated monitor (*Varanus albigularis ionidesi*) for cranial cervical trauma that had resulted in tetraparesis. The monitor had not improved with pharmaceuticals and aqua-therapy, but significant clinical improvement was noted within three acupuncture treatments.

Birds

The neurological components necessary to respond appropriately to painful stimuli in avian species are analogous to those in mammals, with well-developed antinociceptive mechanisms to diminish pain, modulation of pain pathways, and behavioural responses to painful stimuli with pharmacological agents (Gentle 1992; Machin & Livingston 2002; Hawkins 2006; Douglas et al. 2018). Three types of nociceptors have been identified in birds: thermal and mechanical nociceptors, and high threshold nociceptors that are polymodal in nature and respond to mechanical, thermal, and chemical stimulation (Necker & Reiner 1980; Gottschaldt et al. 1982; Gentle 1992; McKeegan 2004; Douglas et al. 2018). Opioid receptors are detectable as early as 10 days in embryonic chicks (Hendrickson & Lin 1980), and the μ, δ, and κ opioid receptors in birds are similarly distributed in the forebrain and midbrain as in mammals, with κ receptors predominating in forebrain of pigeons and songbirds, while μ receptors were most prevalent in chickens. However there have been only a few studied species, with variability existing in receptor density, distribution, and structure, even between strains of the same species (Mansour et al. 1988; Reiner et al. 1989; Csillag et al. 1990; Duhamelle et al. 2018; Douglas et al. 2018). Beta-endorphin has been noted in a wide variety of birds and maintains its structure between different species, indicating that it is important in the resppnse to noxious stimuli or stress (Scanes & Pierzchala-Koziec 2018).

Cyclooxygenase enzymes (COX-1 and COX-2) are widely distributed in birds and can be modulated with NSAIDs (Lu et al. 1995; Mathonnet et al. 2001; Douglas et al. 2018).

Recognition of Pain in Bird Species

In general, similar to many wild species, birds tend not to show overt signs of pain as obvious distress behaviors may attract unwanted attention; rather they will demonstrate more subtle or cryptic behavioural signs of their discomfort. As there are no universal indicators of pain in birds, the assessment of pain must take into account the species-specific normal behaviour and individual behaviour, strain, gender, age, concurrent disease states, type of pain, and the environment. In addition, it is important that behavioural

observations occur at appropriate times for each species, such as observing nocturnal species at night (Hughes 1990; Sufka et al. 1992; Hawkins & Paul-Murphy 2011; Mazor-Thomas et al. 2014; Mikoni et al. 2022).

Birds that are acclimated to handling may mask physiological changes often associated with pain, such as elevations in body temperature, respiratory rate, or stress hormones. However, birds that are comfortable with their environment also may more readily demonstrate painful behaviours such as limb guarding, withdrawal responses, or squinting of the eyes (Heatley et al. 2000; Hawkins 2006; Sneddon et al. 2014). In chickens, elevations in blood pressure were consistently associated with painful procedures, but the measurement of blood pressures is not always feasible (Gentle & Hunter 1991). A study in red-tailed hawks with orthopedic injuries (Mazor-Thomas et al. 2014) demonstrated significant reductions in head movement frequency, beak clacks, and overall movement. Subtle changes to mobility, due to diseases such as pododermatitis and osteoarthritis, can be objectively detected through pressure-sensitive walkways (Sheldon et al. 2019). Immobility is a shared finding across numerous avian species, and in social species isolative behaviour can often be observed (Gentle & Hill 1987; Gentle 1992; Graham 1998; Paul-Murphy & Hawkins 2012; Mikoni et al. 2022). Many bird species that are being handled will respond to acute painful procedures with vocalizations, excessive movement, and escape reactions, but with progression of the painful stimulus will revert to immobility. Normally passive birds may act aggressively when painful. With prolonged pain, decreased appetite and activity are often observed, especially behaviours such as preening or dust bathing, although in some individuals, particularly with psittacines and mynahs, overgrooming and feather destructive behaviour may ensue (Gentle & Hunter 1991; Hawkins & Paul-Murphy 2011; Mikoni et al. 2022).

Analgesia in Birds

Based on pharmacodynamic (PD) studies, clinical reports, and experience, butorphanol is the recommended opioid for use in most avian species at a doses of 1–5 mg/kg intramuscularly every 3–24 hours, as it has poor oral availability (Paul-Murphy et al. 1999; Hawkins 2006; Klaphake et al. 2006; Sladky et al. 2006; Sanchez-Migallon Guzman et al. 2008, 2011; Hawkins & Paul-Murphy 2011). In some species, particularly *Buteo* sp. raptors and corvids, butorphanol can be associated with profound sedation at the higher doses. In PK studies the half-life is only 0.5–2 hours so frequent dosing may be necessary depending on clinical need (Riggs et al. 2008; Sanchez-Migallon et al. 2011a; Paul-Murphy & Hawkins 2012; Singh et al. 2018). A study in common peafowl (*Pavo cristatus*) that utilized subcutaneously implanted osmotic pumps for 7 days maintained serum levels at or above reported antinociceptive concentrations until pump removal with no evidence of sedation (Clancy et al. 2015). Administration of butorphanol tartrate in a long-acting polymer gel formulation (12.5 mg/kg) to Hispaniolan Amazon parrots increases the potential for analgesia for 4–8 hours (Laniesse et al. 2017). An experimental liposome-encapsulated butorphanol also holds promise for the future as it provides analgesic effects for 3–5 days after a single SC injection of 15 mg/kg (Sladky et al. 2006; Paul-Murphy et al. 2009a,b) but commercial development has been slow.

Another κ agonist and partial μ antagonist that may have future clinical use is nalbuphine hydrochloride. In Hispaniolan Amazon parrots (*Amazona ventralis*) it increased pedal thermal withdrawal thresholds for up to 3 hours after single IM administration of 12.5 mg/kg (Sanchez-Migallon Guzman et al. 2011). However, a PK study in the same species (Keller et al. 2011) revealed a short terminal half-life of 30 minutes. Similar to butorphanol, a slow-release formulation has been studied and would be clinically ideal, but is not yet commercially available (Sanches-Migallon Guzman et al. 2013a,c).

The partial μ agonist opioid buprenorphine is being more commonly used and studied with mixed results. In American kestrels (*Falco sparverius*), a dosage of 0.1 mg/kg increased thermal thresholds for at least 6 hours compared with saline controls, with high bioavailability after IM injection (Ceulemans et al. 2014; Gustavsen et al. 2014). At dosages of 0.25 and 0.5 mg/kg in pigeons, it was associated with a positive analgesic response for 2 and 5 hours, respectively (Gaggermeier et al. 2003). In red-tailed hawks (*Buteo jamaicensis)*, buprenorphine ameliorated pain-suppressed behaviours associated with orthopedic injuries, while administration of concentrated buprenorphine (0.3 and 1.8 mg/kg SC) sustained plasma levels >1 ng/mL for 24 and 48 hours, respectively (Mazor-Tomas et al. 2014; Gleeson et al. 2018). A sustained-release buprenorphine formulation at 1.8 mg/kg IM increased thermal thresholds for 24 hours with mild sedation noted (Sanchez-Migallon Guzman et al. 2018a). However, buprenorphine administered intra-articularly in domestic fowl, intramuscularly at 0.1 mg/kg in African grey parrots (*Psittacus erithacus*), or intramuscularly in cockatiels (*Nymphicus hollandicus*) at 1.8 mg/kg failed to demonstrate an analgesic effect (Gentle et al. 1999; Paul-Murphy et al. 1999, 2004a; Sanchez-Migallon Guzman et al. 2018b). Further studies in other avian species are needed.

Other opioids such as fentanyl and hydromorphone have demonstrated mixed results in clinical studies. Fentanyl at 0.02 mg/kg intramuscularly in white cockatoos (*Cacatua alba*) was not effective, but increasing the dose to 0.2 mg/kg

yielded a positive analgesic response but was associated with undesirable hyperactivity (Hoppes et al. 2003). Transdermal fentanyl application at 5 mg/kg in helmeted guineafowl (*Numida meleagris*) sustained plasma concentrations above those associated with analgesia in dogs for at least 7 days (Waugh et al. 2016). In domestic chickens, a 25 μg/h transdermal fentanyl patch (7.23–11.36 μg/kg/h) maintained levels considered analgesic in humans and several mammalian species for the entire 72-hour period that they were applied for (Delaski et al. 2016). Under constant rate infusion studies in red-tailed hawks, fentanyl significantly lowered the minimum anesthetic concentration of isoflurane by 31–55%, supporting its clinical application as an intra-operative analgesic (Pavez et al. 2011).

In American kestrels, IM hydromorphone has a short half-life (1.26 hours) with dosages of 0.1, 0.3, and 0.6 mg/kg IM resulting in antinociception for 3–6 hours with mild sedation noted at the highest dose (Sanchez-Migallon Guzman et al. 2013b, 2014). In contrast, the same dosages of hydromorphone administered to cockatiels failed to provide an analgesic effect but did cause sedation (Houck et al. 2018). Similar to buprenorphine, μ-agonist opioids may not be efficacious in psittacine species, and further study is required in other species.

The PKs of tramadol have been studied in bald eagles (*Haliaetus leucocephalus*), African penguins (*Spheniscus demerus*), red-tailed hawks, peafowl, and Hispaniolan Amazon parrots with oral doses between 5 and 11 mg/kg achieving serum levels equated with analgesia in humans (Souza et al.2009, 2010, 2011; Black et al. 2010; Kilburn et al. 2014). Tramadol (30 mg/kg PO) was as effective as meloxicam (1 mg/kg PO) for providing analgesia for experimentally induced temporary arthritis in ducks (*Cairina moshata domestica*) (Bailey et al. 2019). Preliminary efficacy studies using noxious thermal stimuli in Hispaniolan Amazon parrots reveal that an IV dosage of 5 mg/kg increases the nociceptive threshold for at least 4 hours, while an oral dose of 30 mg/kg provides analgesia for up to 6 hours, indicating that higher doses may be needed for clinical effect (Souza et al. 2010; Geelen et al. 2013). Tramadol administration to common buzzards (*Buteo buteo*) as part of ketamine-based anesthetic protocols provided for analgesia post procedure for up to 3 hours (Raisi et al. 2019). As with other analgesics, significant interspecific PK and PD variability likely exists and deserves further exploration.

The most frequently used NSAIDS in avian species are meloxicam, carprofen, and ketoprofen, with selective use of celocoxib and piroxicam. Meloxicam is the most commonly used NSAID in zoological medicine and has shown a wide margin of safety in a large and diverse number of species (Cuthbert et al. 2007; Naidoo et al. 2008; Hawkins & Paul-Murphy 2011; Whiteside 2014; Dijkstra et al. 2015; Summa et al. 2017; Miller et al. 2019). Significant interspecific variation exists in birds, with elimination half-life in studied species when administered parenterally ranging from as short as 30 minutes in ostrich (*Struthio camelus*), less than an hour in cockatiels, great-horned owls (*Bubo virginianus*), and red-tailed hawks, to approximately 2 hours in American flamingos (*Phoenicopterus ruber*, Caribbean flamingos (*Phoenicopterus ruber ruber*), and lesser flamingos (*Phoeniconaias minor*), over 3 hours in chickens, 4 hours in ring-necked parakeets (*Psittacula krameri*), 5 hours in Bilgorasjka geese (*Anser anser domesticus*) and zebra finches (*Taeniopygia guttata*), 16 hours in Hispaniolan Amazon parrots, 32 hours in African penguins, and as long as 35 hours in African grey parrots (Baert & De Backer 2003; Wilson et al. 2005; Lacasse et al. 2013; Molter et al. 2013; Lindemann et al. 2016; Zordan et al. 2016; Boonstra et al. 2017; Dhondt et al. 2017; Montesinos et al. 2017; Morrison et al. 2018; Miller et al. 2019; Sartini et al. 2020). In Hispaniolan Amazon parrots, IM dosages of 1 mg/kg every 12 hours were needed for effective analgesia for experimentally induced arthritis, but very few long-term studies have been carried out to assess for adverse side effects in birds (Cole et al. 2009). Injectable sustained-release meloxicam formulations yielded highy variable PK results in Hispaniolan Amazon parrots and did not extend the half-lives compared to regular formulations in American flamingos (Sanchez-Migallon Guzman et al. 2017a; Sim & Cox 2018). Until further studies are completed, meloxicam should be used cautiously.

Oral administration of meloxicam yields variable bioavailability, with studied half-lives ranging from less than 1 hour in cockatiels, great-horned owls and red-tailed hawks, 2 hours in Caribbean flamingos, 3 hours in chickens, 4 hours in American flamingos, 5 hours in geese, 6 hours in lesser flamingos, 16 hours in ring-necked parakeets and Hispaniolan Amazon parrots, 29 hours in African penguins, and up to 33 hours in African grey parrots (Wilson et al. 2005; Molter et al. 2013; Lindemann et al. 2016; Zordan et al. 2016; Boonstra et al. 2017; Montesinos et al. 2017; Souza et al. 2017; Morrison et al. 2018; Sartini et al. 2020). Based on the authors' clinical experience a dose range of 1–2 mg/kg SC or IM has proven efficacious in many species, and generally favourable clinical results were noted with chronic oral usage at 0.5–1.0 mg/kg up to twice daily with no complications. As with the other NSAIDS, further studies are needed to evaluate the PK and PD behaviour of meloxicam in various avian taxa, as well as evaluation for adverse effects with chronic administration.

Carprofen has yielded variable results in studied species, with either a very high dose (30 mg/kg) needed to provide

analgesia for experimentally induced arthritis in chickens (McGeown et al. 1999; Hocking et al. 2005) or a very short duration of action noted when a lower dose (3 mg/kg) was administered to Hispaniolan Amazon parrots (Paul-Murphy et al. 2009b). Concerns about its safety have been documented in Cape vultures (Fourie et al. 2015) and high oral doses in feed-induced nephrotoxic and hepatotoxic changes in chickens (Dabhi et al. 2015). Ketoprofen administered orally or parenterally (2 mg/kg) to Japanese quail (*Coturnix japonica*) had a very short half-life of less than 35 minutes despite the route of administration (Graham et al. 2005), while in mallard ducks (*Anas platyrhynchos*), an IM dose of 5 mg/kg was associated with decreased levels of the inflammatory mediator thromboxane for up to 12 hours after administration (Machin et al. 2001), and provided analgesia against a noxious stimulus while under isoflurane anesthesia (Machin & Livingston 2002). However in spectacled (*Somateria fischeri*) and king (*Somateria spectabilis*) eider ducks administration of ketoprofen at 2 and 5 mg/kg IM was associated with severe renal tubular necrosis, visceral gout, acute rhabdomyolysis, and death in 40% and 83% of treated males, respectively, although gender-linked behaviours may have increased the susceptibility of these birds to the side effects of ketoprofen (Mulcahy et al. 2003). In addition, ketoprofen has proven toxic to *Gyps* vulture species at doses above 1.4 mg/kg (Naidoo et al. 2010).

The use of the "coxib" class of NSAIDS (e.g., celecoxib) has been anectodally reported (Dhondt et al. 2017). A potentially promising new "coxib" for birds is mavacoxib. Studies in cockatiels (Dhondt et al. 2017) and Caribbean flamingos (Huckins et al. 2020) demonstrated a long elimination half-life (135 and 75 hours, respectively) after a single oral dose. Clinical efficacy studies remain to be completed. Piroxicam has not been scientifically studied in avian species, but has been used successfully for the chronic treatment of arthritis in cranes (Paul-Murphy & Hawkins 2012). While other NSAIDS, such as flunixin meglumine, have been used historically, they have a very short elimination half-life (<1 hour) in budgerigars (*Melopsittacus undulatus*) and Patagonian conures (*Cyanoliseus patagonus*), and have also been associated with a higher degree of undesirable side effects such renal toxicity and gastrointestinal ulceration (Pereira & Werther 2007; Musser et al. 2013). The most severe example of NSAID-induced renal toxicity is the diclofenac-linked severe decline of Asian *Gyps* vulture species (Green et al. 2004; Oaks et al. 2004; Meteyer et al. 2005; Hussain et al. 2008; Naidoo & Swan 2008).

Unlike other NSAIDS that rely on COX enzyme inhibition, the prostaglandin E_2 (PGE_2) receptor agonist grapiprant binds to the EP4 receptor and blocks the sensitization of sensory neurons and stimulation of inflammation mediated by the PGE2 receptor. Studies in red-tailed hawks administered a 30 mg/kg oral dose indicate excellent bioavailability with no adverse clinical effects noted, although when administered with food, it resulted in mildly lower plasma concentrations and delayed absorption. Further studies are needed to evaluate the PKs, efficacy, and safety in avian species, but it may hold promise (Rodriguez et al. 2021, 2022).

Local anesthetics have been used successfully in a clinical setting, although there are very few scientific studies evaluating efficacy, time to effect, or duration of activity (Lee & Lennox 2016). Historically it was believed that birds may be more sensitive to the effects of local anesthetics owing to more rapid absorption and delayed clearance compared with mammals, thus lower doses were often indicated to avoid signs of toxicity such as drowsiness, recumbency, seizures, cardiovascular effects, and death (Hocking et al. 1997; Hawkins & Paul-Murphy 2011). However in chickens, the toxic dose of intravenous (IV) lidocaine is approximately 30 mg/kg, which is greater in than mammals (Imani et al. 2013), and for IV bupivacaine the effective dose (ED_{50}) to induce cardiovascular effects is 1.96 mg/kg (DiGeronimo et al. 2017). Further studies in different species are required. Regional local anesthetic infiltration is generally effective for joints and soft tissue. In chickens, spinal subarachnoid injection of lidocaine (2 mg/kg) at the synasacrococcygeal space for regional pericloacal anesthesia induced a duration of analgesia of 21 minutes (Kazemi-Darabadi et al. 2019). Sciatic-femoral nerve blocks with lidocaine (1 mg/kg per nerve) in peregrine falcons (*Falco peregrinus*) for pododermatitis surgery provided an analgesic effect for up to 2.5 hours (d'Ovidio et al. 2015). Brachial plexus blockade with lidocaine in Hispaniolan Amazon parrots or high-dose lidocaine with epinephrine or bupivacaine in chickens and mallard ducks failed to prevent nerve transmission (Figueiredo et al. 2008; Brenner et al. 2010; da Cunha et al. 2013). However, a brachial plexus block using ropivacaine (2 mg/kg) was successful in a striped owl (*Asio clamator*) undergoing wing amputation (do Nascimento et al. 2019).

Gabapentin has been used anecdotally, at significantly higher dosages than in mammals, as an adjunctive treatment for suspected neuropathic pain in a few species or for abatement of self-mutilation (Doneley 2007; Siperstein 2007; Shaver et al. 2009). In great-horned owls, oral gabapentin (11 mg/kg) sustained plasma levels associated with therapeutic levels (2 μg/mL) for 8.8 hours, while in Caribbean flamingos a dosage of 25 mg/kg PO maintained plasma concentrations above 2 μg/mL for approximately 12 hours (Yaw et al. 2015; Browning et al. 2018). Based on the authors' experience with gabapentin use in various

species, its efficacy is difficult to determine and highly variable, and further studies are indicated.

Polysulfated glycoaminoglycans (PSGAGs) have been used very cautiously in avian species due to fatal coagulopathies following IM administration of 0.5–100 mg/kg (Anderson et al. 2013). However, Wonn et al. (2022) studied the hypocoagulability of a commonly used veterinary PSGAG product (Adequan 100 mg/mL) and recommend 1 mg/kg subcutaneously once weekly for four doses, followed by once every other week for two doses, then monthly for chronic maintenance.

Other drugs, such as NMDA antagonists, have not been evaluated, while complementary therapies such as acupuncture, physiotherapy, and the use of nutraceuticals have been anecdotally effective and are in need of further study (Crouch 2009; Koski 2011; Rychel et al. 2011; Whiteside 2014).

Mammals

Despite advances in pain management, compared with the lower vertebrate species, there is still a paucity of scientific studies evaluating species-specific pain responses and analgesia in wild mammals. However, studies in laboratory and companion zoological species have increased significantly over the past decade.

Recognition of Pain in Mammals

In general, many of the recognized clinical signs associated with pain in domestic mammals may be seen in wild species, although they are often more subtly expressed, especially in prey species, which may not display behavioural alterations to a painful event. Often remote evaluation is needed to truly evaluate the degree of pain, and advances in wireless monitoring technology can be useful (Oliver et al. 2017; Klune et al. 2019). It is important for clinicians to understand the normal behavior of species in order to evaluate for such changes in behavior that may be related to pain (Hawkins 2002; Flecknell 2008; Whiteside 2014; Dunbar et al. 2016)

Objective assessment of pain can be done through evaluation of physiological and biochemical (e.g., alterations in corticosteroid levels) indices and behaviour. The former indices are often difficult to assess in the conscious animal, although noninvasive biochemical methodologies (e.g., fecal glucocorticoid metabolite monitoring) have become more common (Goldschlager et al. 2013). Nonspecific clinical signs such as tachypnea, trembling, bruxism, salivation, muscle spasms, sweating in species capable of doing so, and dilated pupils can be associated with pain in mammals, while it is often difficult or impossible to evaluate for more specific changes such as tachycardia or pyrexia in the conscious animal. Changes in facial expressions such as wrinkling the brow, frowning, or grimacing are not usually recognized in most species (Williams 2002; Sneddon et al. 2014). However, a small number of studies have validated the use of facial expressions (changes in the shape of the mouth, cheeks, ears, nose, and eyes) to assess for pain in mammals (McLennan et al. 2019). These "grimace scales" have been developed and validated for mice, rats, rabbits, horses, ferrets, and neonatal harbour seals (Leach et al. 2012; Dalla Costa et al. 2014; Hampshire & Robertson 2015; Leung et al. 2016; Reijgwart et al. 2017; MacRae et al. 2018; Klune et al. 2019). Other subjective measures should be evaluated, such as changes in demeanour, altered social interactions, variations in feeding or foraging patterns, changes in posture, mobility, or activity level, alterations of sleep–awake patterns, self-directed behaviours such as looking, biting, kicking, chewing, or rubbing of painful areas, changes in vocalization, and altered response to touch (Bufalari et al. 2007; Walker et al. 2010; Sneddon et al. 2014). Any of these measures may be altered with pharmacologic agents. In some social species, pain responses may elicit assistance or directed aggression from conspecifics within the social group (Sanford et al. 1996).

Analgesia in Mammals

Much of the analgesic drug selection and doses used in mammals are extrapolated from domestic and laboratory species, although much-needed studies of analgesics in wildlife continue to expand.

Opioids are frequently used for analgesia in a zoological setting, but less frequently with free-living wildlife owing to concerns for the potential for sedation. PK and PD studies are limited outside of a laboratory animal setting, but include the PKs of butorphanol in elephants (Tana et al. 2010), PKs and PDs in llamas (Carroll et al. 2001), PKs in ferrets (Katzenbach et al. 2018), the PKs and PDs of morphine in llamas (Uhrig et al. 2007), the PKs of fentanyl patches in llamas (Grubb et al. 2005) and cynomologus macaques (Carlson et al. 2016), the PKs of buprenorphine in macaques (Nunamaker et al. 2013; Mackiewicz et al. 2019), ferrets (Katzenbach et al. 2018), and northern elephant seals (Molter et al. 2015), the PKs of hydromorphone in ferrets (Katzenbach et al. 2018), and the PKs of tramadol hydrochloride in alpacas (Edmondson et al. 2012), macaques (Kelly et al. 2015), and California sea lions (Boonstra et al. 2015). These studies continue to highlight the need for species-specific studies as extrapolation from taxonomically similar species is not always appropriate and the biovailability of parenteral versus oral administration can vary tremendously.

Even though the duration of activity of butorphanol is relatively short compared with other opioids, it is still

frequently used as an analgesic (e.g., maned wolf [McNulty et al. 2000], microchiropterans [Wellehan et al. 2001], African lions [Kolata 2002], Egyptian fruit bats [Lafortune et al. 2004; Tuval et al. 2018], Asian and African elephants [Abou-Madi et al. 2004; Kottwitz et al. 2016], white-tailed deer [MacLean et al. 2006], African hedgehog [Done et al. 2007], otariid and phocid seals [Haulena 2014; Lynch & Bodley 2014], parma wallabies [Okeson et al. 2009], polar bears [Velguth et al. 2009], prehensile tailed porcupine [Guthrie & DeMaar 2011], rhinoceros [Kottwitz et al. 2016], giraffe [Boothe et al. 2016], hippopotamus [Boothe et al. 2016]. Opioid formulations of longer durations such as buprenorphine (e.g., lions [Kolata 2002], polar bears [Velguth et al. 2009], hyena [Hahn et al. 2014], pinnipeds [Moore et al. 2010; Molter et al. 2015], guinea pigs [Smith et al. 2016; Zanetti et al. 2017], chinchillas [Fox & Mans 2018]}, hydromorphone (e.g., squirrel monkey [Wellehan et al. 2004], binturong [Spriggs et al. 2007], chinchillas [Evenson & Mans 2018]) , transdermal fentanyl or fentanyl patches (llama [Grubb et al. 2005], binturong [Spriggs et al. 2007], macaques [Carlson et al. 2016; Salyards et al. 2017]), or epidural morphine are used frequently for analgesia by clinicians in a zoological setting, and are more commonly reported in the literature. Sustained-release formulations of buprenorphine are now available and may offer significant advantage in providing analgesia while minimizing handling (Nunamaker et al. 2013; Molter et al. 2015; Cary et al. 2017; Zanetti et al. 2017; Mackiewicz et al. 2019). Opioid use may result in significant weight loss in some species (Oliver et al. 2017) and care must be taken when utilizing fentanyl patches as ingestion can lead to serious morbidity or mortality (Deschamps et al. 2012).

Based on clinical experience, tramadol also is an effective analgesic in many species (Souza & Cox 2011), with examples of its reported use including large felids (McCain et al. 2008, 2009), Western lowland gorilla (Rush et al. 2010), binturong (Spriggs et al. 2007) pinnipeds (Moore et al. 2010) Atlantic bottlenose dolphin (Schmitt & Sur 2012), elephants, giraffe, rhinioceros, and hippopotamus (Boothe et al. 2016; Kottwitz et al. 2016). A PK study in koalas concluded that SC administration of tramadol at 4 mg/kg was predicted to have analgesic activity based on plasma concentrations (Kimble et al. 2021).

Meloxicam is the most widely administered NSAID in zoological species, with increasing applications in free-ranging wildlife. Its PKs have been studied in nondomestic species such as mini-pigs, baboons, and rodents (Busch et al. 1998), rabbits (Carpenter et al. 2009; Fredholm et al. 2013; Delk et al. 2014), dromedary camels (Wasfi et al. 2012), llamas (Kreuder et al. 2012), koalas (Kimble et al. 2013), macaques (Bauer et al. 2014), ferrets (Chinnadurai et al. 2014), bottlenose dolphins (Simeone et al. 2014), prairie dogs (Cary et al. 2017; Wright et al. 2017), and Malayan flying foxes (Goodnight & Cox 2018). Sex difference in PK behaviour can exist (Chinnadurai et al. 2014). It has been used parenterally or orally in most mammalian families by the authors with no observed or reported side effects. Oral bioavailability may be significantly reduced compared to parenteral administration (Kimble et al. 2013). Based on the reported literature and the authors' experience, oral dosages required for complexed stomached species are higher than those for simple monogastric species. (Whiteside & Black 2004; Whiteside et al. 2006; Pye et al. 2008, 2010; Okeson et al. 2009; Twomey et al. 2010; Dadone et al. 2011; Whiteside 2014).

Carprofen and ketoprofen also are frequently used NSAIDs for captive and free-living mammals. The PKs of carprofen have been established in white rhinoceros (Leiberich et al. 2018). In general, carprofen has been found to be efficacious (Dutton et al. 2002; Mylniczenko et al. 2005; Velguth et al. 2009; Boothe et al. 2016; Kottwitz et al. 2016; Fernando et al. 2016). However, even in taxonomically similar species, there may be profound differences in efficacy. As Walker et al. (2011) reported, it was not effective in controlling postsurgical pain in Stellar sea lions when administered at dosages suggested by Dold et al. (2004) based on PK and PD studies in California sea lions. The PKs of ketoprofen have been studied in camels (Alkatheeri et al. 1999) and elephants (Hunter et al. 2003), and its anecdotal use has been reported in a wide variety of species (e.g., golden lion tamarin [Bronson et al. 2005], exotic ruminants [Howard & Richardson 2005], sun bear [Mylniczenko et al. 2005], pinnipeds [Fauquier et al. 2008; Rush et al. 2012; Dennison et al. 2007], koalas [Pye et al. 2008], bongo [Gyimesi et al. 2008, 2011], agoutis [Zimmerman et al. 2009], giraffes and hippopotamus [Boothe et al. 2016], elephants and rhinoceros Kottwitz et al. 2016]).

NSAIDS such as phenylbutazone and flunixin meglumine are still utilized for analgesia, particularly with larger mammalian species (e.g., rhinoceros [Wack et al. 2010; Harrison et al. 2011; Kottwitz et al. 2016], giraffe [James et al. 2000; Boothe et al. 2016; Gardner & Rourke 2021], elephants [Kottwitz et al. 2016], hippopotamus [Boothe et al. 2016], exotic ruminants [Howard & Richardson 2005; Gyimesi et al. 2011], deer [Mansfield et al. 2006], elk [Larsen et al. 2000], Stellar sea lions [Walker et al. 2009], bison [Minter et al. 2011]). The PKs of phenylbutazone have been carried out in Asian and African elephants (Bechert et al. 2008) and dromedary camel (Kadir et al. 2003), with the PKs of flunixin also studied in African and Asian elephants (Bechert et al. 2021), dromedary camel (Oukessou 1994), and white rhinoceros (East et al. 2019).

The PKs of ibuprofen have been studied in Asian and African elephants (Bechert & Christensen 2007), and its use has been reported in primates (Wellehan et al. 2004; Bronson et al. 2005; Robbins et al. 2009), rhinoceros (Bertelsen et al. 2004; Kottwitz et al. 2016), elephants (Kottwitz et al. 2016), giraffe, and hippopotamus (Boothe et al. 2016). Its use in carnivore species is not recommended based on side effects noted in domestic canids and felids. Increasingly the 'coxib' NSAIDs (e.g., deracoxib, robenacoxib, firocoxib) are being used (Boothe et al. 2016; Kottwitz et al. 2016). Other sporadically used NSAIDs include tepoxalin, etodolac, tolfenamic acid, and naproxen, which are occasionally reported in the literature (Hahn et al. 2014; Williams & Junge 2014; Stringer et al. 2012). Care should be exercised if using these, as the PK or PD behaviour, and the potential negative side effects, are not known.

Corticosteroids are infrequently used for pain management in exotic species owing to the potential negative side effects, but medium- to long-acting steroids such as triamcinolone acetate and medroxyprednisolone acetate have been used successfully for joint infusions in mammals with arthritis refractory to other therapies.

Local anesthetics are frequently used with zoological species, and their use continues to expand in a free-range setting. Doses are extrapolated from domestic mammals. They are effective when used topically, epidurally, intra-articularly, intrapleurally, or intra-abdominally for specific nerve blocks (such as dental blocks for tooth extractions or endodontic procedures (Fig. 2.4) or regional nerve blocks), nonspecific infiltration such as ring blocks or line blocks, or for IV regional blocks (Mylniczenko et al. 2005; Mansfield et al. 2006; Beasley & Rhodes 2007; Borkowski et al. 2009; Morges et al. 2009; Pye et al. 2010; Schroeder et al. 2010; Clarke & DeVoe 2011; Dadone et al. 2011; Schäffer et al. 2017). The combination of lidocaine and bupivacaine is often advantageous due to a faster onset of action and prolonged effect (Anagnostou et al. 2015; Vicente & Bergström 2018). Care must be taken, particularly with smaller species, to avoid approaching toxic dosages (Heard 2014a; Gyimesi & Burns 2009; Flecknell 2018; D'Ovidio & Adami 2019).

In a clinical setting, the use of alpha-2 agonists, such as medetomidine, or NMDA antagonists, such as ketamine or amantadine, for analgesia independent from anesthesia is rarely described in the literature for exotic species. In a giant panda, amantadine in combination with carprofen provided effective analgesia (Fernando et al. 2016). Amantadine also was anecdotally used as part of multimodal analgesia in a Southern white rhinoceros (Gardner & Rourke 2021). Anecdotal evidence suggests that ketamine at 1/10th of the anesthetic dose for a species can be efficacious for analgesia, or as a constant rate infusion at 0.01–0.02 mg/kg/min, which limits its use in a field setting (Cracknell 2007). The addition of magnesium (Mg^{+2}) with ketamine enhances its analgesic effect (Liu et al. 2001).



Figure 2.4 Rostral mandibular (middle mental) nerve block with bupivicaine in an Amur tiger (*Panthera tigris altaica*) for an endodontic procedure. This dental block would be useful for premolar extraction for aging studies as well.

Gabapentin use, particularly as part of multimodal therapy for chronic neuropathic pain or chronic disease states such as osteoarthritis or cancer pain, is apparently effective and warrants further study (Adkesson 2006; Bronson et al. 2008; Vonsy et al. 2009; Boothe et al. 2016; Kottwitz et al. 2016; Huckins et al. 2018; Gardner & Rourke 2021). Other adjunctive therapies, such as oral glucosamine sulfate, chondroitin, omega-3 fatty acid supplementation, or injectable polysulfated glycoaminoglycans, are frequently utilized in a zoological setting for chronic arthritides and are anecdotally effective (Stringfield & Wynne 1999; Whiteside et al. 2006; Pye et al. 2008), but there are no supporting scientific studies that clearly demonstrate a benefit with oral products, and there are legitimate questions of oral bioavailability, especially in herbivores. Recent analyses of multiple studies in dogs and humans indicate there is conflicting evidence as to the benefit to glucosamine, chondroitin, green lipped mussels, or methylsulfonylmethane supplementation (Neil et al. 2005; Aragon et al. 2007; Teets et al. 2010; Vandeweerd et al. 2012). Further research associated with their use in zoological species is indicated. Maropitant, a neurokinin-1 antagonist, also is being studied and used anecdotally as a potential analgesia, especially

for abdominal pain (e.g., abdominal surgeries), often in combination with other analgesics (Corrêa et al. 2019; Karna et al. 2019). However, a recent meta-analysis (Kinobe & Miyake 2020) concluded that although maropitant definitively reduced the minimum alveolar concentrations for isoflurane and sevoflurane, there was not strong enough evidence that it has significant analgesic or anti-inflammatory effects at recommended manufacturer doses. Other modalities, such as acupuncture or cold laser therapy, also have produced favourable analgesic responses for osteoarthritis or neuropathic pain, and deserve further study (Maenaka et al. 2006; Cassu et al. 2008; Teets et al. 2010; Koski 2011; Rychel et al. 2011; Dadone & Harrison 2017).

Pain in Invertebrates

There is growing scientific evidence suggesting that invertebrate species, especially the more advanced species found in the phyla Arthropoda and Mollusca, have the ability to experience pain, rather than just respond to nociceptive stimuli. This is based on the presence of suitable receptors and the central nervous system, responsiveness to analgesics and anesthetics, physiological changes, avoidance learning, protective motor reactions, and cognitive abilities and sentience (Barr et al. 2008; Crook & Walters 2011; Elwood 2011, 2019; Sneddon et al. 2014; Rotllant et al. 2023). Many of the advanced invertebrate species have brains that, relative to their body weight, are larger than those in many vertebrates species. In addition these invertebrate species have complex brain structures for sensory analysis, memory, learning, and decision making, which are analogous to the functions of the cerebral cortex in vertebrate species (Smith 1991; Sandeman et al. 1992; Elwood et al. 2009; Sneddon et al. 2014; Sneddon 2015; Burrell 2017).

Behavioural evidence for the likely experience of pain has been demonstrated in several invertebrate species through avoidance learning research and protective motor reflexes. Algae octopus (*Abdopus aculeatus*) demonstrate increased sensitivity and targeted wound tending behaviour after injury (Alupay et al. 2014). Estuarine crabs (*Chasmagnathus granulatus*) associated an electrical shock with a particular location for a minimum of 3 hours after the event, and even 24 hours later in multiple trials (Denti et al. 1988; Fernandez-Duque et al. 1992). Long-term behavioural changes were observed in hermit crabs (*Pagurus bernhardus*) within their shell after they were shocked on the ventrum compared with crabs that were not shocked, which included sustained grooming of the ventral shock location (Elwood & Appel 2009; Elwood 2011). Acetic acid or sodium hydroxide applied to the antenna or eye of glass prawns resulted in an immediate tail-flick response followed by increased grooming or rubbing of the affected area. Topical application of the local anesthetic benzocaine markedly decreased these responses but did not interfere with swimming, indicating that analgesia and not anesthesia was achieved (Barr et al. 2008). Finally, some arthropods such as spiders or crabs will automize limbs when injected with noxious substances known to be painful in vertebrates, such as the bee or wasp venom or acetic acid, or when exposed to a hot plate or electric shock (Eisner & Camazine 1983; Fiorito 1986; Elwood 2011).

Further research is needed to fully characterize the pain experience and the PKs and PDs of analgesic drugs in invertebrate species. However, until such research is available, clinicians should consider the administration of analgesics to patients that are being subjected to a procedure that is deemed painful in vertebrates. This includes general anesthesia with a volatile anesthetic such as isoflurane or sevoflurane, and administration of peri-procedural analgesics such as local anesthetics (diluted lidocaine, bupivacaine, and benzocaine) (Mosley & Lewbart 2014; Cooper 2011; Lewbart & Mosley 2012; Andrews et al. 2013; Rottlant et al. 2023).

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3

Effective Anesthetic Monitoring

Sathya Chinnadurai

Physiologic monitoring is critical to help an anesthetist achieve and maintain an appropriate plane of anesthesia, anticipate and detect when changes in delivery of anesthetic drugs are required, and promptly identify preoperative, intraoperative, and postoperative complications. Without detailed monitoring, accurate record keeping, and careful assessment and reassessment of the patient, it is nearly impossible to provide effective, safe anesthesia to an animal (Chinnadurai et al. 2016). With the constant discovery of new drugs and the development of anesthetic induction protocols, it is easy to focus on finding the mythical "safe" protocol instead of developing a safe anesthetist. Regardless of the induction protocol used, an anesthetist must be ready and able to assess the patient and make adjustments to anesthetic maintenance based on that assessment. This includes increasing and decreasing anesthetic depth, maintaining normothermia, ventilatory support, and maintenance of normotension.

This chapter serves as a refresher on the effective use of common anesthetic monitors, including the challenges of using those monitors in nondomestic species. In addition, we will discuss a systematic approach to the diagnosis and treatment of common anesthetic problems. The most basic anesthetic monitoring consists of measuring heart rate, respiratory rate, and body temperature. Monitoring of blood oxygenation, ventilation (carbon dioxide excretion), and blood pressure requires additional monitors. Pulse oximeters, capnographs, electrocardiograms (ECGs), and oscillometeric blood pressure monitors are the commonly used standard anesthetic monitors in veterinary anesthesia but require some accommodation for use in nondomestic species, especially in a field setting (Chinnadurai et al. 2016). It is important to remember that even though these devices are widely used in wildlife medicine, very few have been objectively evaluated in nondomestic species (Watson et al. 2019).

This chapter discusses monitoring individual body systems, with a focus on respiratory and cardiovascular monitoring. Detail of the individual monitors themselves is given and some of the nuances in using those monitors in nondomestic species are discussed. Finally, the treatment of common anesthetic complications is covered.

Anesthetic Monitor Review

Prior to any anesthetic procedure, a plan for appropriate monitoring should be developed. This plan should be based on the anesthetic risk to the animal based on the species of interest, the anesthetic drugs used, the proposed procedures, the environment, and the anticipated complications. The remote setting of field anesthesia often dictates the limitations of equipment and personnel that are available for patient monitoring during the anesthetic event. While the most basic forms of anesthetic monitoring consist of measurements of heart rate, pulse quality, respiratory rate, and body temperature and can be carried out by the anesthetist with the use of their eyes, ears, a stethoscope, and a rectal thermometer, more advanced monitoring equipment is now available for field use. Ideally, monitoring of the cardiovascular and respiratory systems should be continuous, with intermittent recordings of the parameters every 5–10 minutes on a designated anesthetic record. In addition to these continuously monitored parameters, the anesthetic depth and temperature should be monitored intermittently.

While it is critical to interpret monitoring devices simultaneously and in relation to one another, it is helpful to categorize monitors based on function and body system, specifically, those used for respiratory, cardiovascular, thermal, and, less commonly, depth of anesthesia monitoring. Each of the anesthetic monitoring parameters simply evaluates a relationship of metabolic supply and demand.

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The most simplistic and yet most critical aspect of respiratory physiology is knowing that the respiratory system is always serving metabolic demand by performing two primary tasks: (i) absorbing oxygen and (ii) eliminating carbon dioxide (ventilation). To complete these tasks, the cardiovascular system must ensure the delivery of oxygen and the removal of carbon dioxide from distant parts of the body through blood flow (perfusion). Assigning numerical values to the interplay of oxygenation, ventilation, and perfusion is the sole function of an anesthetic monitor.

Anesthetic monitoring devices are categorized as either direct (invasive) or indirect (noninvasive) indicators of respiratory and cardiovascular function (Dorsch & Dorsch 2008). Direct monitoring devices are often considered the most accurate and applicable across taxa. Noninvasive monitors carry many benefits for the anesthetist and the patient, but can be hampered by inaccuracy and species-specific nuances. For this reason, indirect devices need to be validated in the species of interest (Brown et al. 2007; Mosley 2015).

Respiratory Monitoring Devices

The primary means of assessing oxygenation and ventilation are visual assessment of respiratory depth and frequency, indirect monitoring with pulse oximetry and capnography, and direct monitoring with blood gas analysis (Dorsch & Dorsch 2008). While visual assessment is crucial in each anesthetized case, without objective quantification of oxygenation and ventilation complete assessment of the respiratory system is impossible. States of hypoxia and hypercapnia can both affect respiratory rate and rhythm, necessitating deeper evaluation.

The Pulse Oximeter

The pulse oximeter is a commonly used, noninvasive device that uses photoplethysmography to determine arterial hemoglobin saturation. It uses light-emitting diodes (LEDs) and photosensors to detect pulsatile blood flow and determine a ratio of oxygenated to deoxygenated hemoglobin based on differential light absorption. Its primary purpose is to provide real-time assessment of changes in oxygenation. As values are generated with each beat of the heart and subsequent pulse wave, changes can be detected almost instantaneously. The limitations come from the fact that a pulse oximeter can only provide information about the oxygen saturation of hemoglobin in pulsatile arterial blood (SaO_2) (Dorsch & Dorsch 2008). Oxygen is carried bound to hemoglobin (Hb) in red blood cells and dissolved in the blood (measured as the partial pressure of dissolved oxygen in arterial blood, PaO_2). Total arterial oxygen content (CaO_2) is determined by the following equation: $CaO_2 = (1.34 \times Hb \times SaO_2) + (0.0031 \times PaO_2)$. Because hemoglobin carries the majority of oxygen, total content can be heavily influenced by both hemoglobin saturation and hemoglobin content.

Because the pulse oximeter is a simple and easily available, near-instantaneous monitor, it is very widely used and is capable of providing real-time indications of changes in oxygenation and heart rate. This timely feedback allows an anesthetist to intervene quickly to control hypoxemia.

The pulse oximeter probe typically consists of two light emitters and one or more light sensors. Each of the two LEDs projects a different wavelength of light through the tissue bed it is contacting. The two different wavelengths correspond to the wavelengths of light absorbed by oxygenated and deoxygenated hemoglobin. Opposite the LED, a photosensor measures the light that is transmitted (i.e., not absorbed) through the tissue and the machine calculates the ratio of oxygenated to deoxygenated hemoglobin (Dorsch & Dorsch 2008).

Accurate performance depends on multiple factors, including good tissue perfusion, good pulse quality, light-permeable epidermis, and hemoglobin and oxyhemoglobin, which absorb light at preset wavelengths. Pulse quality can be affected by hypotension and low cardiac output, and regionally affected by vasoconstriction and vasodilation. Species differences in hemoglobin structure could affect the accuracy of the reading. In cases of anemia, a patient may have excellent hemoglobin saturation, but an overall deficiency in hemoglobin will still result in poor oxygen delivery. Other sources of error include patient movement, bright ambient light, and the fact that most devices are not calibrated to read accurately below 80%.

Capnography

Capnography is arguably the most useful anesthetic monitoring technique and often the most underused (Fig. 3.1). Effective capnography can identify conditions that might lead to hypoxia before a patient is hypoxic and is one of the most reliable ways of detecting cardiac arrest and airway obstruction. The capnograph can also be used for confirming endotracheal tube placement in challenging intubations, detecting disconnections and leaks, and problems with sodalime and one-way valves. The capnograph typically uses infrared spectrometry to determine the partial pressure of CO_2 in expired gas (Bednarski et al. 2011; Mosley 2015). This generates three pieces of information (i) the end-tidal CO_2 ($ETCO_2$) partial pressure, (ii) the capnograph waveform, and (iii) the respiratory rate. The accuracy of capnography has been evaluated in very few nonmammalian species (Desmarchelier et al. 2007).



Figure 3.1 Monitoring a dolphin with mainstream capnography at the blowhole. The animal is lightly sedated and manually restrained, and ventilation is monitored continuously. Electrocardiography leads are placed on either side of the thorax behind the pectoral flippers for two-lead electrocardiography. Photo credit: Chicago Zoological Society.

For CO_2 to be detected on a capnograph, three critical physiologic processes must be happening: (i) cellular metabolism has to produce CO_2, (ii) circulation has to bring CO_2 from the periphery to the lungs, and (iii) the lungs have to be ventilating for the CO_2 to be exhaled and detected by the monitor. Abnormalities in $ETCO_2$ can occur due to derangements in any of those three processes. In a healthy "normal" animal, $ETCO_2$ provides a close approximation of the arterial partial pressure of CO_2 ($PaCO_2$), the indicator of ventilatory function and respiratory pH balance. Typically, $ETCO_2$ underestimates $PaCO_2$ by 2–5 mmHg. Hypoventilation can cause increases in $ETCO_2$ and $PaCO_2$. Hyperventilation can cause decreases in both. There are also numerous scenarios when the discrepancy between expired and arterial CO_2 may grow (Morkel et al. 2010). These include any state of poor perfusion, which decreases cardiac output and pulmonary perfusion. With less blood delivered to the lungs, there is less CO_2 exhaled, but there is no change in CO_2 production.

Many practitioners use their capnograph simply for one value, the $ETCO_2$. That single number can be used as an effective indicator of ventilatory function, but the capnograph waveform provides many more valuable pieces of information about equipment and animal function. It can track changes in not only ventilation, but cardiac output and metabolic rate.

Blood Gas Monitoring

Blood glucose, systemic lactate, and blood gases can be easily assessed with point-of-care portable analyzers (Burgdorf-Moisuk et al. 2012; Posner et al. 2005). These measurements, in conjunction with other monitoring techniques, allow an overall assessment of the animal, including cardiopulmonary stability, tissue perfusion, and likelihood of intraprocedural or postcapture complications.

Deleterious changes in blood pH, oxygenation, and ventilation can be rapidly diagnosed and treated. Point-of-care blood gas analyzers are ideally suited for use in field and zoological settings. The most commonly used analyzers are battery operated and require only a small volume of blood (0.2–0.5 mL). This allows them to be used in remote settings and with small patients. Additionally, results are generated in 2–3 minutes, which can satisfy the needs of many impatient zoo clinicians (Fahlman et al. 2010). Most analyzers can provide immediate information about blood oxygenation, ventilation, blood pH, glucose, and electrolytes. Immediate information also allows rapid adjustment of anesthetic management.

Maintenance of normal blood pH (approximately 7.4 for most mammals) is crucial for homeostatic function. As such, respiratory and metabolic processes have evolved with multiple redundancies to preserve physiologic pH. Most ectothermic species, and some mammals and birds (especially diving animals) have adaptations which allow for a much wider range of acceptable blood pH. While this provides an additional safety buffer for these animals, it does complicate interpretation of blood gases and determining what is normal and what requires correction. Hypoxemia, hypoventilation, and poor perfusion are some of the most significant anesthetic complications experienced in the anesthesia of captive and free-ranging wildlife. With routine use of blood gas analyzers many of these complications can be detected early and potentially corrected. While pulse oximetery and capnography provide useful, noninvasive, second-to-second assessments of ventilation and oxygenation, both methodologies can have some drawbacks that compromise their accuracy. Direct blood gas analysis can identify abnormalities in species for which noninvasive methodology is not validated. A capnograph can provide a noninvasive assessment of expired CO_2, which should be similar to arterial CO_2. Without blood gas analysis, it is possible that an increase in physiologic dead space could compromise the accuracy of the capnograph. In species capable of pulmonary shunting, such as reptiles, the expired CO_2 may not represent the arterial CO_2 at all.

Sample Collection

Blood should be collected anaerobically into a heparinized syringe. Excessive heparin can affect parameters, including hematocrit and ionized calcium. Samples should be analyzed as quickly as possible and care should be taken to not

introduce air bubbles into the sample. In reality, small air bubbles may not affect the accuracy of the sample significantly, but can cause the analyzer to malfunction. Excessive room air contamination can cause a decrease in the measured CO_2 and an increase or decrease in PaO_2 depending on the percentage of inspired oxygen.

- Arterial collection sites:
  - auricular artery: elephants, rhinoceros, most ruminants
  - facial, transverse facial artery: equids, some ruminants
  - radial artery: apes
  - dorsal pedal artery: large carnivores
  - femoral artery: small carnivores, small primates
  - superficial ulnar artery: birds
- Venous collection sites: jugular, auricular or lingual veins

Jugular and auricular sites provide the easiest sampling and jugular sampling also provides the closest approximation of a true mixed venous sample. Lingual samples provide a close approximation of arterial gas tensions.

Arterial versus Venous Comparison

Arterial samples are crucial for assessing pulmonary performance, especially oxygenation. A venous blood gas can provide pH, CO_2, and a crude estimate of body oxygen demand. The oxygen content of venous blood varies greatly depending on the sampling site and level of metabolism and should not be used to approximate arterial oxygen content. A central mixed venous sample can provide very useful information about oxygen consumption and anaerobic metabolism, but requires an arterial sample for comparison.

A blood gas report contains multiple values, some of which are directly measured and some of which are calculated from the measured parameters based on algorithms validated for human use. Measured parameters include pH, partial pressure of CO_2 ($PaCO_2$), partial pressure of oxygen (PaO_2), hematocrit, and lactate. Most analyzers also measure certain electrolytes, including Na, Cl, K, and ionized Ca. From these measurements, the machine will calculate hemoglobin, bicarbonate (HCO_3), base excess, and oxygen saturation (SO_2). The formulae for calculated parameters are given in Appendix 3.1. Oxygen saturation is calculated assuming a "normal" adult human hemoglobin oxygen dissociation curve. Some machines will correct for changes in electrolyte concentrations based on changes in blood pH.

All blood gas analyzers measure dissolved gases at a standard temperature (usually, 37°C). When the patient's body temperature differs significantly from 37°C it may be useful to "correct" the sample data to the body temperature (Dorsch & Dorsch 2008). Temperature correction of blood gases is fairly controversial, even in human medicine. In short, the concern is that in a hypothermic patient, reported values (measured at 37°C) may not represent the true values in the patient. At the same time, corrected values are not applicable to any known reference ranges. Human reference ranges are designed to be used with a blood temperature of 37°C. For near-normothermic mammals, temperature correction does not make a significant difference and the difference is not usually a reason to change the course of treatment. For ectotherms and severely hypothermic mammals, temperature correction may be more valuable (Hanley et al. 2010). Most analyzers use a built-in algorithm for temperature correction. There are multiple published references detailing correction formulae for ectotherms (Keller et al. 2012).

Basic interpretation should be a straightforward, step-by-step process.

Six-step interpretation:

1) What is the pH? Normal pH for most mammals is 7.35–7.45. Is the patient's pH low (acidemia) or high (alkelemia)?
2) What is the PaO_2 (arterial sample)? Normal arterial PaO_2 is 100 mmHg, while breathing room air. Is the patient hypoxemic? Is the patient's oxygen tension appropriate for the fraction of oxygen that it is breathing?
3) What is the $PaCO_2$? Normal $PaCO_2$ is 35–45 mmHg. $PaCO_2$ represents the respiratory component of the acid-base derangement. Changes in $PaCO_2$ result in respiratory acidosis and alkalosis.
4) What is the metabolic component (HCO_3 and base excess)? Are the changes appropriate for the changes in $PaCO_2$ or is there a metabolic acidosis or alkalosis?
5) What is the level of compensation? Derangements of either respiratory or metabolic acid-base balance often result in compensatory change from the other system, i.e. metabolic acidosis often results in a compensatory respiratory alkalosis (hyperventilation).
6) Are there abnormalities in electrolytes or lactate?

1) pH: pH only gives us the direction and extent of the derangement, but does not tell us the source of the problem. It does help narrow down the differentials for the primary problem and the list of actions that need to be carried out to correct the problem. Carnivores tend to have slightly more acidic pH, while herbivores and omnivores with high carbohydrate diets tend to have more alkaline blood pH.
2) PaO_2: Normal PaO_2 (arterial partial pressure of oxygen) is 100 mmHg when breathing room air and 400–500 mmHg when breathing 100% oxygen. Hypoxemia is defined as $PaO_2 < 60$ mmHg. Calculating an alveolar-to-arterial oxygen gradient (A-a gradient)

provides useful information about the cause of the hypoxemia. In addition, calculating a PaO_2/FiO_2 (partial pressure to fraction of inspired oxygen) ratio provides a very easy means of assessing pulmonary function. The A-a gradient is most accurate when the patient is breathing room air (21% oxygen) while the PaO_2/FiO_2 ratio can be done with any FiO_2.

A measured hypoxemia is typically the result of one of five problems (Paterson et al., 2009):

1) Hypoventilation: The patient is not breathing frequently or deeply enough. In cases of hypoventilation, the PaO_2 is low but there is a normal A-a gradient.
2) Low FiO_2: The inspired percentage of oxygen is too low. This is rare as most anesthetized animals are breathing an enriched oxygen mixture. The animal is hypoxemic with a normal PaO_2/FiO_2 (partial pressure of arterial oxygen/fraction inspired oxygen) ratio.
3) Ventilation/perfusion mismatching: This is quite common and is likely the main source of hypoxemia in anesthetized large animals. It is often associated with atelectasis and can be exacerbated by poor cardiac output and poor pulmonary perfusion (Morkel et al. 2010).
4) Diffusion impairment: Rare, will not discussed.
5) Anatomic right-to-left shunt: Rare, rare will not be discussed.

3) $PaCO_2$: Carbon dioxide tension quantifies the balance between cellular metabolism and alveolar ventilation. Hypercapnea typically results from a decrease in ventilation, but can be a result of increased metabolism (exertion). Hypocapnea could be from hyperventilation or decreased metabolic activity. $PaCO_2$ can also be compared to $ETCO_2$ to determine if there is an increase in physiologic dead space. $ETCO_2$ should slightly underestimate arterial CO_2 by 5 mmHg. An increase in this difference indicates that there are areas of lung that are ventilated, but not perfused. This occurs with pulmonary thromboembolism and decreased pulmonary perfusion secondary to decreased cardiac output.
4) Bicarbonate and base excess: Both of these calculated parameters provide information about metabolic alkalosis or acidosis. These are indirect measures as both are derived from the measured CO_2 on the blood gas (formulas given above). A typical reference range for HCO_3 is 19–24 mEq/L. To account for the effect of CO_2 on HCO_3 calculation, base excess (BE) can be used. BE determines the amount of bicarbonate that needs to be added to blood to bring the pH back to 7.4, when $PaCO_2$ is set at 40. Essentially, BE factors in the effect of body buffer systems and factors out the effect of CO_2 on bicarbonate to determine the metabolic contribution to the acid-base balance. The reference interval for bicarbonate is −4 to 4 mEq/L. While not a perfect system, the BE provides a rapid way of determining the metabolic disturbance. If the BE is high, there is a metabolic alkalosis and if it is low there is a metabolic acidosis, regardless of the respiratory disturbance.
5) Compensation: Before evaluating compensation, look back at the pH. If the pH is low, the primary process is an acidosis and the compensatory process (if present) is an alkalosis. Compensation rarely brings the patient back to a normal pH and never overcompensates. A primary chronic respiratory acidosis (hypoventilation) will lead to a compensatory metabolic alkalosis, but pH will not return to normal and will not become alkalotic. Methods of compensation include chemical buffers (few seconds), respiratory (few minutes), and metabolic compensation (few days).
6) Lactate and electrolytes: Blood lactate is a by-product and indicator of anaerobic metabolism (Harms et al. 2003). Increases in blood lactate typically accompany decreases in tissue perfusion. This could include ischemic muscle from a positional or exertional myopathy in which metabolic oxygen demand has outstripped the available oxygen delivery. Focal ischemia (strangulated intestine, compromised blood flow to a limb after trauma) can also increase lactate production, and in some cases the hyperlactatemia will only be seen after perfusion is reestablished. Electrolyte interpretation is similar to routine chemistry interpretation.

Effect of Capture on Blood Gases

Typically changes seen during capture include hypoxemia, hypercapnea, lactic acidosis, and hyperkalemia from acidosis and myocyte rupture. Strenuous capture can result in metabolic acidosis from increased production of lactate. Hypoxemia can exacerbate lactate production and hypercapnea from increased metabolic production of CO_2 during exertion can lead to worsening of acidosis (Fahlman et al. 2011; Hanley et al. 2005; Mans et al. 2012). Similar changes in blood oxygenation, CO_2, and lactate production can result from body positioning during anesthesia. For example, moving a rhinoceros from lateral to sternal recumbency may improve its ventilation and oxygenation while compromising muscle perfusion and increasing lactate build-up (Morkel et al. 2010).

Ectotherm Blood Gases

There are a number of published reports on the use of blood gases for evaluating reptiles, fish, and invertebrates (Hanley et al. 2010; Lewbart et al. 2014; Sheldon et al. 2019).

Important aspects to keep under consideration include the role of temperature compensation and the wide range of acceptable blood pH in most ectotherms (Keller et al. 2012). Most of the referenced studies use a taxon-specific formula for correcting pH and dissolved gases for body temperature. In many cases, body temperature is assumed to be the ambient temperature. In some instances, clinically significant abnormalities were not noted unless temperature correction was performed. While the correction formulas may be valid, it is important to remember that corrected values should not be compared to standard reference ranges. Species- and temperature-specific ranges should be established.

Cardiovascular Monitoring

Cardiovascular monitoring consists of assessing the heart rate and rhythm with auscultation, palpation, and electrocardiography and quantifying perfusion with direct and indirect measurement of blood pressure.

Electrocardiography

Electrocardiography is applicable to a wide ranges of species and not only provides information about heart rate and rhythm, but can be used to diagnose conduction abnormalities associated with electrolyte abnormalities and myocardial ischemia (Bartlett et al. 2009; Harms et al. 2013; Hassanpour et al. 2013). Accurate diagnosis of the rhythm is imperative for guiding treatment. Some anesthetic agents, especially the alpha-2 agonists, can induce bradyarrythmias and atrioventricular nodal blocks, which may be difficult to discern by auscultation alone. Ventricular arrhythmias may be associated with hypoxia, myocardial damage, and excessive catecholamine release seen with ultrapotent opioid administration. Diagnosis of the rhythm is imperative for guiding treatment. For routine anesthetic monitoring, a three-lead ECG is typically employed, utilizing the principles of Einthoven's triangle. The three leads are positive, negative, and ground (neutral) leads; animal body confirmation may affect the necessary lead placements to create an appropriate vector across the heart (Dorsch & Dorsch 2008; Schumacher et al. 2003). In typical small quadrupedal species, the most common recording is a lead II ECG with the negative electrode at the right forelimb and the positive electrode at the left hindlimb (Fig. 3.2). In larger animals, a base–apex placement is used, with the positive electrode on the left thorax caudal to the heart, the negative electrode on the skin over the right jugular furrow, and the ground electrode attached to the skin far from the heart (Gandolf et al. 2010; Pourjafar et al. 2011). These basic techniques for ECG recording have been modified and normal values have been described for cetaceans, elephants, reptiles, and a wide variety of birds (Bartlett et al. 2009; Harms et al. 2013; Hassanpour et al. 2013).

Blood Pressure Measurement

In many cases, blood pressure itself is not a primary concern and is an easily measured surrogate for cardiac output and perfusion (Mosley 2015). Blood pressure is product of two values: cardiac output and systemic vascular resistance (SVR). Cardiac output itself is determined by two values, heart rate (HR) and stroke volume (SV). Based on these relationships, derangements of blood pressure typically result



Figure 3.2 Surgical monitoring of a smokey jungle frog (*Leptodactylus pentodactylus*). Two-lead electrocardiography is used to monitor heart rate and rhythm, and a pulse oximeter has been placed on the left hind foot for approximation of hemoglobin oxygen saturation. The animal is endotracheally intubated and monitored with capnography. Photo credit: Chicago Zoological Society.

from a change in HR, SV or SVR or some combination of these three parameters. Unfortunately, cardiac output and SVR are not easily measured in clinical patients and thus blood pressure is the most convenient and reliable surrogate.

There are two means of collecting blood pressure: direct or indirect methods. Direct, or invasive, measurement of blood pressure requires inserting a catheter in a suitable artery and measuring arterial pressures with a transducer. This remains the gold standard, although it can be technically challenging (Brown et al. 2007; Watson et al. 2019).

Indirect, or noninvasive, blood pressure measurement is typically performed with an oscillometric monitor. The device inflates an air-filled cuff to occlude blood flow in an artery. It then decreases pressure in the cuff in a stepwise fashion to detect changes in the frequency of oscillation produced by pulses in blood vessels. If the time between successive pulses is sufficiently long, the device may provide an inaccurate reading (Dorsch & Dorsch 2008). This source of error is commonly seen when oscillometric devices are used on animals with low heart rates, such as reptiles or equids (Chinnadurai et al. 2009). Other sources for failure of the oscillometric device include movement by the patient and poor signal quality. Hypotensive patients with poor peripheral perfusion often generate errors in blood pressure measurement. Unfortunately, these are often the patients that need accurate readings the most.

Due to the high potential for inaccuracy with commercial oscillometric units in veterinary medicine, the American College of Veterinary Internal Medicine released a consensus statement outlining guidelines for blood pressure measurement in dogs and cats. Those guidelines state that "ideally blood pressure should be measured with devices that have been validated in the species of interest and under the circumstances in which the patient is being tested" (Brown et al. 2007). Given the wide range of animals that are housed and treated in zoological collections, this bar is rarely ever met, but should be a goal for ideal patient care.

Various oscillometric methods and devices have been evaluated for use in nondomestic species, including megavertebrates, nondomestic felids, Hispaniolan Amazon parrots, lizards, and snakes, with varying results (Acierno et al. 2008; Bertelsen et al. 2017; Chinnadurai et al. 2009, 2010; Sadler et al. 2013). Many have reported that indirect methods cannot be substituted for direct blood pressure measurements. These findings are important because often oscillometric blood pressure is used across taxa in veterinary medicine without questioning the validity. Doppler ultrasound devices can be used for detection of heartbeat or peripheral pulsations and, in some species, approximation of blood pressure when used with a sphygnomanometer.

There are intrinsic limitations when devices designed and validated for humans or domestic mammals are applied to nonmammalian species. Two studies in avian species showed poor correlation between direct systolic arterial blood pressure measurements and indirect measurements using either Doppler or oscillometric devices (Acierno et al. 2008; Zehnder et al. 2009). In fact, studies in multiple parrot species raised doubts that indirect measurements of blood pressure by Doppler are even repeatable in the same animal at the same time point due to disagreement between cuff placements on the same limb from the same bird (Acierno et al. 2008). The overall precision of Doppler blood pressure measurements was poor. Based on these findings, even using Doppler blood pressure measurements to monitor trends in an individual bird is dubious clinical practice.

Similar findings have also been reported in boid snakes and green iguanas. In iguanas, an oscillometric device failed to provide reading for most attempts and had poor correlation when compared to directly measured pressures (Chinnadurai et al. 2010). When used on the tail of anesthetized boid snakes, the same device had a much lower failure rate and consistently overestimated systolic blood pressure, while underestimating diastolic and mean pressures (Fig. 3.3) (Chinnadurai et al. 2009).

The most accurate technique for blood pressure assessment involves placement of an arterial catheter and measurement through an arterial blood pressure (Saugel et al. 2014). Invasive blood pressure monitoring with an intraarterial catheter requires continuous connection of the animal to a monitoring device, limiting movement. These devices can be technically challenging to place and operate, and carry the risk of thrombosis and hemorrhage. Placement sites for arterial catheters are the same as those listed for arterial sampling of blood gases.

Body-temperature Monitoring

Peri-anesthetic hypothermia is one of the most common complications in veterinary anesthesia (Ko & Krimins 2014). Anesthetic drugs often cause blunting of normal physiologic thermoregulation and shivering, inhalants, and some injectables cause direct vasodilation, increasing heat loss from the skin. During field captures, especially with high ambient temperatures, hyperthermia can easily occur (Chinnadurai et al. 2016). Even short-duration derangements in body temperature can alert metabolic oxygen demand, affect recovery time, and increase the risk of wound infection as well as contribute to arrhythmias and coagulation defects (Pottie et al. 2007; Torossian 2008), making temperature monitoring and thermal support essential, especially in field settings.

During an anesthetic episode, body heat may be lost by four mechanisms: radiation, convection, conduction, and



Figure 3.3 Doppler ultrasound placement over the heart on an anesthetized snake for monitoring heart rate. Photo credit: Chicago Zoological Society.

evaporation. Radiation is loss of heat through infrared emission to the environment surrounding the patient. This does not include heat lost through direct contact with a cold surface. Radiation accounts for 60–70% of heat loss in anesthetized humans. Convection is loss of heat to air currents around the body. Most hospital situations involve conditioned air moved through ventilation systems with a high turnover rate. This results in a continuous loss of heat to the air. Conduction consists of direct loss of heat to surfaces in contact with a patient. This includes the operating table, as well as intravenous fluids, ultrasound gel, and water on the patient. Evaporation is the loss of warm, humid air from the respiratory tract, skin, or an open surgical wound (Ko & Krimins 2014; van Zeeland et al. 2012). Alcohol application can accelerate evaporative cooling from the skin.

Inexpensive thermometers designed for home use by people often have a narrow working range of temperatures and may fail to give a reading in hypothermic and hyperthemic patients or ectothermic patients. Thermistor probes associated with anesthetic multiparameter monitors maintain a much larger working range and can be used as esophageal or rectal probes. To assess core body temperature, it is important to position the tip of an esophageal thermistor probe close to the heart (Dorsch & Dorsch 2008; Machon 1999). In some species, cloacal or distal rectal temperatures may underestimate core temperature.

Systematic Assessment and Treatment of Anesthetic Complications

Veterinary students are taught to use subjective and objective data to identify a problem, generate a list of differentials, and systematically rule in or rule out those differentials until coming to a diagnosis that dictates treatment. Unfortunately, when it comes to anesthetic management, skilled veterinarians often fail to take the same linear and logical approach of identifying changes in vital parameters as data to be used in the diagnosis of a problem and its treatment.

The first step in diagnosing an anesthetic problem is determining if you have an equipment problem or a patient problem. We do this by instinct sometimes, but too often, we write off a real problem as an equipment problem. The easiest way to distinguish patient problems from equipment problems is to employ redundant monitors. If the patient is bradycardic on the ECG, check the pulse oximeter or auscultate with a stethoscope. Sometimes the interpretation of the redundant monitor is less straightforward. If the patient's blood pressure drops suddenly, check the heart rate. A normal animal should compensate for a sudden drop in blood pressure with a compensatory increase in heart rate. Very rarely does an acute change in heart rate, respiratory rate, blood pressure, oxygen saturation, or expired CO_2 occur without deviation in another parameter. Years of clinical practice often result in some instinctual responses to anesthetic problems. The patient is tachycardic, therefore it must be light, and the anesthetist should turn up the inhalant anesthetic. This approach is piecemeal and often ends up in misdiagnosis and mistreatment. We will look here at some of the most common anesthetic complications that we deal with every day, but we will look at them with a problem-based approach. With each problem "symptom" we will list three or four differentials.

Hypotension

Most causes of hypotension involve a change in HR, SV, or SVR, as mentioned above. Changes in the different parameters are interrelated. Aside from being important for basic physiology, remembering these three components gives you a set list of differentials for why your patient is hypotensive. Decreased heart rate can be caused by drugs, such as opioids or alpha-2 agonists, or simply high vagal tone in the patient. Decreased systemic vascular resistance is often

drug-induced vasodilation from inhalant anesthesia, acepromazine, or azaperone. It can also be inappropriate vasodilation, which occurs with sepsis. Decreased strove volume occurs with decreased preload or venous return. This can accompany true hypovolemia with dehydration or blood loss, mechanical obstruction to venous return from an abdominal mass, or as a side effect of positive pressure ventilation.

Steps in treating hypotension:

1) Assess and adjust anesthetic depth. Inhalant anesthetics affect vascular tone and contractility, and are potent hypotensive agents. Too often, a vaporizer is set at a given percentage and forgotten for the remainder of the procedure. Use only as much as you need.
2) Address preload. Hypovolemia can be temporarily addressed with intravenous fluids such as crystalloids and colloids. Animals with high volume abdominal contents, like a rumen, fetus, or abdominal mass, may have decreased return of venous blood through the caudal vena cava to the heart, especially in dorsal recumbency, and may benefit from being rolled into lateral recumbency. Additionally, positive pressure ventilation also decreases venous return and may need to be adjusted in the face of hypotension.
3) Improve vascular tone. Adjusting depth may increase sympathetic stimulation and promote vasoconstriction. Drugs such as ephedrine, phenylephrine stimulate alpha-1 receptors and cause vasoconstriction.
4) Increase cardiac output:
   - If the animal is bradycardic, consider atropine or glycopyrrolate.
   - Increase the contractile force of the heart by using pressors such as dopamine or dobutamine.

Treating Tachycardia and Bradycardia

Changes in heart rate are integrally tied to changes in blood pressure. In many situations, the absolute heart rate is not nearly as important as the role heart rate plays in cardiac output and perfusion. It is crucial to interpret heart rate in relation to blood pressure and cardiac output. It is rarely necessary to treat bradycardia in a normotensive, nonarrhythmic patient. For abnormalities in heart rate, treating the primary problem is the primary concern.

Reasons for tachycardia:

1) compensation for low blood pressure (baroreceptor response)
2) compensation for hypoxemia (chemoreceptor response)
3) sympathetic stimulation from noxious stimuli (i.e. patient is too light)

Reasons for bradycardia:

1) response to high blood pressure (baroreceptor response)
2) direct vagal stimulation from anesthetic drugs (opioids, alpha-2 agonists)
3) excessive anesthetic depth.

Hypoxemia

In terrestrial mammals, hypoxemia is defined as an arterial partial pressure of oxygen less than 60 mmHg or an SpO_2 of less than 90%. Reasons for hypoxia are defined in the blood gas section above.

Tachypnea

We often assume that if a patient's respiratory rate increases, that it is light. In truth, there are likely four reasons why a patient is tachypneic under anesthesia:

1) they are hypercapneic
2) they are hypoxemic
3) they are at a light plane of anesthesia and responding to noxious stimulus
4) they are hyperthermic and trying to lose heat

When noticing any change in respiratory rate and character it is critical to evaluate the four possibilities above: the $ETCO_2$, the SpO_2, body temperature, and depth of anesthesia.

Effective anesthetic monitoring requires a basic understanding of the function of the monitor and the function of the body systems being monitored. Understanding that interaction will allow a safe anesthetist to make timely and accurate assessments and interventions to preserve organ function and the life of the patient (Fig. 3.4).



Figure 3.4 Multiparameter monitoring of a gorilla. Monitoring includes capnography, pulse oximetery, electrocardiography, and both direct and indirect blood pressure monitoring. Overall anesthetic monitoring is managed by a dedicated anesthetist. Photo credit: Chicago Zoological Society.

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Appendix

Formulae used by blood gas analyzers to calculate parameters:

1) HCO_3: $\log HCO_3 = pH + \log(PaCO_2 - 7.608)$
2) Base excess = $HCO_3 - 24.8 + 16.2(pH\ 7.4)$
3) Anion gap: $([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$
4) A-a gradient = $PaO_2 - PaO_2 = (FiO_2 \times (P_{bar} - PH_2O) - PaCO_2/0.8) - PaO_2$

   If performed at standard atmospheric pressure (760 mmHg) and room air (21% oxygen) the formula is simplified to $150 - 1.2(PaCO_2) - PaO_2$. The normal A-a gradient is 10–15 mmHg.
5) Physiologic dead space: $Vd/Vt = (PaCO_2 - EtCO_2)/PaCO_2$. The normal dead space is 0.3–0.5.

4

Emergencies and Complications

Nigel Caulkett, Søren Boysen, and Jon M. Arnemo

Emergency Preparedness

A key element of any successful anesthetic procedure is to anticipate and prepare for potential complications. This is particularly important in zoo and wildlife situations because anesthesia may take place in remote environments with limited availability of equipment and drugs for supportive care. Careful consideration of potential complications prior to the anesthetic procedure will help improve outcomes when emergencies occur. This section provides a summary of considerations prior to an anesthetic or capture event. More complete guidelines can be found in Chinnadurai et al. (2016) and Arnemo et al. (2014).

Environmental Considerations

Prior to any capture event careful consideration should be given to the environment in which the event will take place. With zoo animals it is sometimes possible to plan the event in a relatively controlled environment, but with free-ranging wildlife that is rarely the case. Consideration should be given to ambient temperature because this can increase the risk of thermoregulatory complications. The type of terrain should be considered, particularly the presence of waterbodies or cliffs. Forested terrain can mean challenges in tracking animals and telemetry darts may need to be considered. Access to the capture site is a consideration. If only foot access is available there will be a limit on how much equipment can be carried and careful consideration must be given to the type and amount of equipment carried.

Pre-immobilization Plan and Briefing

Prior to any immobilization a plan should be formulated based on the environmental conditions and the necessity to perform the procedure, i.e. is the procedure elective or emergent. The plan should include a human safety briefing and include how the team will respond to a human or animal emergency. Personnel should be familiar with the contents of the emergency pack and should be aware of their individual roles in an emergency.

Emergency Pack

An emergency pack should be carried during any immobilization procedure. At minimum it should contain the following:

- Equipment to provide airway support.
- Equipment to provide ventilation (if possible).
- Equipment to provide supplemental inspired oxygen.
- Intravenous catheters and tape.
- Intravenous fluids and administration sets.
- Emergency drugs, at minimum epinephrine, atropine, dexamethasone, and lidocaine without epinephrine.
- Equipment and supplies to treat trauma (wounds).
- Long-acting antibiotics and a nonsteroidal anti-inflammatory drug.
- A rumen tube to treat bloat.
- A means of providing euthanasia.

Immobilization, Sedation, and Anesthesia

The reliability of a capture technique is a major consideration during the capture process. The choice of technique can vary between captive and free-ranging animals, and depending on the ability to safely physically restrain the animal if arousal occurs. The process of zoo animal and wildlife capture and handling has improved dramatically over the years. Early techniques relied on the use of muscle relaxants alone. These drugs would paralyze the animal but not render them unconscious. The techniques were not humane or safe for the animals and sudden recoveries

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could place capture crews at risk. These techniques were simply a form of chemical immobilization. Potent opioids will induce a state of immobilization where the animal may still be responsive to external stimulation and may still have the potential to injure handlers if care is not taken around limbs, horns, or antlers. These drugs are often combined with a tranquilizer or sedative to induce a state of neuroleptanalgesia (Kreeger et al. 2009). Sedation is a component of anesthesia but differs from anesthesia in that stimulation may rouse the patient from their soporific state. Sedative techniques may be used to capture and restrain wildlife, particularly wild ungulates. The use of alpha-2 agonists alone can be unreliable. Combining alpha-2 agonists with tranquilizers and/or opioids will induce a synergistic effect and a deeper plane of sedation. The butorphanol-azaperone-medetomidine (BAM) combination is a good example of this synergism. Studies in American elk, using the bispectral index (BIS) to determine the plane of anesthesia, demonstrated that elk receiving BAM developed a deeper state of anesthesia than elk receiving carfentanil-xylazine. The BIS values reported with BAM were consistent with deep sedation (Kreeger et al. 2009). Caution should always be exercised to avoid arousal of animals restrained with deep sedation. Noise should be kept to a minimum, animals should be repositioned or moved in a cautious manner, and appropriate analgesia should be used to prevent painful stimulation. Sedation is appropriate in many capture situations, but anesthesia should be considered for larger or more dangerous species. Anesthesia differs from sedation in that the patient loses consciousness and cannot be roused until the drugs are metabolized. The most commonly used anesthetic drugs for wildlife capture and handling are the dissociative anesthetics, ketamine and tiletamine. Alfaxalone is a more recent addition to capture protocols. These drugs are typically used in addition to a sedation protocol. Dissociative anesthetics produce dose-dependent effects ranging from sedation to anesthesia. It is important to choose an appropriate intramuscular dose if anesthesia is desired. In some situations, intravenous (IV) titration and maintenance is advisable to achieve a desired plane of anesthesia, particularly if surgical interventions are to be performed. Dissociatives should be combined with a tranquilizer or sedative to reduce the risk of muscle rigidity or convulsive activity.

Inadequate Drug Dosing

Anesthesia and immobilization of zoo and wild animals is a particularly challenging field of veterinary anesthesiology. There are many factors that contribute to these challenges but a major one is the delivery of an appropriate drug dose to achieve reliable sedation or anesthesia. The use of remote drug-delivery techniques can pose a particular challenge. Injection site, needle length, and complete or partial failure of drug delivery from the dart can result in either failure to deliver the complete dose or delayed absorption into the circulation (Bergvall et al. 2015). The clinical impact is that the induction period may be very prolonged, the animal may completely fail to become recumbent, or it may be aroused when approached. Pharmacodynamics also play an important role. It is common for free-ranging or very excited animals to require a greater dose of capture drugs compared to calm or captive animals (Kreeger et al. 2023). This phenomenon can be particularly apparent when protocols based on alpha-2 agonists are utilized because competition for noradrenergic receptors increases in the face of elevated endogenous catecholamines. As sedation, with these drugs, occurs from reduction of sympathetic outflow in the central nervous system these animals may take longer to sedate or may fail to sedate adequately. The drug doses outlined in this textbook will serve as a good starting point for immobilization or anesthesia of a given species. It is important to note if the recommended dose was determined in captive or wild animals and the delivery technique used. There has been a great deal of good science performed to develop these capture techniques, but they will fail on occasion. The art of anesthesia comes into play when a decision must be made on how to best re-dose the animal. In some situations, a full dose of the drugs may be required, particularly if dart failure is suspected, if the animal is showing no signs of drug effect, or if human or animal safety is at risk. If the animal is showing some signs of drug effect a decision may be made to deliver a partial dose of the drugs. It can be challenging to determine what dose to deliver and the experience of the capture team plays an important role. It is always best to learn from experienced people who have mastered the art of these techniques to make the best judgement call on additional dosing in these situations.

Airway Support

Airway support can be challenging during an immobilization event as the induction period may be prolonged and with many species it is important to ensure that the animal is safely anesthetized prior to approach. The airway may be lost in this time period, with severe consequences. During the induction period it is important to observe the animal for chest excursions and to listen for upper airway noise. As soon as it is safe to approach the animal, the airway should be checked for patency and the head and neck placed in a

position to maximize ventilation. A complete discussion of airway support can be found in Cracknell (2014).

Unsupported Airway

Wild animals are frequently maintained with an unsupported airway during capture procedures. Unfortunately, this will place the animal at risk of hypoventilation, hypoxemia, and aspiration. Ideally the airway should always be supported, but logistically this may be a challenge under field conditions. If the animal is maintained with an unsupported airway, it should always be closely monitored to ensure that adequate chest excursions are present and that oxygenation is appropriate. Equipment should always be available to provide airway support in the event of loss of airway or apnea.

Infraglottic Airways

Endotracheal intubation via either the nasotracheal or orotracheal approach is the ideal method to provide airway support. A variety of endotracheal tube styles are available. The choice of a particular endotracheal tube depends on the species and the procedure being performed. Various methods are also available to facilitate endotracheal tube placement, including manual manipulation, laryngoscopy, and fiberoptic-guided placement. The equipment required and the technique is very species dependent. Please refer to individual species chapters in this textbook for recommendations on each species.

Supraglottic Airways

Supraglottic airways include nasopharyngeal airways and laryngeal mask airways (LMAs). Commercial veterinary LMAs are currently available for cats and rabbits (Croatz 2010). Human LMAs have been adapted for a variety of species (Cracknell 2014). The use of these devices has recently been described in calves (Armstrong et al. 2018) and free-ranging bighorn sheep (Hee et al. 2020). One major advantage of LMAs is the fact that they can readily be placed with a blind technique. This is a potential advantage in emergent situations, particularly for individuals who are not proficient at laryngoscopy (Fig. 4.1).

Confirmation of Airway Placement

It is always important to confirm correct airway placement immediately following intubation. The most rapid method to confirm placement is with capnography (Fig. 4.2). Placement of a capnograph and visualization of a normal capnograph waveform should be used whenever equipment is available. Alternate techniques can include palpation of the trachea and esophagus to determine if inadvertent esophageal intubation has been performed. Chest auscultation for bilateral lung sounds during ventilation will also assist in confirmation that placement is endotracheal rather than endobronchial.



Figure 4.1 Placing a laryngeal mask airway in a Bighorn sheep lamb.

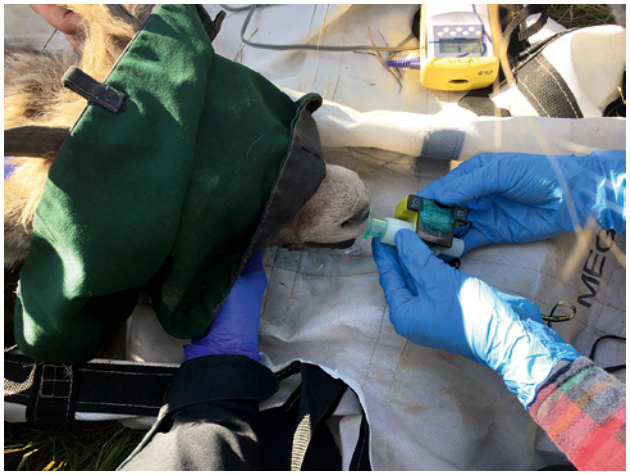


Figure 4.2 Capnography can be used to determine correct placement of endotracheal tubes or supraglottic airways.

Hypoventilation

Hypoventilation during zoo animal and wildlife anesthesia is typically the result of drug-induced respiratory depression. Potent opioids, alpha-2 agonists, dissociative anesthetics, GABAergic induction agents, and volatile anesthetics can all contribute to hypoventilation. Hypoxemia may be a consequence of hypoventilation,

particularly if the animal is breathing ambient air. Hypoxemia is exacerbated by ventilation-perfusion mismatching induced by drugs, positional changes, or recumbency. Given the frequency and potential adverse consequences of these complications, availability of equipment for ventilation and oxygenation is advocated as a best practice guideline during wildlife anesthesia (Chinnadurai et al. 2016). Hypoventilation can be challenging to treat under field conditions. Pharmacological interventions may include partial antagonism of potent opioids (Moresco et al. 2001; Buss et al. 2018) or the use of respiratory stimulating drugs (Haw et al. 2016). These methods may be useful in specific situations and deserve more study. Currently the definitive treatment for hypoventilation is the use of intermittent positive pressure ventilation (IPPV). In zoo situations ventilation can typically be performed with a small or large animal ventilator attached to an anesthetic machine. In field situations a bag valve mask (BVM) may be an option in animals up to 100 kg. A demand valve can be used in animals >100 kg. Both of these techniques will require placement of an airway prior to use.

Bag Valve Mask

The BVM or ambu bag is a self-inflating bag with a valve that directs inspiratory and expiratory flow to provide ventilator support. The bag can be used with a mask in humans, but in veterinary patients it is typically attached to an endotracheal tube. Flow is typically adjusted to obtain adequate chest excursions and rate is adjusted by the operator. Ideally a BVM with a pressure relief valve should be used to help avoid barotrauma. Adult and pediatric bags are available and can be readily adapted to many veterinary patients. The BVM can be used with ambient air or enriched oxygen if a tank and regulator are available.

Demand Valves

In field situations, IPPV of large animals can be accomplished with a demand valve. The demand valve has been used to successfully ventilate horses for many years, particularly in the postoperative period (Waterman et al. 1982). The use of demand valves has also been described in extremely large mammals. Horne et al. (2001) described a technique whereby two demand valves combined with a Y connector can be used to ventilate African elephants. Demand valves offer an advantage over large animal ventilators for field use as they are compact and easy to transport. They must be manually cycled, however, which ties up personnel, and high flows of oxygen are required to run them, but oxygen supply can be a challenge in the field.

Hypoxemia

Hypoxemia is a very common complication associated with immobilization and anesthesia. It is often defined as partial pressure of arterial oxygen (PaO_2) <60 mmHg or hemoglobin saturation <85%, but a number of factors, particularly the species or altitude, can influence normal values. Several factors contribute to the development of hypoxemia during wildlife capture and handling. Hypoventilation, induced by potent opioids, can result in hypoxemia (Buss et al. 2018; Haw et al. 2016; Paterson et al. 2009; Moresco et al. 2001). Many other drugs, including ketamine, alfaxalone, and propofol, can contribute to hypoventilation. The alpha-2 agonists will exacerbate ventilation:perfusion (V/Q) mismatching and contribute to hypoxemia (Kästner 2006; Lakhdhir et al. 2020; Read 2003). Other factors that can contribute to hypoxemia include positional changes (Cattet et al. 1999), ruminal tympany, and compromised airways. Severe hypoxemia may induce arrhythmias (Caulkett et al. 1994, 2000) and potentially acute death. The impact of mild to moderate hypoxemia in wildlife is not well described. Hypoxemia will result in prolongation of recovery time following reversal (Paterson et al. 2009; Risling et al. 2011). The impact on the animal post recovery has not been determined. It is considered good anesthetic practice to prevent or treat hypoxemia. In controlled settings an anesthetic machine with an appropriate circuit is the simplest way to provide supplemental oxygen to an anesthetized patient. Treatment of hypoxemia in the field is typically achieved via the provision of intranasal or intratracheal oxygen. A complete discussion of hypoxemia can be found in Fahlman (2014).

Intranasal and Intratracheal Oxygen Administration

Intranasal administration of oxygen can be used to increase the fraction of inspired oxygen (FIO_2), which will help offset the decrease in PaO_2 observed during immobilization. In this technique a cannula is placed into the nostril and advanced to the level of the medial canthus of the eye. The cannula is connected via an oxygen line to an oxygen tank with a regulator or to an oxygen concentrator. Variations of delivery include the use of a cannula in each nostril or the use of human nasal prongs. The oxygen flow rate is adjusted with a flow meter. In general, higher flow rates will typically increase FIO_2, resulting in a greater PaO_2. In field situations flow is adjusted to the lowest flow required to maintain greater than 95% hemoglobin saturation to preserve the oxygen supply in the tank. Flows required to offset hypoxemia in different species are variable and the



Figure 4.3 Delivery of supplemental inspired oxygen to an anesthetized moose.

literature should be reviewed for guidance on flows to initiate therapy. Higher flows are typically required in larger species. A flow rate of 10 L/min has been used in American elk, which typically weigh 300–400 kg (Read et al. 2001). In female reindeer, typically weighing 50–100 kg, a flow of 1–2 L/min will effectively treat hypoxemia (Evans et al. 2013). Flow rates of oxygen as low as 1 L/min effectively treated hypoxemia in female white-tailed deer weighing 55–65 kg (Fahlman et al. 2014). If the patient is intubated a cannula can be placed into the endotracheal tube and oxygen delivered by the transtracheal route. Lower flow rates are required than via the intranasal route and greater FIO_2 values can be achieved.

Oxygen Delivery Equipment

In clinical situations oxygen can be delivered to deeply sedated patients via an anesthetic machine, with an appropriate circuit and a face mask or endotracheal tube. In field situations a D or E oxygen cylinder coupled with a regulator and flow meter can be used to deliver supplemental inspired oxygen (Fig. 4.3). It may be challenging to restock cylinders in remote areas and portable oxygen concentrators can be valuable in these conditions as they are battery operated and can be recharged overnight. The use of portable oxygen concentrators has been described in wildlife (Fahlman 2014; Fahlman et al. 2012).

Cardiovascular Complications and Emergencies

Bradycardia

In defining bradycardia it is important to know normal values for the species and the impact of the anesthetic technique being used. Vagally mediated bradyarrhythmias are very common in animals anesthetized with alpha-2 based protocols. These bradyarrhythmias are often not treated. Profound bradyarrhythmias may result from a variety of causes, including vagal stimulation, profound hypoxemia, hyperkalemia, and cardiac disease. In general, the underlying cause should be identified, and if the situation is life-threatening atropine should be administered at a dose of 0.02–0.04 mg/kg (Lerche 2015). Glycopyrrolate can also be used to treat vagal arrhythmias but due to its slow onset it is less useful than atropine in emergent situations. Hyperkalemia has been reported in a number of exotic felids anesthetized with protocols containing alpha-2 agonists. This complication can be severe and may result in cardiac arrest. It is good practice to monitor cardiac rhythm and electrocardiograph (ECG) morphology when anesthetizing wild felids (Romano et al. 2018).

Tachycardia

Tachycardia is often an indication of underlying complications under anesthesia and can be associated with pain, awareness, hypotension, hypoxemia, or hypercarbia. These conditions often induce a stress response. It is important to rule out these complications when attempting to determine the root cause of the tachycardia. Primary tachyarrhythmias can originate anywhere in the heart. An ECG is required to characterize the arrhythmia prior to treatment. Treatment of ventricular tachycardia is typically initiated with a class 1B antiarrhythmic drug such as lidocaine (1–2 mg/kg). Initial treatment of supraventricular tachyarrhythmias is typically achieved with a beta-blocking drug. Esmolol is often the drug of choice during anesthesia as it can be readily titrated in an acute setting. Esmolol is typically administered to dogs and cats at a loading dose of 2 μg/kg followed by a constant rate infusion (CRI) of 50 μg/kg/min (Murrell 2015).

Hypotension

Hypotension is a relatively common complication during anesthesia, particularly when volatile agents such as isoflurane or sevoflurane are used for maintenance of anesthesia. Hypotension is typically defined as a systolic arterial pressure <90 mmHg or a mean arterial pressure <60 mmHg. This definition is based on humans and may vary amongst other species. When treating hypotension it is important to identify the underlying cause. Pre-existing or ongoing fluid deficits or hemorrhage should be treated with volume replacement. Depending on the situation, isotonic replacement fluids, hypertonic fluids, colloids, or whole blood may be indicated. In field situations it can be challenging to carry large volumes of crystalloid fluids and

low volume resuscitation fluids such as hydroxyethyl starch can be a useful addition to resuscitation with isotonic crystalloids. Hypotension induced by isoflurane or sevoflurane may be treated by reducing the inspired concentration of volatile agent. Additional drugs such as alfaxalone, opioids, lidocaine, or alpha-2 agonist CRIs can be considered to maintain an appropriate plane of anesthesia when the volatile agent is reduced. Alpha-2 agonist CRIs have an additional benefit as they will increase peripheral vascular resistance and counter vasodilation. Pharmacological treatment of hypotension can include the use of dobutamine, dopamine, ephedrine, and norepinephrine. Most of these drugs must be administered as CRIs. Ephedrine is potentially useful in field situations because it can be administered at a bolus dose of 0.06 mg/kg (equine dose). The onset is approximately 5 minutes and effects will last approximately 30 minutes. Boluses can be repeated if needed to prolong drug effects (Trim & Shepherd 2015).

Hypertension

Acute hypertension during the capture and handling of wildlife is often drug related. Protocols based on alpha-2 agonists or potent opioids are often associated with hypertension. Normal blood pressure is difficult to define in zoo and wildlife species, therefore it can be difficult to define hypertension. Systolic pressure >160 mmHg is often used in domestic mammals. Hypertension may also result from a stress response due to light anesthesia, hypoxemia, or hypercarbia. It is important to identify the root cause of hypertension in order to treat it appropriately.

Shock

Shock during wildlife capture and handling can result from many different causes. The underlying cause should be identified, if possible, to determine appropriate treatment. During wildlife capture and handling hypovolemic shock resulting from trauma and capture shock syndrome are probably the most common forms of shock encountered. Shock can be very difficult to treat under field conditions, particularly in large animals. Generally, therapy should be directed at maintaining oxygen delivery to the tissues. Supplemental inspired oxygen should be considered to maximize arterial oxygen content and appropriate fluid replacement is vital in most forms of shock. Availability of blood products and large volumes of fluid is a challenge in zoo and wildlife anesthesia but an isotonic replacement fluid such as lactated Ringer's solution should always be available. If large animals are anesthetized hypertonic saline may be considered and/or a colloidal solution. Vasoconstrictive and/or inotropic drugs should also be considered. Given the challenges in treating shock under field conditions, every step should be taken to prevent trauma or capture myopathy during the capture process.

Hyperthemia

Hyperthermia can be challenging to define as normothermia may vary considerably between species and over seasons. Recent approaches have proposed that hyperthermia should be defined as an increase of >2°C from normal body temperature for a certain species in a certain season. Hyperthermia is a very common complication during wildlife capture and handling. It is important to monitor body temperature throughout an immobilization procedure, particularly if an animal has undergone a chase prior to induction. It is important to note that rectal temperature measurement may underestimate core temperature by as much as 1°C (Ozeki et al. 2015). Factors that increase the risk of hyperthermia during capture include prolonged pursuit and interference of thermoregulation from capture drugs. Alpha-2 agonists promote heat conservation via peripheral vasoconstriction. Symptoms of hyperthermia include rapid breathing, weak, rapid, or irregular heartbeat, and finally convulsions and death. In many mammalian species a body temperature greater than 41°C results in an emergent situation that requires immediate intervention. Treatment in the field may include immersion in cool water, movement into a shaded area, packing the inguinal or axillary areas with snow or ice, or fanning the animal. Cold water enemas combined with cold IV fluid administration have been shown to reduce the core temperature of hyperthermic bears (Ozeki et al. 2015). If cold water enemas are used, rectal temperature measurement is no longer reliable and another route of temperature measurement, such as esophageal or tympanic, should be considered. Antagonism of alpha-2 agonists can also help to normalize body temperature (Ozeki et al. 2015). It is always best to prevent hyperthermia as it can be difficult to treat. Try to avoid capture procedures during the warm hours of the day, minimize pursuit times, and avoid prolonged physical restraint.

Hypothermia

Hypothermia is typically encountered in very young animals, animals that have small body masses, and animals in poor body condition. It is difficult to define a temperature where hypothermia becomes a concern because there is a wide variation in normal body temperature among species. It is probably simplest to define hypothermia as a body temperature >2°C lower than normal. Marsupials can have

particularly low normal body temperatures. In many mammalian species hypothermia is defined as a core temperature less than 34°C. Hypothermia may lead to arrhythmias, prolonged recovery, or acidosis. Causative factors can include low ambient temperature, wind chill, precipitation, or drugs that impair thermoregulation. If body temperature is declining and trending towards hypothermia it is best to proactively treat it. Treatment may include drying wet animals, covering the animal, or providing external heat sources. In controlled settings convective warming can be particularly effective. It is always best to try to prevent hypothermia from occurring. Insulate the animal from the ground to prevent conductive heat losses and cover the animal to prevent losses from radiation or convective cooling.

Vomiting and Regurgitation

Vomiting and regurgitation are emergencies in an immobilized animal. If inhalation of stomach contents occurs, aspiration pneumonia can result, requiring prolonged intensive care that usually is not possible for wild animals. Animals should be positioned so that the nose is sloping downwards from the back of the head to decrease the risk of inhaling regurgitated materials. If vomiting occurs in smaller moveable animals, the animal should be placed in sternal recumbency with the head pointed downwards. A long-acting broad-spectrum antibiotic should be considered for animals showing signs of aspiration such as witnessed aspiration events, rumen contents in the nostrils, or harsh lung sounds.

Bloat

Bloat during wildlife capture is usually caused by lateral recumbency or by ruminal atony following administration of alpha-2 agonists. Ruminants should be positioned in sternal recumbency to reduce the risk of ruminal tympany. Tympany results from the inability to relieve gases from the rumen or stomach through eructation. Supportive treatment consists of placing the immobilized animal in sternal recumbency with the neck extended and the head forward, permitting saliva to drain. Move the animal from side to side over the brisket and elevate the front quarters of smaller animals. If positioning does not relieve the bloat, insert a lubricated and properly sized tube via the esophagus into the rumen to relieve pressure. Generally, in animals immobilized with alpha-2 agonists, bloat will resolve following the administration of an alpha-2 antagonist. In the face of severe bloat, procedures should be completed and the immobilization should be reversed. The last resort is trocharization of the rumen using a large-bore (2.5 mm), long (60–80 mm) needle.

Trauma

During the process of immobilization and capture, physical injuries, such as contusions, lacerations, abrasions, punctures, and fractures, may be inflicted on the animal accidentally or as a result of mishandling. Minor lacerations may be flushed, cleaned, and protected with an insect repellant. An appropriate long-acting antibiotic may be given to help prevent infection. Closure may be considered for large lacerations, and they should be flushed copiously, cleaned, and debrided. These lacerations are often contaminated and if they are closed appropriate drainage must be considered in the closure. Fractures and other serious conditions are difficult to treat effectively and will often require that the animal be euthanized for humane reasons.

Physical trauma may be prevented by taking notice of any hazard in the environment that may cause injury to the animal during capture and by careful handling. If traps, snares, nets, or other forms of manual capture or restraint are used, they should be appropriate for the species and set by well-trained individuals.

Pneumothorax

An uncommon cause of hypoxemia is pneumothorax. Dart penetration of the thoracic cavity can result in open or closed pneumothorax. It may be possible to treat pneumothorax with thoracocentesis. Equipment should be carried to perform thoracocentesis in the field. See Sigrist (2008) for instructions on thoracocentesis.

Myopathy

Most free-ranging wild animals exert themselves only infrequently to escape danger. They are not conditioned for running hard over long distances. Chasing wild animals by helicopter or motor vehicle for capture causes a tremendous amount of stress, resulting in intensive muscular activity. The effects of sympathetic exhaustion from sustained stress, combined with intense muscular exertion, are causative factors of various life-threatening syndromes known as *capture myopathy*. Capture myopathy is difficult to treat and prevention is of utmost importance. Capture myopathy may be prevented by reducing capture stress, fear, and exertion (by limiting chasing time), minimizing visual and auditory stimulation, careful handling and restraint of the captured animal, and providing a stress-free recovery environment. For a complete discussion of capture myopathy refer to Paterson (2014) and Breed et al. (2019).

Cardiopulmonary Resuscitation

Evidence-based cardiopulmonary resuscitation (CPR) guidelines do not exist for wildlife; recommendations are based on human medicine, small animal RECOVER guidelines, experimental animal models, and expert opinion.

Several concepts are universally accepted regardless of species: preparedness and prevention, basic life support (BLS), advanced life support (ALS), monitoring, and post-cardiac arrest care. This chapter focuses on the first four concepts.

In an ideal setting CPR success is <6% in veterinary patients (Hofmeister et al. 2009), with numbers likely much lower in wildlife, particularly in the field. This emphasizes the need to be prepared. All members should be familiar with a designated crash cart or mobile CPR kit containing the necessary supplies, drugs, equipment, and documents, which should be routinely checked on a per-use basis to ensure it is properly stocked, that all equipment functions properly, and that nothing has expired.

It should take <10–15 seconds to confirm cardiopulmonary arrest (CPA) through auscultation of the heart, palpation for pulses, and observation for breathing, which is immediately followed by BLS if an arrest is suspected. There is no evidence that initiating compressions when an animal is not in arrest causes significant harm (Fletcher et al. 2012; Fletcher & Boller 2015).

Presence of Apnea

If there is any doubt act as if the patient is not breathing and intervene. Apnea in an unresponsive patient with an inability to locate a pulse within 10 seconds should trigger CPR (Fletcher et al. 2012). Agonal breaths preceding an arrest are sometimes confused for respirations; CPR should proceed in the presence of agonal breaths.

Absence of a heartbeat and/or pulses (femoral artery) should prompt initiation of BLS. Prolonged efforts to locate a pulse should be avoided if the patient is apneic and unresponsive; proceed with BLS.

BLS should be initiated if the patients is apneic, a pulse is not identified within 10 seconds, and there is loss of consciousness with fixed, dilated (unresponsive) pupils.

Pulmonary Arrest without Cardiac Arrest

When respiratory arrest occurs without cardiac arrest (absence of respiratory effort with a palpable pulse) intubate and give two to four large breaths. If apnea persists after several seconds, start positive pressure ventilation (PPV). If the patient progresses to CPA, begin chest compressions immediately.

Arrests during Anesthesia

Consider discontinuation of volatile anesthesia or administration of a specific antagonist in anaesthetized wildlife if it is safe to do so; this will depend on the species and the environment.

Basic Life Support

BLS is the attempt to sustain life by artificially maintaining blood flow through performing chest compressions and artificially maintaining oxygenation of the blood and removal of carbon dioxide through PPV.

The Alphabet of an Arrest: A, B, C or C, A, B

After confirming CPA, the ABC of CPR is essential. Recent evidence suggests the algorithm of CAB (circulation, airway, breathing) is preferred over ABC (airway, breathing, circulation) as blood flow is the highest priority and chest compressions provide ventilation even prior to intubation and PPV (Fletcher & Boller 2015).

Circulation

Under ideal conditions only 30–45% of normal cardiac output is achieved during BLS, emphasizing the importance of proper CPR (Plunkett & McMichael 2008; Andreka & Fenneaux 2006).

Although chest compressions and internal cardiac message are both applicable in emergency critical care, because of the unlikelihood of performing open chest CPR in wildlife field conditions, only chest compressions will be discussed in this chapter.

Chest Compressions

Although chest compressions only generate a small amount of blood flow, if started early and performed properly they can provide critical blood flow to the brain and myocardium, which may be sufficient to achieve the return of spontaneous circulation (ROSC).

Start compressions immediately on identification of CPA; interruptions of compressions must be minimal and only for essential interventions (i.e., endotracheal intubation, defibrillation, or catheter placement). Even short interruptions to compressions negatively impact outcome in humans and continuous effective compressions must be maintained throughout the resuscitation attempt (Deakin et al. 2010; Neumar et al. 2010).

When an essential intervention is deemed necessary, interruption in compressions should not exceed 5–10 seconds (Deakin et al. 2010; Neumar et al. 2010).

Technique for Chest Compressions: General Delivery of chest compressions will vary according to the wildlife species in which it is performed (Table 4.1).

If at least two people are present, the goal should be to provide respirations and chest compressions. If only one person is present, chest compressions take precedence (Deakin et al. 2010; Neumar et al. 2010). Intubate and start PPV when help arrives.

If only one person is present and the patient is already intubated, give 30 chest compressions and two ventilations (Deakin et al. 2010; Neumar et al. 2010).

Providing good-quality chest compressions is exhausting; chest compressors should be alternated every 2 minutes (Malzer et al. 1996; Orliaguet et al. 1995). Interruption of compressions to alternate compressors should take <5 seconds.

A CPR leader should monitor the quality of CPR and alternate CPR providers or technique if quality is poor.

Maximizing Blood Flow during Chest Compressions The chest should be compressed by approximately one-third of the thoracic width at its widest point (Plunkett & McMichael 2008).

Frequency of compressions should follow guidelines for the species and weight (see Table 4.1). Exceeding recommended rates is not beneficial and can decrease filling time during the chest recoil phase. Compressions below the recommended rate are associated with poorer outcomes.

Chest compression to relaxation time should be approximately 1:1, making sure full chest recoil is attained between each compression relaxation cycle (Plunkett & McMichael 2008).

In general, there are two theories to explain blood flow during chest compressions: the cardiac pump theory and thoracic pump theory. With the cardiac pump theory, direct compression of the heart between the two sides of the rib cage results in forward blood flow. This mechanism is most likely prominent in animals less than 15 kg or during internal cardiac massage (Plunkett & McMichael 2008).

With the thoracic pump theory changes in intrathoracic pressure during compressions and relaxation of the chest (not direct cardiac compression) result in blood flow. This mechanism likely accounts for the majority of blood flow in animals greater than 15 kg (Plunkett & McMichael 2008).

Airway

Maintain the airway, provide oxygen support as soon as possible, and ventilate the lungs with the most appropriate equipment immediately available (see breathing).

Confirm the airway is not obstructed and intubate as quickly as possible; if possible, avoid stopping compressions for >5–10 seconds to intubate.

If the animal is intubated, make sure the tube is patent (not obstructed with mucous or kinked) and in the right location (not esophageal). Ensure the cuff is inflated to allow PPV. High-volume, low-pressure cuffs are preferred over low-volume, high-pressure cuffs due to the risk of pressure necrosis of the tracheal mucosa (Plunkett & McMichael 2008).

If intubation is not possible (e.g., masses or laryngeal collapse), a tracheostomy tube may be required. Minimize interruption of chest compressions to perform a tracheostomy. Tracheostomy closure is usually through second intention healing, although primary closure may be preferred in the field setting, particularly if animals may enter bodies of water.

Breathing (Ventilation)

The optimal tidal volume, respiratory rate, and inspired oxygen content to use during CPR are unknown and may vary between individuals, breeds, and species. Slow delivery of breaths, with an inspiratory time of 1 second and enough volume (10 mL/kg) to produce a normal chest rise is recommended (Plunkett & McMichael 2008). Hyperventilation can be harmful because it increases intrathoracic pressures, decreases venous return, and subsequently decreases cardiac output and cerebral perfusion pressures (Aufderheide & Lurie 2004). Therefore, a balance between hypoventilation (too few breaths or incomplete expansion of the lungs) and hyperventilation must be achieved.

Avoid overinflation of the lungs (if a pressure gauge is available, do not exceed 20 cmH_20 pressure), but make sure the chest visibly rises with each breath (Plunkett & McMichael 2008).

PPV can be delivered by connecting the patient to an anesthetic machine and using the rebreathing bag (rare in field settings), ambu bag, or demand valve depending on the size of the animal and environment encountered.

Time permitting, confirm proper connection and function of anesthetic machines (tubing free of obstruction, oxygen on and flowing, proper connection to the endotracheal tube, etc.). Begin PPV using the reservoir bag and pop-off valve. The pop-off valve can be closed or partially closed during compression of the reservoir bag to allow filling of the lungs; do not to exceed 20 cmH_2O of pressure during compression of the reservoir bag.

An ambu bag is inexpensive and can be used with room air until connected to an oxygen source. Although not common, pressure gauges can be used with ambu bags. Use of a reservoir bag with the ambu bag (available on some ambu bags) increases the inspired oxygen content during PPV (the reservoir bag fills with oxygen, which the ambu bag draws from, decreasing the chance of mixing oxygenated air with room air).

Oxygen content should initially be set at 100% if it is available (Plunkett & McMichael 2008). Following ROSC and spontaneous respirations, the inspired oxygen content

Table 4.1 CPCR techniques for avian and mammalian patients

Species	Position	Compression Site	Technique	Rate/Minute	Ventilation	Notes
Avian patients (small)	Dorsal	Sternum	One or two fingers	Up to 200	20–30 bpm	Intubation is challenging in very small birds, consider chest compressions only with oxygen supplementation provided by mask or flow by
Avian patients (large)	Dorsal	Sternum	Palm of the hand on the keel bone	100–120	10 bpm	Very large birds such as larger ratites may require a similar technique to 100–250 kg mammals
Mammals ≤1 kg	Right lateral	Caudal to the forelimb	Two fingers	150–200	20–30 bpm	If intubation is not possible, mask ventilation may be attempted
Mammals 1–10 kg	Right lateral	Fifth to sixth intercostal space over the heart (cardiac pump)	Palm of the hand on the sternum with the fifth to sixth intercostal space between the finger and thumb	100–120	10–15 bpm depending on weight	Direct compression of the heart when the fingers and thumb are squeezed together Fingers and thumb of the opposite hand can be placed over the first hand if more vigorous compressions are required Avoid using only the fingertips to compress the chest as this may result in poorer efficacy and decreased blood flow
Mammals 10–100 kg	Right lateral	Widest point of the chest (thoracic pump)	Keep shoulders, elbows, and hands in a straight line so the weight of the upper body is transferred into the compressions via the arms	100–120	10 bpm	Consider approach for patients >250 kg if technique fails and animal is >70 kg
Mammals 100–250 kg	Right lateral	Widest part of the chest (thoracic pump)	Use one foot, with the knee and hip in a line over the foot	100	8–10	There is no published literature on any technique to perform cardiopulmonary cerebral resuscitation in patients between 100 and 250 kg in body weight If this technique fails, consider technique for patients >250 kg
Mammals >250 kg	Right lateral	Widest part of the chest (thoracic pump)	Use one knee to "fall" on the patient at the widest point of the chest just caudal to the left elbow	80	8–10	Technique is physically demanding for the operator and it may be best used intermittently for short periods

For all species: Compress the chest by approximately 30% in a 1:1 compression to relaxation rate, allowing full chest recoil between each compression. Switch out chest compressors every 2 minutes or less if fatigue sets in earlier. Minimize interruption in compressions to less than 5–10 seconds at any time.
bpm, breaths per minute.

is titrated to a level that provides adequate partial pressure of arterial oxygen or hemoglobin saturation ($PaO_2 \geq$ 70 mmHg and $SaO_2 \geq 93\%$) while minimizing the risks of oxygen toxicity.

Advanced Life Support: D, E, F

ALS interventions are unlikely to lead to ROSC without effective BLS, and thus should be instituted without interruption of BLS.

Drugs

There are generally five routes of drug administration; central venous catheter (jugular vein), peripheral venous catheter (i.e., cephalic or saphenous), intraosseous (IO) catheter, intratracheal (IT), and intracardiac (only recommended during open chest CPR). Do not discontinue compressions during the administration of drugs via any route!

Central line administration is the most rapid and preferred CPR route (Emerman et al. 1988). However, unless already in place, a peripheral catheter is recommended over a central line due to increased ease of placement and decreased risk of complications. With difficult IV access a venous cutdown (<60 seconds) or automated IO catheters (<10 seconds) can be placed. IO catheters show equal efficacy to peripheral lines and may be equivalent to central lines when placed in proximity to the heart (e.g., proximal humerus) (Neumar et al. 2010). In general, if a drug can be given IV it can be given IO at the same dose.

Drugs delivered IV or IO should be followed by a bolus of fluids (10–20 mL/kg) to "push" administered drugs more rapidly towards the heart (Emerman et al. 1990).

The IT route is less frequently used in human CPR due to unpredictable plasma concentrations (Neumar et al. 2010). However, it is still frequently used in veterinary patients due to its low cost and ease of use. The optimal IT dose for most drugs is unknown but should be two to three times the IV dose. Evidence suggests the IT epinephrine dose may need to be three to 10 times the IV dose (Hörnchen et al. 1987). With the exception of bicarbonate, all drugs given IV can be given IT. To ensure the drug reaches the small airways administer the drugs via a long 5–8 Fr red rubber feeding tube passed through the endotracheal tube. A small bolus of air equal to the volume of the feeding tube is administered after the drug to ensure the drug reaches the lungs and does not remain within the feeding tube. Ventilate the patient with two or three rapid breaths to help distribute the drug within the lungs.

Intracardiac administration is no longer recommended due to the risk of lacerating coronary vessels, injury leading to arrhythmias, and accidental intracardiac muscle injection.

A drug dose chart is given in Table 4.2.

Epinephrine

Epinephrine remains the gold standard CPA drug because of its alpha sympathomimetic effects (Deakin et al. 2010).

The dosage and frequency vary from 0.01 to 0.1 mg/kg of 1:1000 ratio repeated at 3–5-minute intervals (Neumar

Table 4.2 Cardiopulmonary cerebral resuscitation drug doses

Drug	Dose	2.5 kg	5 kg	10 kg	15 kg	20 kg	25 kg	30 kg	40 kg	50 kg
Epinephrine 1:1000 1 mg/mL	0.01 mg/kg (0.1 mg/kg)	0.025 0.25	0.05 0.5	0.1 1	0.15 1.5	0.2 2	0.25 2.5	0.3 3	0.4 4	0.5 5
Atropine 0.5 mg/mL	0.05 mg/kg	0.25	0.5	1	1.5	2	2.5	3	4	5
Lidocaine 20 mg/mL	2 mg/kg	0.25	0.5	1	1.5	2	2.5	3	4	5
Bicarbonate 1 meq/mL	1 meq/kg	2.5	5	10	15	20	25	30	40	50
External defibrillation	4–6 J/kg	10	20	40	60	80	100	120	160	200
Internal defibrillation	0.5–1 J/kg	2	3	5	8	10	15	15	20	25
Vasopressin 20 U/mL	0.8 U/kg	0.1	0.2	0.4	0.6	0.8	1	1.2	1.6	2

Drugs are in mL per kg, administration IV, double or triple the dose if given endotrachealy.

et al. 2010), making every other compression cycle an ideal time for administration. The low dose (0.01 mg/kg IV or IO) is associated with a higher rate of survival to discharge, while the high dose (0.1 mg/kg IV or IO) is associated with a higher rate of ROSC (Rozanski et al. 2012). Until further studies show otherwise, the standard of care is to administer epinephrine at 0.01 mg/kg. If 0.01 mg/kg fails to provide ROSC after one or two boluses, a 0.1 mg/kg dose or use of vasopressin can be considered.

Vasopressin

The only promising alternative to epinephrine is vasopressin. Vasopressin is a vasoconstrictor and antidiuretic that can be used in lieu of or in conjunction with epinephrine. Increased responsiveness in acidic environments and a lack of inotropic and chronotropic effects that can add to myocardial ischemia when ROSC is achieved may be an advantage of vasopressin over epinephrine. The current trend is to administer vasopressin in place of the first or second dose of epinephrine (Neumar et al. 2010; Fletcher & Boller 2015; Rozanski et al. 2012). The suggested dose in companion animals is 0.8 U/kg IV or IO.

Atropine

Atropine is a parasympatholytic agent. It inhibits the effects of acetylcholine and increases heart rate. Its primary indication is when increased vagal tone is the suspected cause of CPA. It is no longer routinely used for treatment of pulseless electrical activity (PEA)/asystole in people (Neumar et al. 2010), however, given there is no evidence to suggest it has detrimental effects during bradycardic or asystolic CPA, it may still play a role in the veterinary profession (see sections on PEA and asystole below).

Bicarbonate

Routine administration of sodium bicarbonate during CPA or after ROSC is not recommended in humans. It may be beneficial in cases where the arrest was caused by hyperkalemia (i.e., urethral obstruction, uroabdomen, or addisonian crisis etc.) or pre-existing metabolic acidosis was present. If given, blood gases should be followed serially to determine response to therapy and the possible need for repeat doses. It is important that ventilation be maintained if bicarbonate is administered to prevent paradoxical central nervous system acidosis.

Lidocaine and Amiodarone

There is no evidence that antiarrhythmics given during cardiac arrest increase survival. They may be considered in ventricular fibrillation or pulseless ventricular tachycardia when defibrillation is not available. Amiodarone is recommended over lidocaine in the human literature (Neumar et al. 2010).

Calcium Gluconate and Glucose

Both have been used during cardiopulmonary cerebral resuscitation (CPCR), but they should only be given when indicated (i.e., pre-existing conditions).

Electrocardiogram

There are three common fatal arrhythmias reported in association with CPA. One may proceed to another.

Ventricular Asystole

Ventricular asystole is characterized by an absence of all electrical ventricular activity: the ECG tracing is a flat line (Fig. 4.4a).

Atropine is no longer recommended for asystole in humans due to a lack of demonstrable benefit. However, given asystole in veterinary patients may be the result of increased vagal tone, until proven otherwise, atropine in conjunction with epinephrine may still be beneficial.

Pulseless Electrical Activity

This is the most common arresting arrhythmia reported in veterinary patients. PE) is characterized by a visible ECG tracing (electrical activity present) in the absence of myocardial contractility (Fig. 4.4b). Treatment is difficult and often unsuccessful. Epinephrine is recommended in cases of PEA. Although atropine is no longer recommended in humans, CPA in veterinary patients often results from increased vagal tone, therefore atropine may still play a role in conjunction with epinephrine, particularly if the cause of CPA was not witnessed, in veterinary patients.

Ventricular Fibrillation

This is the most common arresting rhythm in people, often secondary to myocardial infarctions. It is characterized by a completely disorganized and anarchic rhythm, which results in complete absence of coordinated or effective ventricular contractions. It may be coarse or fine (Fig. 4.4c–e). Electrical defibrillation is the recommended treatment for this arrhythmia, which transiently depolarizes all cardiac cells simultaneously (complete cardiac standstill), with the hope they will restart in a synchronized pattern (Deakin et al. 2010; Neumar et al. 2010).

Given defibrillators are not common in most wildlife field settings, a precordial thump (strong quick thump on the chest wall over the heart) can be attempted. The idea is to traumatically depolarize the heart or stun it.

Fluids

Resuscitation with fluids is only recommended in cases of confirmed hypovolemia to avoid volume overload and pulmonary edema (Deakin et al. 2010). IV administration is

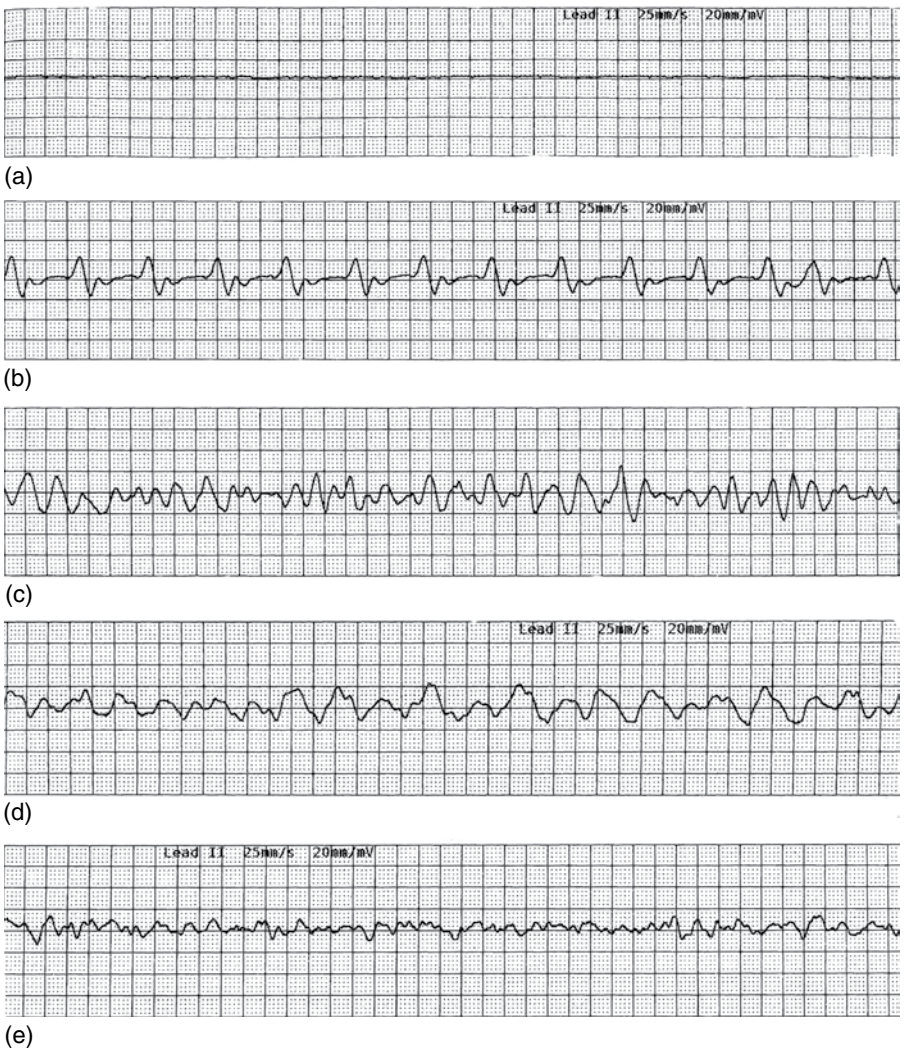


Figure 4.4 (a) Electrocardiograph tracing of ventricular asystole. Note the absence of any electrical activity. (b) An example of pulseless electrical activity. Note that the ECG tracing can vary from near-normal to very bizarre depending on the electrical activity present. The key thing to note is that there is synchronous electrical activity from the heart in the absence of a detectable pulse. (c–e) ECG tracing of coarse ventricular fibrillation progressing to fine ventricular fibrillation.

the preferred route. Alternatively, the IO route can be used. Any fluid boluses given to "chase" CPR drugs should be included in fluid volume calculations.

Monitoring Efficacy of CPCR

Femoral pulse palpation is an easy technique to monitor the efficacy of CPR. If compression efforts fail to produce a palpable pulse, then a change in compression technique should be considered. Palpation of a pulse when chest compressions are stopped is a fairly reliable indicator of ROSC (Neumar et al. 2010). Do not discontinue chest compression for more than 10 seconds to assess ROSC.

Measurement of end-tidal CO_2 is one of the most consistent and reliable measures of CPR and detection of ROSC. Unlike ECG analysis, it does not require an interruption in chest compressions to monitor (Neumar et al. 2010). Although specific parameters have not been established, an end-tidal CO_2 of >18 mmHg likely represents efficacious CPR (Grmec & Klemen 2001; Kolar et al. 2008; Pokorna et al. 2009). With ROSC the end-tidal CO_2 will rapidly rise and likely exceed 30 mmHg (Fig. 4.5) (Sehra et al. 2003; Ahrens et al. 2001).

End-tidal CO_2 may also be used to confirm endotracheal tube placement in some animal species, particularly those that are difficult to intubate.

Discontinuing CPCR

The risk of permanent severe neurologic injury is significant after 15–20 minutes of decreased cerebral blood flow, therefore it is reasonable to discontinue CPR if ROSC is not re-established within this timeframe (Plunkett & McMichael 2008). However, the prognosis will vary depending on the underlying cause, the conditions under which CPCR is performed, and ultimately the quality of life of the patient.

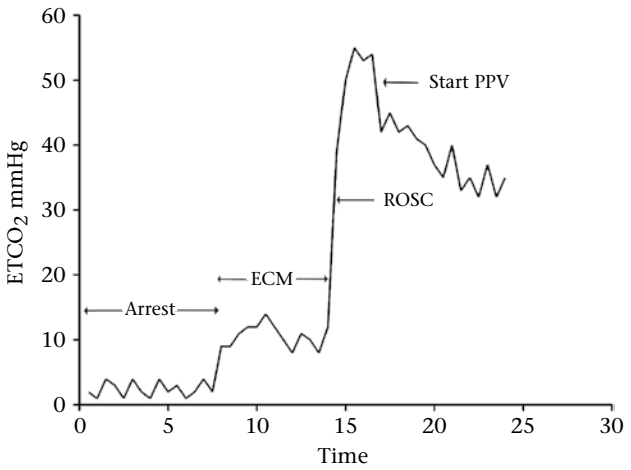


Figure 4.5 End-tidal carbon dioxide ($ETCO_2$) measurement and its association with cardiac arrest, effective external cardiac message (ECM), return of spontaneous circulation (ROSC), and initiation of positive pressure ventilation (PPV).

Prognosis and Return of Spontaneous Circulation?

Outcome depends on the underlying cause, the training of personnel, species, duration of the arrest, and the equipment available. The prognosis is generally poor, with very few patients achieving normal neurologic function (although this varies with the underlying cause). Studies in small animals demonstrate that 30% of patients will have ROSC, re-arrest occurs in 35–70% of ROSC patients, 5–10% will be discharged from the hospital, and 1% will have a return to normal function. Discharge from respiratory arrest alone varies from 25% to 60% in small animals.

CPA caused by anesthesia, drug overdose, increased vagal tone, or electrolyte imbalances tends to have a better prognosis than patients with serious underlying critical illnesses such as sepsis, systemic inflammatory response syndrome, or neoplasia. Early intervention is critical and patients with significant underlying illness should be monitored closely to allow earlier intervention. In addition, well-trained staff (frequent practice of CPR) with properly equipped facilities oxygen, suction, etc. will further increase success rates. Finally, the prognosis changes by species: small animal veterinary patients have a better prognosis compared to large animal patients.

If ROSC is achieved close intensive monitoring is needed to prevent a second CPA and most patients require vasopressors. Mechanical ventilation may also be necessary for a period of time following ROSC to decrease the chance of a second arrest.

Euthanasia

Equipment or drugs for humane euthanasia should always be carried during animal captures. The method of euthanasia depends on the situation and species. In many countries, the veterinarian is legally responsible for the death of animals, including endangered species, that eat a euthanized carcass. If firearms or bolt guns are used (recommended if the meat will be salvaged), personnel must be trained in the use of the firearms and the appropriate bullet/bolt placement. In anesthetized animals, potassium chloride may be considered as an option for euthanasia as there is less risk of death to animals that may consume the carcass when compared to pentobarbital. Animals that die or are euthanized during a capture procedure should be removed from the site and transported for necropsy. These animals should not be left in the field due to the risk of intoxication of scavengers. A more complete discussion of euthanasia in zoo animals and wildlife can be found in American Veterinary Medical Association (2020), Canadian Council on Animal Care (2003), and Woodbury (2014).

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5

Remote Drug Delivery

Ramiro Isaza

Introduction

Prior to the development of effective anesthetics and remote delivery systems, veterinary procedures on nondomestic species were either impossible to accomplish or associated with unacceptably high mortality rates. This chapter examines the methods of anesthetic drug delivery with an emphasis on the commercial equipment available to the zoological medicine practitioner in North America.

Direct Delivery for Cooperative Animals

Animal Training for Direct Drug Administration

The technique a clinician selects to administer anesthetic drugs to an animal depends largely on whether the animal is cooperative during the preinduction period. Too often the clinician assumes that most nondomestic species are either uncooperative or too dangerous for traditional routes of drug administration such as hand injection. However, through proper training, many nondomestic species can be behaviorally restrained and will allow the veterinarian to perform a routine physical examination or administer medications on a regular basis. Animals trained for voluntary behavioral restraint are usually well socialized and become tolerant of human manipulation. For these animals, intramuscular and even intravenous injections can be administered as would be typical for domestic species in a traditional veterinary practice. For example, a chimpanzee can be trained to place its arm through the cage bars to receive intramuscular injections rather than be subjected to darting. More extreme examples are well-trained elephants or whales that permit direct manipulation despite their overwhelming size.

For some nondomestic species, combinations of mechanical restraints and behavioral training are viable options. With proper techniques and safety precautions, manual restraint of smaller nondomestic species for direct drug administration is often possible. Various mechanical restraint devices typically associated with domestic hoofstock, such as horse stanchions or cattle chutes, can be adapted for the treatment of nondomestic species (Haigh 1999). An example would include teaching a giraffe or rhinoceros to walk through and stand in a chute for daily physical examinations and routine treatments (Fig. 5.1). Once mechanically restrained, the animal can be induced with injectable agents or forced to breathe inhalant anesthetics.

It must be restated that for any of these methods of direct drug administration to succeed, prior training of the nondomestic animal is critical. Attempting to restrain an animal in an unfamiliar environment for direct drug administration is often stressful, dangerous, and ultimately unsuccessful for both the animal and the staff. Consultation with professional trainers and a clearly defined set of target behaviors needed for drug administration should be the first step, and the trainer's relationship and trust with the animal should not be underestimated. Often an animal will refuse medication offered by a stranger yet will subsequently accept the same medication if presented by the trainer. Ultimately, effective training prior to the anesthetic procedure can reduce the stress associated with anesthesia and increases the likelihood of compliance.

Nevertheless, the veterinarian must be aware of the limitations of a priori training. Quiet, well-trained animals may become dangerous if placed in unfamiliar environments such as hospitals, separated from their conspecifics, or given unexpected painful stimuli such as injections. Some of these issues, however, also can be minimized with advanced planning. For example, having the anesthetic procedures begin in the animal's regular enclosure with its usual handler will often facilitate induction, but equipment should be brought to the enclosure well in advance of the procedure to minimize disruption.

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Figure 5.1 Mechanical restraint of a giraffe using a chute.

Manual Drug Delivery Routes for Cooperative Animals

Oral

Oral anesthetics are occasionally useful in zoological medicine. Some induction agents can be simply sprayed into the oral cavity or placed inside a food item that is then offered to the animal. Oral administration of various anesthetics has been accomplished using various juices, maple syrup, peanut butter, marshmallow cream, and honey (Thurmon et al. 1996). Oral carfentanil was administered to chimpanzees, tapirs, and bears transmucosally by mixing the injectable formulation of the drug into food (Kearns et al. 2000; Pollock & Ramsay 2003; Mortenson & Bechert 2001). The transmucosal formulation of fentanyl was evaluated for use as part of a preanesthetic protocol in great apes (Hunter et al. 2004).

Wild animals can be baited with medicated food that is placed in traps or spread out on the ground. One example is the use of oral alpha-chloralose to capture birds (Hayes et al. 2003; Loibl et al 1988). In situations where animals aggressively open their mouths when provoked, injectable anesthetics can even be sprayed into the mouth or the nose for mucosal absorption (Grove & Ramsay 2000). In practice, all these methods of oral administration are difficult to apply consistently as they require some measure of voluntary cooperation. Also, because the drug needs to be absorbed through the oral or nasal mucosa, it must remain in contact with the mucosa and not swallowed. Generally, such inductions are prolonged and frequently unpredictable, but may occasionally work as preinduction sedation.

Hand-held Injection

Hand injection is the most direct method of administering induction agents to an animal, requiring either exceptionally cooperative behavior or good restraint for proper placement. For an effective intramuscular injection, even a restrained animal must be approached quietly and given the injection quickly.

Administering a hand injection generally involves the following steps:

1) A sterile plastic disposable syringe with a Luer-lock hub is selected to avoid needle detachment.
2) A sterile large 18–14-gauge needle is chosen to prevent breaking the needle during injection and allow fast deposition of the drug.
3) The needle is firmly attached to the syringe hub and the attachment double-checked prior to injection.
4) The syringe is filled with an appropriate dose of the drug.
5) The loaded syringe is grasped with the thumb over the plunger.
6) The injection site is selected.
7) Using a quick flick of the wrist, the plunger is rapidly pressed down as the needle begins to penetrate the skin.

Slower placement of the drug, with aspiration prior to injection, rarely succeeds in unrestrained nondomestic species. The hand injection method of drug administration is considered dangerous for the person injecting the anesthetic. Trauma from bite wounds, kicks, and crushing injuries are common. Of equal concern is the possibility for self-injection after the animal's sudden movements or exposure to aerosol sprays from a broken syringe. Hand administration of potent narcotics such as carfentanil is therefore not recommended.

Pole Syringes

A pole syringe is essentially a hand injection with the added safety of a long pole. Pole syringes were primarily developed for use in chute, cage, or trap-restrained animals and they enable the operator to avoid some of the potential trauma associated with direct hand injections. This added safety is, however, at the expense of control of the injection process. Poorly restrained animals invariably react to the needle by moving away or attacking prior to full injection. As with hand injection, this technique requires a quick delivery through a large-gauge needle (14–18 gauge). The needle is inserted in a large muscle, and then the pole is held in position until the drug is deposited.

Three types of pole syringes are available. The manual pressure pole syringe has a typical syringe body with an extended plunger to provide extra length. Once inserted into the animal, the plunger is pushed against the resistance of the animal's body. In the second type, an extension pole is attached to the body of the syringe with a second internal extension of the syringe plunger that is manually depressed to deposit the drug. The final type incorporates a mechanism with a spring or pressurized gas-loaded plunger that is triggered when the needle presses on the skin. Although considered safer than hand injection, animals may still react to the needle and injure themselves by moving or misdirecting the pole syringe.

Remote Delivery Systems for Uncooperative Animals

Unfortunately, in zoological medicine, many anesthetic procedures must be performed on uncooperative animals for various reasons. Animals that are not acclimated to human contact generally become agitated and aggressive when approached. This is typically the case in free-living species or in captive animals where routine direct human contact is discouraged. Second, some species, such as large carnivores or hoofstock, pose significant inherent risks to the veterinarians and keepers that preclude the possibility of using behavioral or physical restraint. Finally, even in cooperative or human-habituated animals, trained behavior can significantly change due to illness or pain so that the training no longer helps facilitate direct anesthetic drug delivery methods (Fig. 5.2).

When injectable anesthetic agents are used in unrestrained nondomestic species, a remote delivery system consisting of a dart and projector is often the most practical option. Darts can be projected via a blowpipe, compressed air projector, or gunpowder cartridge rifle (Bush 1992). All darts have four basic components: a drug storage compartment, a method of injecting the drug, a needle to penetrate the skin, and a stabilizer on the tail for accurate flight. Commercially available darts differ in their methods of drug expulsion, materials used in their construction, drug payload volumes, and dart attachments such as the needle or tail. In this chapter, the method of drug delivery will be used to distinguish the darting systems.



Figure 5.2 Use of a blowpipe for short-range injection of a white rhinoceros that would react if hand injected.

Several homemade dart and projector systems have been described in the literature (Haigh & Hopf 1976; Warren et al. 1979; Barnard & Dobbs 1980; Lochmiller & Grant 1983). Here, descriptions and discussions of equipment will be limited to those drug delivery systems that are currently commercially available. The choice of delivery system is subject to the clinician's preferences, needs, or experience, but almost any commercial system can be effective when used by experienced operators. The similarity between available equipment systems allows some interchange of components that can be configured to meet the clinician's specific preferences. However, this interchangeability can also be somewhat misleading and may lead to dart failure caused by subtle differences in the darting systems. Generally, it is recommended that one manufacturer's system be purchased along with the relevant product lines to ensure that they are effective and reliable when used as designed.

Historical Development of Remote Delivery Systems

Remote delivery of drugs was first used globally by indigenous hunters with poison-tipped projectiles (Nielsen 1999; Bush 1992). For example, plant extracts containing curare were used by pre-Columbian South American Indians to produce effective neuromuscular blockage and muscle paralysis in animals and are still used by some aboriginal groups that continue to hunt. When these poison-tipped darts are projected with long blowpipes they can be delivered by experienced hunters with extraordinary precision and to lethal effect. The precise dosage, relevant to delivery and margins of safety, was not an important consideration since the purpose of darting was to kill the animal.

In the first half of the twentieth century, zoological collections relied on manual restraint as the primary means of administering veterinary care. These restraints were dangerous for both the humans and the animals, often resulting in stress, injury, and occasional animal mortalities. In the mid-1950s the first remote delivery device was described in the literature (Hall et al. 1953). It consisted of a modified metal drill bit with a gallamine and glucose paste packed into the groves. The bit was attached to a dart and delivered with a Crossman air gun. Once the animal was paralyzed

and the procedure completed, the gallamine was reversed. Although effective, the paste was absorbed slowly, leading to development of a "flying syringe" to deliver liquid injections (Crockford et al. 1958). This aluminum dart used an acid-base reaction to inject the drug. After extensive modifications and improvements, this dart became the prototype for many of the modern darts in use today (Bush 1992). Around the same time, Colin Murdoch, a veterinarian and inventor from New Zealand, also developed a series of darts and projectors that became known as Paxarms. Subsequently, plastic two-chambered gas darts were introduced to zoological medicine and developed into several commercial darting systems (Bush 1992). Several authors have reviewed the development of darting equipment over the past 40 years (Bush 1992; Nielsen 1999; Fowler 1995; Harthoorn 1976; Fritsch 1982). A listing of some currently available darts and delivery systems can be found in Table 5.1:

Table 5.1 Description of currently available darts by manufacturer.

Manufacturer and Dart Description	Dart Type	Payload Volume (mL)	Dart Diameter (mm)	Needle Sizes (mm)	Tailpieces	Recommended Projector
Dan-inject blow dart syringe	Two-chambered	1.5, 3	11.8	1.1 × 25 or 1.2 × 38	Orange cloth	12-mm Dan-inject 1.25- or 1.8-m (2 piece) blowpipe
Telinject blow dart syringe	Two-chambered	1, 2, 3	10.8	0.9 × 25 to 1.2 × 38 (3 gauges and 4 lengths)	Orange cloth or plastic tailpiece	11-mm Telinject 1- or 2-m blowpipe or 16-mm, 2.2-m high-performance blowpipe with plastic tailpiece
Telinject blow dart syringe	Two-chambered	5	14.0	0.9 × 25 to 1.2 × 38 (3 gauges and 4 lengths)	Red with yellow cloth or plastic tailpiece	14-mm Telinject 1.5-m blowpipe or 16-mm, 2.2-m high-performance blowpipe with plastic tailpiece
Dist-Inject "Softy" blow dart syringe	Two-chambered	3.8	10.8	1.2 × 25 or 1.6 × 38	Red cloth or PVC tailpiece	11-mm mini-Ject 0.9-m blowpipe or 16-mm Dist-Inject 1.5 cm with PVC tailpiece
Maxi-Ject veterinary syringe dart	Two-chambered	1, 2	9.7	1.9 × 25 or 1.2 × 38	Yellow cloth	10 mm Maxi-Ject 2-piece, 1-m blowpipe
Maxi-Ject veterinary syringe dart	Two-chambered	1, 2, 3	10.7	1.9 × 25 or 1.2 × 38	Orange cloth	11-mm Maxi-Ject 2-piece, 1-m blowpipe
Maxi-Ject veterinary syringe dart	Two-chambered	5	13.7	1.2 × 38	Red with yellow cloth	14-mm Maxi-Ject 2-piece, 1-m blowpipe
TeleDart veterinary syringe blow dart	Two-chambered	1, 2, 3	10.7	0.9 × 25 to 1.2 × 38 (3 gauges and 4 lengths)	Pink cloth with yellow base	11-mm B11 or 16-mm B16 TeleDart blowpipes with plastic tailpiece
TeleDart veterinary syringe blow dart	Two-chambered	5	13	0.9 × 25 to 1.2 × 38 (3 gauges and 4 lengths)	Pink cloth with red base	14-mm B14 or 16-mm B16 TeleDart blowpipes with plastic tailpiece
Telinject "Vario" molded polyamide nylon syringe	Two-chambered	1, 3	10.8	1.5 × 20 to 2.0 × 100 (2 gauges and 10 lengths)	Red cloth	11-mm Telinject Vario pistol or Vario 1V and 3V rifles
Telinject "Vario" molded polyamide nylon syringe	Two-chambered	5, 10, 15, 20	12.2	1.5 × 20 to 2.0 × 60 (2 gauges and 10 lengths)	Red with yellow cloth	13-mm Telinject Vario pistol or Vario 1V and 3V rifles
Dan-inject "S" series molded nylon syringe	Two-chambered	1.5, 3	10.7	1.5 × 20 or 2.2 × 100 (3 gauges and 9 lengths)	Red cloth	11-mm Dan-inject model PI pistol or JM/IM injection rifles

Table 5.1 (Continued)

Manufacturer and Dart Description	Dart Type	Payload Volume (mL)	Dart Diameter (mm)	Needle Sizes (mm)	Tailpieces	Recommended Projector
Dan-inject "S" series molded nylon syringe	Two-chambered	5, 10	12.5	1.5 × 20 or 2.2 × 100 (3 gauges and 9 lengths)	Red with white cloth	13-mm Dan-inject model PI pistol or JM/IM injection rifles
Dist-Inject "Mini-Ject 2000" molded nylon syringe	Two-chambered	1, 2, 3, 5	10.8	1.1 × 25 or 1.2 × 35	Red cloth	11-mm model 45 delta pistol, model 35N pistol, or model 50N, model 70, model 72 rifles
Dist-Inject "easy" butane charged molded nylon syringe	Two-chambered	3, 5	10.6	1.1 × 25 or 1.2 × 35	Orange and yellow fins	11-mm model 45 delta pneumatic 0.35-m blowpipes
TeleDart "TD" veterinary syringe molded plastic dart	Two-chambered	1, 2, 3, 5	10.8	1.5 × 20 to 2.0 × 60 (2 gauges and 8 lengths)	Pink cloth with orange base	11-mm model RD206 pistol, RD406 pistol, or model RD706 TeleDart injection gun
TeleDart "TD" veterinary syringe molded plastic dart	Two-chambered	1, 2, 3, 5, 10, 15, 20	12.6 or 15.5	1.5 × 20 to 2.0 × 60 (2 gauges and 8 lengths)	Pink cloth with orange base	16-mm model RD206 pistol, RD406 pistol, or model RD706 TeleDart injection gun
Palmer Cap-Chur "Aero" clear plastic dart	Two-chambered	1, 2, 3, 4, 5	12.5	2.5 × 19 to 2.5 × 38 (11 lengths)	Tetra plastic tail	12.7 Palmer Cap-Chur short, mid, and long-range CO_2 projectors
Pneu-Dart "P" polycarbonate dart with "Slo-inject"	Explosive	0.5, 1, 1.5, 2	12.5	2.1 × 9.5 to 2.0 × 50.8 (7 lengths) Open or tri-port	Yellow plastic	12.7-mm Blo-Jector blowpipe
Pneu-Dart "P" and "U" polycarbonate or aluminum darts with "Slo-inject"	Explosive	0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10	12.5	2.1 × 9.5 to 2.0 × 50.8 (7 lengths) Open or tri-port	Yellow plastic	12.7-mm G2 X-Caliber rifle, X-2 pistol, model 178BS air rifle, or Model 190B pistol
Pneu-Dart "C" polycarbonate or aluminum darts with "Slo-inject"	Explosive	0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 10	12.5	2.1 × 6 to 2.0 × 50.8 (7 lengths) Open or tri-port	Orange plastic	12.7-mm model 193, 194, 196 and 2000 Pneu-Dart cartridge fired rifles
Clear Dart "Petite" clear plastic dart	Explosive	0.5, 1, 1.5, 2	12.4	2.1 × 9.5 to 2.0 × 50.8 (7 lengths) Open or side port	Pink plastic	Any 2.7–13-mm barrel
Clear Dart "Original" clear plastic dart	Explosive	3, 5, 7.5, 10	12.4	2.1 × 9.5 to 2.0 × 50 (7 lengths) Open or side port	Pink plastic	Any 2.7–13-mm barrel
Palmer Cap-Chur aluminum dart	Explosive	0.5, 1, 2, 3, 4, 5, 7, 10, 15, 20	12.5	2.5 × 13 to 2.5 × 76 (11 lengths)	Yarn or plastic "Tetra"	12.7-mm #1300 Mid-range pistol, #1200 long range CO_2 rifle
Dist-Inject aluminum dart	Explosive	1, 2, 3, 4, 5, 7, 10, 15	12.5	2.5 × 19 to 2.5 × 78	Yarn, plastic finned, and feathered	13-mm model 30N pistol, model 60N rifle
Dist-Inject disposable molded nylon "Speedy" dart	Explosive	3	12.5	2.5 × 20 to 2.5 × 30 barbed	Yellow plastic finned	13-mm model 30N pistol, model 60N rifle

PVC, polyvinyl chloride.

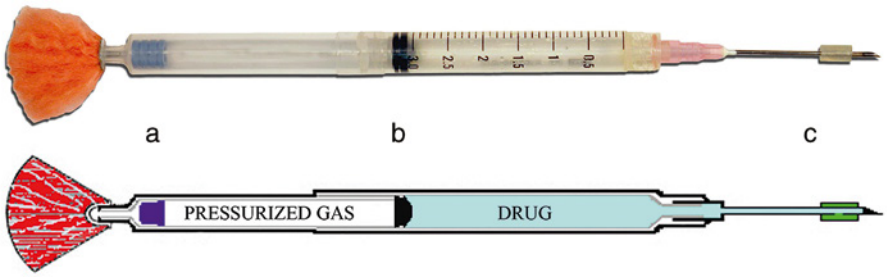


Figure 5.3 Photograph and illustration of a two-chambered compressed gas dart. (a) Posterior plunger that acts as a one-way valve allowing compressed gas to be introduced, but preventing gas escape. (b) Movable central syringe plunger that divides the two chambers of the dart. (c) Side-ported needle with a silicone sleeve occluding the port.

Dart Types

Two-chambered Compressed (Pressurized) Gas Darts

These darts are lightweight and usually made of plastic or occasionally aluminum. They are made of a variety of injection-molded plastic materials. The exact composition of the plastic and manufacturing process is often proprietary information. The dart body is divided into dual chambers by a movable, rubber syringe plunger in the center, with the anterior chamber holding the anesthetic drug and the posterior chamber for compressed gas (Fig. 5.3).

The anterior drug chamber is bounded by the central plunger and by a syringe hub that accepts a needle at the front of the dart. The posterior gas chamber is enclosed by the central plunger in front and by a second, smaller movable rubber plunger at the back. The posterior plunger acts as a one-way valve that allows gas to be inserted through the posterior hub, but then occludes the posterior hub to prevent gas escape. The caudal part of the dart body has a syringe hub that accepts a tailpiece. The dart needles for this system are hollow with a sharp, sealed tip and an opening cut into the side a few millimeters away from the tip from which the medication is expelled. A small silicone sleeve is placed over this opening before the needle is attached to the anterior hub of the dart (Fig. 5.4).

The drug is instilled into the anterior chamber of the dart, then the needle with the silicone sleeve is securely attached to the hub. These darts are then charged by placing the compressed gas into the back chamber. The pressurized gas may be room air introduced manually with an adapter attached to a second air-filled syringe or compressed butane liquid inserted into the posterior chamber of the dart (Fig. 5.5).

Leakage of drug too early in the darting process is prevented by the silicone sleeve occluding the needle vent but as the needle enters the animal's skin, the sleeve remains on the skin surface, exposing the needle vent. The pressurized gas then pushes the central plunger forward and forces the drug out of the anterior chamber and through the needle. If the darts and needles are cleaned and maintained between usages, they are usually reusable at least a few times. For cleaning, the plastic darts can be gas sterilized and the needles can be autoclaved or gas sterilized.

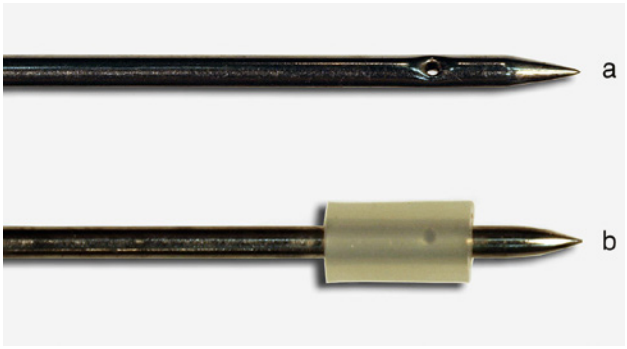


Figure 5.4 Photograph of two side-ported needles. (a) Needle with its side port exposed. (b) Similar needle with a silicone sleeve occluding the port.

Because this dart type is relatively lightweight with a slow deposition of drug over several seconds, the injection is relatively nontraumatic to the animal. The dart's sharp needles make them ideal for penetration of most skin types. With proper selection of needle lengths and dart sizes, these darts can be used safely on a large variety of species. They are generally used for short ranges, and because their trajectories are easily affected by wind gusts, they are preferably used during calm weather conditions. Their primary disadvantages are that they can be destroyed by hitting unintended solid objects and their complexity makes them prone to dart failures.

Loading a two-chambered plastic dart involves the following steps:

1) An appropriate-sized clean or sterilized dart is removed from the package.
2) The dart is inspected for cracks and abnormal shape.
3) The dart is tested by placing air pressure in both compartments to make sure that the plungers move easily and that the dart does not leak. A metal connector is required to attach regular 6 or 12 cc syringes to the hub of the dart to inject air into the posterior chamber.

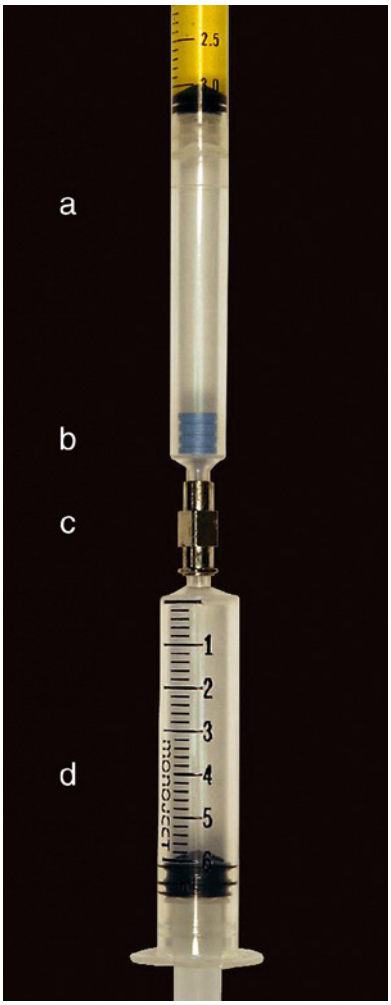


Figure 5.5 Photograph of a two-chambered compressed gas dart being filled. (a) Posterior chamber of the dart. (b) Posterior plunger acting as a one-way valve to allow introduction of compressed gas, but preventing its escape. (c) Coupler that is needed to allow air to pass from the syringe to the dart. (d) Standard syringe used to force air into the dart.

4) Next an appropriately sized, sterile needle is selected. The needle must be inspected for patency and for the presence of a sharp tip. It must be free of burrs or bends from previous impacts.
5) A silicone sleeve is placed over the needle tip and slid down over the needle vent. Many dart manufactures have proprietary colored sleeves to fit their different needle diameters. Some people chose to place sterile ointment on the needle surface to provide lubrication. The sleeve is moved up and down the needle several times to be sure it moves easily before it is placed over the vent opening in the needle.
6) The needle with the silicone sleeve in place is placed onto a clean, empty syringe. To confirm that the sleeve has completely occluded the needle vent, an attempt should be made to force air through the needle.
7) Prior to loading the dart with drugs, the posterior plunger (one-way valve) should be displaced with a venting pin to make sure the posterior chamber is not pressurized.
8) The central plunger is then positioned to provide the correct volume for the drug in the anterior chamber.
9) The needle of a second syringe containing the drug is inserted through the anterior hub and the anterior chamber is slowly filled with the drug to avoid creating bubbles by too rapid filling.
10) The occluded needle with the preplaced silicone sleeve is attached to the dart. This attachment must be secure, with the needle firmly seated on the anterior dart hub. A hemostat or pliers is sometimes used to tighten it in place, being careful not to damage the dart with these tools.
11) A transparent safety cover, such as a syringe casing, is placed over the end of the needle.
12) The dart is held in a vertical position with the needle pointing upwards.
13) The dart is charged with either air or butane placed into the posterior chamber. The air or gas is forced in through the posterior hub, around the one-way valve, and into the posterior chamber of the dart. When properly charged, the rubber plunger at the back of the dart will be firmly pressed against the caudal portion of the posterior chamber.
14) An appropriate tailpiece for the dart is selected. The tailpiece should be inspected to ensure that it is clean, dry, and symmetrical.
15) The tailpiece is firmly attached to the posterior hub of the dart, making the dart ready for use.

Two-chambered Blow Darts

Several types of two-chambered darts use pressurized gas to push the drug into the animal (Fig. 5.6).

The first is the blow dart, which is constructed of very lightweight, clear medical-grade plastic similar to the material used in disposable plastic syringes. The blow dart body usually has a Luer-lock syringe tip hub on the anterior drug compartment. The blow dart needle is exceptionally sharp, constructed from a modified hypodermic needle with a tip that is soldered closed and an opening cut into the side (Fig. 5.7).

The blow dart's lightness and sharper needles make it ideal for use with blowpipes. These darts are most accurate when used indoors. Blow darts should never be used in carbon dioxide (CO_2) or gunpowder cartridge-propelled projectors as their light construction causes erratic flight at high velocities and because they often shatter on impact.

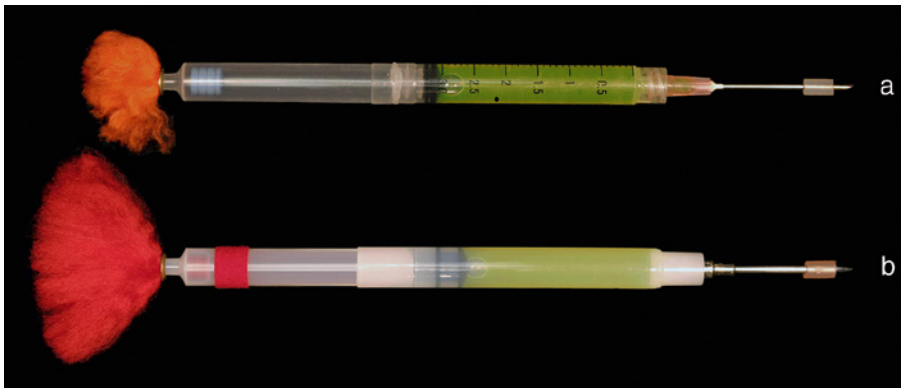


Figure 5.6 Photograph showing the difference between two types of two-chambered compressed gas darts. (a) Blow dart. (b) Injection-molded plastic dart.



Figure 5.7 Photograph of two needle types used in different types of two-chambered compressed gas darts. (a) Hypodermic needle with a sharp tip occluded with solder and used in blow darts. (b) Thicker, blunter, machined needle used in injection-molded plastic darts.

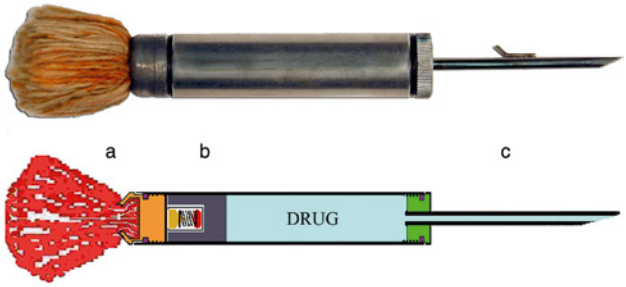


Figure 5.8 Photograph and illustration of a gunpowder explosive powered dart. (a) Yarn tailpiece that is threaded into the back of the dart body. (b) Movable central syringe plunger which contains the explosive charge. (c) Forward ported needle with a wire barb is threaded into the front of the dart body.

Injection-molded Two-chambered Plastic Darts

These darts are heavier than blow darts and are constructed of a variety of synthetic plastic materials. The construction of the dart body is more robust and often reinforced. The anterior hub has a thick collar to better seat the needle and to provide additional strength to the needle attachment. The needles are machined from a thicker metal that resists bending and breaking better than the modified hypodermic blow dart needles.

Injection-molded plastic darts are designed for use in CO_2 or compressed air-powered projectors. Improved ballistic properties enable them to fly true at higher velocities. They are also made to withstand greater impact forces. This gives them a much greater range and allows them to be used outdoors in moderately windy conditions. The blunter needles have no difficulty penetrating most animal skin when powered by these projectors, but are ineffective when projected with a blowpipe. When used correctly and at appropriate distances, these injection-molded plastic darts are safe for the animal and cause only minor trauma (Cattet et al. 2006). A variety of needle sizes are available. Needles can be fitted with barbs to reduce bouncing out of the animal. Impact absorbers can also be placed at the base of the needles to prevent them from penetrating beyond the intended depth and decrease dart trauma (Wiesner 1998). The potential problems associated with these darts are that they can cause significant trauma when used with gas-powered projectors at inappropriately close ranges. Such trauma includes soft tissue damage resulting from the dart embedding too deeply and even long bone fractures.

Gunpowder Explosive Darts

Explosive powered darts use a black gunpowder explosive cap to generate the force needed to discharge the drug. A movable plastic plunger is placed into the center of the dart body to separate the drug from the explosive cap and trigger mechanism (Fig. 5.8).

The anterior chamber holds the drug. The posterior chamber holds a metal explosive unit that contains an explosive cap, a weighted firing pin, and a spring that keeps the firing pin away from the cap prior to dart impact (Fig. 5.9).

The explosive unit is set behind the caudal aspect of the central plunger, and the back of the dart is sealed with a tailpiece. The needles are hollow, forward, or side ported, and do not need to be capped. They come in a large variety of lengths and are usually barbed.

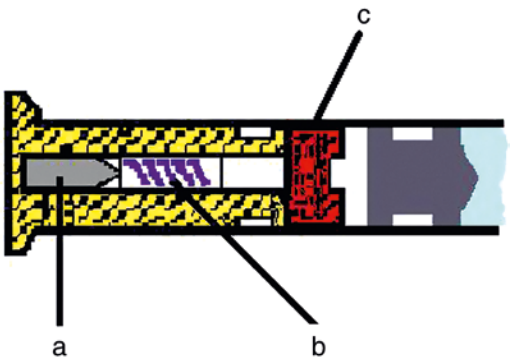


Figure 5.9 Illustration of the tail section and trigger mechanism of a Pneu-Dart gunpowder explosive-powered dart. (a) Movable weight. (b) Spring that holds the weight back. (c) Explosive cap.

Gunpowder charged darts are loaded by placing the drug through the needle lumen and into the anterior chamber. When the dart hits the skin of the animal, the needle penetrates and the body of the dart is stopped by the skin surface. The forward momentum of the dart is carried to the metal firing capsule, where the small spring is overpowered and the firing pin impacts the cap, resulting in an explosion. Expanding gas within the posterior chamber then rapidly forces the plunger cranially, thus pushing the drug out through the needle. Drug injection occurs within approximately 0.001 seconds and can cause considerable tissue trauma (Kreeger et al. 2002; Cattet et al. 2006). Additionally, the explosive rate of the injection causes a rocket effect that propels the dart out of the animal. For the explosive unit to work, the dart must strike the animal with enough force at a perpendicular angle to the target. This necessary force can result in significant dart trauma, particularly in small or delicate species.

Modular Gunpowder Explosive Powered Darts

The Palmer Cap-Chur syringe is an example of a modular gunpowder-explosive powered dart because the operator can build a highly specific dart configuration by choosing different available components. The body of each dart is an aluminum 12.6-mm diameter (.50 caliber) tube with internally threaded ends. The aluminum syringe barrel comes in various lengths that can hold 0.5–20 mL of drug. The Palmer Cap-Chur gunpowder charges come in three different power strengths, each appropriate for a different dart volume. The charges are color-coded: yellow for 0.5–3 mL, orange for 4–10 mL, and red for 15–20 mL. Dart failure can occur with improper charge selection. The metal explosive charge fits with its closed, rounded, cranial end into a pocket in the caudal aspect of the central plunger (Fig. 5.10).

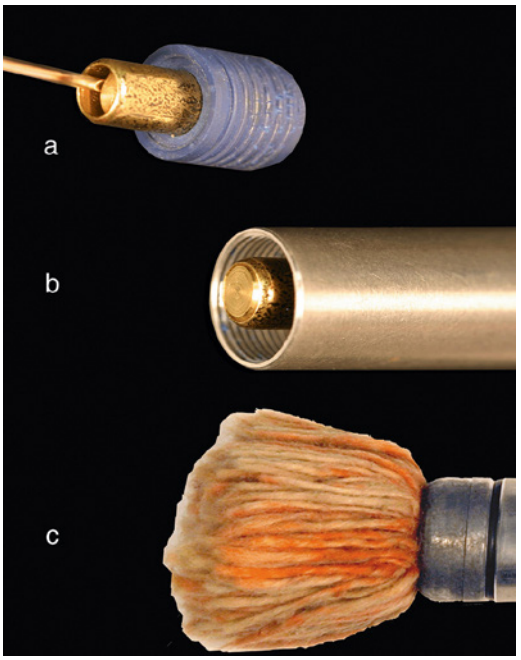


Figure 5.10 Photograph demonstrating the steps in assembling the tail section and trigger mechanism of a Palmer Cap-Chur gunpowder explosive powered dart. (a) The charge has been placed into the caudal pocket of the central plunger. The needle is pressing against the weight and spring to demonstrate the proper orientation of the explosive charge. (b) The plunger and explosive charge have been inserted into the posterior part of the dart body. (c) The yarn tailpiece has been threaded into place.

The explosive unit must be oriented correctly with the open end facing caudally for the dart to discharge. The back of the dart is sealed with a tailpiece that screws into the internally threaded dart body. The needle is threaded into the anterior end of the dart. The needles are hollow and do not need to be capped. Forward-ported and side-ported needles are available in a variety of lengths and with several barb styles (Fig. 5.11).

These modular systems are the oldest commercially available darts and have many years of proven reliability. The many possible dart configurations that can be created depending on choice of needle length, needle style, and payload volume (i.e., tube length) make this the most versatile darting system available. From one set of dart components, darts can be configured with short needles for carnivores or very large needles and barrels for elephants and rhinoceroses. The dart components, except the explosive units, are reusable if cleaned and maintained properly. Keeping the dart components sterile is challenging, but using unsterilized equipment may lead to dart-induced infections (Bush & Gray 1972). The biggest weakness of the system is that the heavy darts and the explosive discharge of drug can lead to significant tissue damage.



Figure 5.11 Photograph of the three needle types used in gunpowder explosive powered darts. (a) Pneu-Dart needle with a green gel cone collar barb. (b) Palmer Cap-Chur needle with a small metal collar. (c) Palmer Cap-Chur needle with a wire barb.

Loading a Palmer Cap-Chur dart involves the following steps:

1) The appropriately sized and sterilized dart components are removed from their packages.
2) The dart parts are inspected for cracks and abnormal shape. The needle, body, and tail are preliminarily assembled to ensure proper threading and then passed through the syringe barrel of the projector to ensure that the dart passes freely.
3) A sterile, central, rubber plunger is selected and then lubricated. It is placed inside the body of the dart, and the plunger is moved back and forth within the length of the dart body to ensure that it moves easily.
4) The plunger is positioned in the caudal part of the dart body.
5) An appropriate strength metal explosive unit is fitted into the pocket in the caudal aspect of the rubber plunger. It is crucial to make sure that the explosive unit is oriented correctly, with the movable plate exposed caudally.
6) A tailpiece is selected and threaded into the caudal part of the dart body.
7) An appropriately sized sterile needle with an acceptable barb style is selected. It must be inspected for patency and to make sure that it does not have a burr at the tip or is bent from a previous impact.
8) The needle is then threaded onto the cranial part of the dart body.
9) The dart is loaded by passing the needle of a syringe containing the drug through the dart needle lumen and depositing the drug into the anterior chamber of the dart. The syringe needle should be longer than the dart needle and the drug introduced slowly to avoid drug back flow from that dart needle.
10) Sterile water is used to completely fill the remaining volume in the anterior chamber of the dart.

Prefabricated Gunpowder Explosive-powered Darts

Pneu-Darts and Clear Darts are examples of prefabricated rather than modular gunpowder explosive-powered darts. The explosive mechanisms are similar, except that they come already positioned in the dart by the manufacturers. The darts, which come as complete units that cannot be taken apart, are made of a combination of aluminum or polycarbonate plastic bodies, a hollow needle, and a plastic tailpiece. The function and limitations of this type of darts are similar to those of modular systems.

The simplicity of the prepurchased dart makes them appealing products. The operator selects the dart volume, needle length, and barb configuration that will be needed for the anesthetic event. Most needles come with a green gelatin collar or barb to prevent the dart from being ejected from the skin when the dart discharges. Loading the dart is a simple matter of placing the drug through the dart needle and into the anterior chamber.

Pneu-Darts come in three types. The first is the "P" dart line, with a yellow tailpiece, designed for blowpipes or CO_2 powered projectors. The second is the "U" dart with yellow tailpieces fitted with an orange plastic spacer that retains the dart in the rifle barrel. The final dart line is the "C" dart, with orange tailpieces that are designed for the 22 blank-powered cartridge projectors. They differ only in the diameter of the tailpieces: larger in the "C" dart to help engage the rifled barrel and in the tensile strength of the spring in the explosive unit, which is weaker in the "P" and "U" darts. The Pneu-Dart line offers several available dart configurations that include clear polycarbonate plastic or aluminum bodies and are available with tri-ported needles.

Loading a Pneu-Dart or similar dart involves the following steps:

1) Select a dart with the appropriate drug payload size and needle length from the package.
2) Note the tailpiece color and package label to make sure that the dart type selected matches the intended projector. A yellow tailpiece indicates the "P" and "U" dart lines designed for blowpipes or CO_2 powered projectors. An orange tailpiece indicates the "C" dart line designed for the 22 blank-powered cartridge projectors.
3) Inspect the dart for cracks and other manufacturing abnormalities.
4) Inspect the dart for dirt or moisture damage that may compromise sterility or dart function.
5) Load the dart by passing the needle of a syringe containing the drug through the dart needle lumen and depositing the drug into the anterior chamber of the

dart. The syringe needle should be longer than the dart needle and the drug introduced slowly to avoid drug back flow from the dart needle.

6) Use sterile water to completely fill the remaining volume in the anterior chamber of the dart.

Miscellaneous Dart Types

Modified Two-chambered Compressed Gas Dart

Palmer Cap-Chur produces a modified clear plastic two-chambered compressed gas dart that uses the projector's CO_2 to automatically pressurize the dart. The dart has a unique one-way valve system in the tailpiece that allows entry of pressurized CO_2 from the projector into the posterior chamber of the dart. The dart has an open needle that is occluded with a plastic tip. The function and loading of this dart are like that of two-chambered gas darts, without the need for prior pressurization.

Chemical-powered Darts

Chemical darts use an effervescent acid/base reaction to produce gas and thus inject the anesthetic (Fig. 5.12).

The design has a two-chamber configuration with the chemicals placed in the posterior chamber. Prior to discharge the chemicals are kept apart. On impact, a variety of mechanisms have been devised to allow the chemicals to mix and produce gas (Bush 1992). Because the drug compartment is not under pressure, open-ended needles can be used. These darts are easy to load and are reliable in most field situations. The injection speed is slower than that of compressed gas or explosive charged darts, but this slow discharge is usually acceptable and in fact beneficial in that it causes minimal injection trauma and limited blow-back from the dart. No chemical darts are commercially available in the United States, but they are used and available in Africa and Europe (Nielsen 1999).

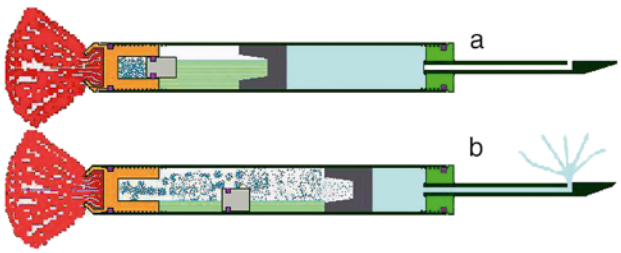


Figure 5.12 Illustration of a chemical reaction-powered dart. (a) Representation of the loaded dart prior to impact. The chemical reagents are kept separated by a weight occluding the chemical chambers. (b) Representation of the dart after impacting the target and during discharge of the drug. The weight is now dislodged and the chemicals have mixed and produced a gas that pushes the central plunger forward.

Spring-powered Darts

Spring-powered darts are also not currently commercially available in the United States. The design is like that of the two-chambered dart, except that the posterior chamber is replaced with a spring to provide the injection force. The spring is attached anteriorly to the central plunger and posteriorly to the back of the dart body. Trigger mechanisms usually involve silicone-capped needles that function similarly to those in two-chambered darts. The dart body is constructed of plastic or aluminum depending on the projector that will be used. The major problem with these darts is that the process of loading the dart is both difficult and dangerous due to inadvertent spraying of the drug during the loading process.

Solid Drug Darts

Solid drug projectiles are constructed in a manner similar to the original gallamine paste projectiles used in the 1950s. Several attempts have been made to develop a solid, lightweight, absorbable bullet (Bush 1992). Current versions are made of various materials, such as hydroxypropylcellulose, that dissolve and absorb into the muscle of the animal (Jessup 1993; van de Wijdeven 2002). An example is the Ballistivet system, which was developed for vaccination of domestic livestock, but can be applied to anesthesia of both captive and wild nondomestic species. As in the original descriptions of solid drug injection systems, the limitations of payload size and slow absorption are persistent obstacles in their use for primary induction of anesthesia.

Remote Delivery Projectors

Compressed Gas Projectors

Blowpipes

Blowpipes are by far the most versatile, inexpensive, silent, lightweight projectors available. In short ranges, an experienced darter can have exceptional accuracy. The light darts combined with their slow velocity produce minimal impact and tissue trauma. The operator can adjust the dart speed instantly and therefore deliver the dart as gently as needed.

Blowpipes consist of a long lightweight tube with a mouthpiece on one end. A blow dart is placed in the end of the pipe and compressed gas is provided by the operator blowing with a rapid, strong breath through the tube. The longer the pipe, the greater the accuracy of the dart. Commercial blowpipes are available from several manufacturers in various pipe lengths, diameters, and shapes of mouthpieces. Selection is based on personal preference for the mouthpiece and the diameter of the dart type selected.

Using a blowpipe requires practice. The pipe is held horizontally and grasped in the hand opposite to the dominant eye. The operator should look at the tip of the pipe and aim

it at the target. Compressed air is provided following a deep inhalation then a rapid exhalation in a manner somewhat approximating a combination of coughing and blowing through the pipe. Because of the slow dart velocity, the dart will tend to fly in an exaggerated downward arc instead of a straight line. Effective blowpipe range is about 0.5–10 m. Because darts may occasionally leak and the mouth must be placed on the mouthpiece, darts containing dangerous drugs such as concentrated narcotics should not be projected using a blowpipe.

Gauged Blowgun Projectors

A modification to the blowpipe is to add an external source of compressed gas, thereby eliminating the need for the operator to exhale through the pipe (Fig. 5.13).

Gauged blowgun projectors are designed to shoot heavier injection molded two-chambered plastic darts or type "P" or "U" Pneu-Darts. These projectors utilize a source of compressed gas, a combination pressure gauge and valve system to control the gas pressure, and a trigger mechanism. Gas power can be provided either by air via a foot pump or by compressed CO_2 from a pressurized cylinder. Pressure gauges and release valves allow the pressure to be increased or decreased as needed during darting. A detachable, long barrel is then mounted on either a pistol handle or a rifle stock. The projectors can be equipped with a telescopic sight. Different diameter barrels can be interchanged to accommodate either 10.8- or 12.5-mm darts. Pistols are used for short range or indoors where space is limited, but are less accurate than rifles, which are used outdoors over longer distances. Careful selection of the dart type is important, as lightweight plastic blow darts will often not fly correctly in these CO_2-powered projectors.

Gauged blowgun projectors are quiet, reasonably accurate, and provide a simple means of darting exotics for distances between 5 and 30 m. Many veterinarians in zoological collections use this system exclusively.

Air and CO_2 Rifles and Pistols

Pistols and rifles are compressed gas projectors with their barrel permanently mounted onto a triggered compressed gas power source (Fig. 5.14).

The compressed gas power source can be provided by CO_2 cylinders or using an attached air pump similar to a pellet gun. These projectors generally lack accurate pressure gauges and valve systems with the ability to change the gas pressure. Instead, they typically have two or three presets that can be dialed in for selecting power levels. These systems are usually designed for 12.5-mm metal darts such as Palmer Cap-Chur and type "P" or "U" Pneu-darts. Due to their short barrels, the pistols are notoriously inaccurate at long range. In contrast, rifles can be very accurate at moderate distances. Both systems, when used at short range, can cause significant trauma due to the lack of accurate pressure control.

Gunpowder Cartridge-powered Rifles

These rifles have permanently mounted barrels on a rifle stock. They are powered by .22 caliber blanks that come in several charge strengths with different amounts of gunpowder. Charge strengths are color-coded. In the Palmer Cap-Chur system, brown is the weakest cartridge, followed by green, yellow, and red as the strongest (Fig. 5.15).

Lacking pressure gauges, preset lower power levels can often be manually selected. Although these rifles are too powerful for short-range or indoor use, they have the longest effective range of any projector and can be used in



Figure 5.13 Photograph of two Dan-Inject blowgun type projectors. (a) Model CO_2 PI pistol with an 11-mm barrel. The pistol is powered with a compressed CO_2 cartridge. (b) JM Special rifle with 11-mm barrel. It is also powered by a compressed CO_2 cartridge.



Figure 5.14 Photographs of three compressed gas-powered 12.7-mm (.50 caliber) projectors. (a) Palmer Cap-Chur Model #1300 mid-range pistol powered with two compressed CO_2 cartridges. (b) Pneu-Dart Model 178B air pump rifle. (c) Palmer Cap-Chur Model #1200 long-range rifle powered with two compressed CO_2 cartridges.



Figure 5.15 Photographs of two cartridge-powered 12.7-mm (.50 caliber) projectors. These powerful guns are used only outdoors for long-range targets. (a) Palmer Cap-Chur Model #1000 extra long-range rifle. (b) Pneu-Dart Model 196 rifle.

windy conditions. With a 12.7-mm (.50 caliber) bore, these rifles are designed for 12.5-mm metal darts such as Palmer Cap-Chur or type "C" Pneu-Darts.

Miscellaneous Projector Types

Crossbows and Bows

Although uncommon, commercially available darts can be mounted on arrow shafts and delivered with either crossbow or conventional bows. In Africa, several Ju/'Hoan bushmen were given arrows with Pneu Darts attached at the tips. Using these arrows and their archery hunting techniques, they were successfully able to immobilize free-ranging lions and leopards (Stander et al. 1996). Archery-based projectors are accurate, but if not properly controlled the velocity of the heavy arrows will cause trauma to the animals.

Injection Collars

Remote injection collars can be placed on an animal prior to release and used to inject the animal later (Jessup 1993). Commercially available products have been used in white-tailed deer and wolves. The injection is triggered by remote control. Combined with telemetry and a safety collar release if the batteries that power them run low, they can be a valuable tool for use in wildlife. Application of these collars in zoological collections has been limited, but may be practical in situations that require multiple immobilizations in animals that are difficult to dart.

Darting Accessories

Many manufacturers provide practice darts and targets for their equipment. These practice darts are cheaper than operational darts and are consistently weighted to help improve accuracy. Through practice the operator will develop proficiency with the equipment and reliable accuracy. During practice it is important to develop a feeling for the proper impact velocity required to prevent excessive trauma.

Laser range finders, scopes, and binoculars are useful in outdoor darting procedures. Calibrating the projector for selected distances is the best method of consistently producing accurate and atraumatic shots. Once the calibration is completed during practice sessions, using the range finder significantly improves range estimates and allows the operator to make confident and accurate projector settings. The binoculars are useful for selecting the target and then confirming that the dart has hit the animal.

Cleaning and Reusing Darts

Many of the remote drug delivery systems, such as pole syringes, two-chambered compressed gas darts, and modular gunpowder explosive powered darts, are designed to be reusable. However, for proper function these darts must be cleaned, maintained, and stored correctly. Specific procedures and maintenance recommendations should be obtained from the dart manufacturer based on the preferences of the individual practitioner.

General dart cleaning and storage procedures:

1) Every effort should be made to locate and retrieve the dart after the procedure.
2) The retrieved dart should be placed in a labeled and secure container during transport prior to dismantling and cleaning.
3) Using gloves and proper eye protection, the dart should be inspected for residual drug or unreleased internal pressure.
4) While submerged under water the dart is carefully disassembled. The water provides protection from drug aerosolization and also dilutes any residual drug from the dart. Alternatively, disassembly can be performed under flowing tap water or in a safety cabinet.
5) After disassembly, each component of the dart is individually cleaned with warm soapy water and then inspected. The dart bodies are inspected for bending or cracks. Needles are inspected for patency, bending, or damaged retention barbs. Needle tips are inspected for sharpness and tip burs. Damaged parts should be discarded or repaired.
6) The dart parts should then be soaked in a disinfectant solution, carefully rinsed, and individually dried.
7) The dart components should be lubricated according to the manufacturer's recommendations.
8) The darts components are then sorted and packaged in sealable containers or surgical instrument wrappers.
9) Finally, the dart components can be sterilized according to manufacturer's recommendations.

Drug Delivery Problems

Dart Failure

Although darts and their projectors have become indispensable tools in zoological medicine, dart failures are common. The most important factor causing a dart to miss the target is operator error from inexperience with the darting system. Each darting system has individual characteristics that must be learned by the operator. Accuracy and consistency are only developed with persistent practice.

Unfortunately, all darting systems are prone to high failure rates, and even when the darts hit their intended target, many fail to discharge. More complex darting systems are more likely to fail. Careful preparation and testing of the darts are essential steps prior to each darting. Each darting system has critical or failure-prone components that must be carefully checked by the operator. Maintaining the equipment in portable organized kits helps ensure that the proper components are available and facilitates the darting procedures (Fig. 5.16).

Examples of common problems are explosive charges that fail to fire, blocked dart needles, and central plungers that stick. Ambient temperatures can affect dart function and the performance of compressed gas darts. In very cold temperatures darts may fracture on impact, drugs can freeze or become thick, and compressed gas exerts less pressure, causing incomplete discharges.

Drug Failure

The selection of anesthetic drugs is beyond the scope of this chapter, but inappropriate choices can definitely result in immobilization failures. Improper deposition of the darted drugs can also produce unexpected results. Darts that deposit drugs into vascular structures or medullary cavities of bones can have rapid onset similar to intravenous administration. Conversely, deposition into skin, subcutaneous space, tendons, fat deposits, or other poorly vascularized tissues can result in unacceptably slow absorption. Some clinicians recommend the usage of hyluronidase to improve absorption of drugs injected with darts (Kock 1992).

Drug interactions when mixed into a syringe must be considered, but have been poorly studied. Environmental conditions such as freezing or heating may also alter drug potency. Long-term storage of drugs in preloaded darts is questionable because the drug's potency and purity may change with time (Kreeger 2002).

Aerodynamics of Darts

Darts have poor ballistic properties compared to bullets or arrows. Their variable shapes and shifting liquids often cause their flight to be very erratic. Bent darts or needles damaged by previous impacts can radically alter a flight trajectory. Aside from the shape, the velocity of the dart as it exits the projector is another important variable in



Figure 5.16 Photograph of a darting kit with essential components separated into compartments. Note that a radio is included to provide emergency communications.

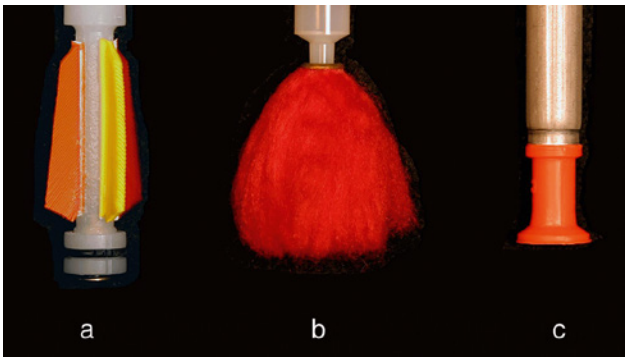


Figure 5.17 Photograph of three types of dart tails. (a) Four fin tail from a Dist-Inject mini-ject easy dart. (b) Cloth tail from a Dan-inject S series plastic dart. (c) Plastic tail from a Pneu-Dart type C dart.

determining the dart's trajectory. Fast muzzle velocities produce flat flight trajectories similar to those of a bullet. Although accurate, these faster velocities are associated with severe impact trauma and dart malfunctions. Furthermore, all darts, even when properly loaded and balanced, will destabilize at very high velocities. As a result, all darting systems are forced to use relatively slow muzzle velocities. At these slower velocities, the dart's trajectory becomes a downward arc which increases with darting distance. This arc must be anticipated, and an experienced darter will compensate appropriately.

The tailpiece is designed to provide the dart with aerodynamic stability (Fig. 5.17).

Available tails range from finned tails like archery arrows to wool and cloth tail stabilizers. Finned tails are considered very reliable, whereas wool and cloth tail stabilizers can cause problems if they are asymmetrical. Rifling of the projector barrel is a method of increasing flight stability by forcing the projectile to spin on its horizontal axis. Although available in some projectors, few darts can engage the rifled barrel surface and therefore do not actually spin well in flight (Fig. 5.18). Additionally, some dart tails, such as cloth and finned configurations, actually resist the horizontal spin that the rifled barrel is intended to provide.

Environmental conditions can also have significant effects on dart trajectories. Objects such as trees or large plants may deflect the dart. Winds and wind gusts can cause darts to fly in unexpected directions. Helicopter down drafts can affect darts as well. Due to their light weight, plastic darts are more prone to this problem.

Animal Injury

Severe tissue injury, including hemorrhage, necrosis, and bone fractures, can occur whenever darts are used. Any projectile with a needle can cause injury when it hits an animal in an unintended location. Sudden movements



Figure 5.18 Photograph through the barrel of a rifle barrel showing the spiral riffling intended to cause a dart to spin on its horizontal axis during flight.

from the targeted animal can lead to inadvertent injury to either the target or other animals in the group. Common examples include dart injuries to the eye, thorax, abdomen, and testicles. It is ultimately the operator's responsibility to only take shots that are likely to hit the expected target in an anatomically appropriate location.

In choosing the site selection on the animal, the operator must evaluate whether enough muscle mass is present to allow for injection of the drug and safe impact of the drug. In most animals the muscles of the upper hind legs are the safest selection. Occasionally the base of the neck or the triceps can be targeted. In addition, the choice of needle should limit tissue trauma while effectively providing adequate penetration for injection of the drug into the muscle. Needle length is selected based on the thickness of the animal's skin and the expected depth of the muscle mass. Inappropriately long needles have the potential to fracture bones on impact. Choice of needle diameter requires consideration of the potential for the needle to break on impact. Broken dart needles retained in muscle tissue have been reported when too thin a needle diameter was chosen (Cohn 1998).

Trauma to an animal from a dart is directly related to the kinetic energy (KE) of the dart (Karlsson & Stahling 2000; Kreeger et al. 2002). This energy can be estimated by knowing the mass and speed of the dart at impact in the following relationship: $KE = \frac{1}{2}(\text{mass}) \times (\text{velocity})^2$. Since velocity is squared it therefore has the greatest influence on the injuries caused on impact and means that heavy darts are not always more harmful for the animal than lighter ones (Kreeger et al. 2002). Although all darts require enough kinetic energy for the needle to enter the

skin and trigger discharge, excessive amounts of energy are associated with trauma and dart failure. In extreme situations the whole dart can become imbedded into the muscle or fracture a bone.

Darts can also injure tissues by overly forceful injection of drug (Cattet et al. 2006). This is particularly true of large-bore, open-ended needles that are discharged with explosive force. Both severe tissue injury and tissue necrosis have been documented with these types of darts (Wiesner 1998; Cattet et al. 2006).

Needle trauma caused by movement of the needle after discharge can similarly be significant. Often the first reaction of a darted animal is to jump, run, or remove the dart. Barbs and collars on dart needles are designed to keep the darts lodged in the animal, but if retained in live tissue for long periods or forcefully removed, they can lead to injury.

Infection of the dart site is generally rare, but can be another cause of serious complications to routine darting procedures. Unavoidably, needle penetration of the dart occurs through unclipped, unprepared, and often grossly contaminated skin. Some darts have been shown to directly introduce hair and other foreign material deep into the dart injection site (Cattet et al. 2006). Unsterile darts and contaminated drugs can further inoculate the injection site with bacteria. Once introduced into the dart wound, bacteria may grow rapidly in the traumatized tissues associated with the dart site, resulting in significant and deep wounds that develop into gross clinical infections. Inspection of the dart site and local wound care during the anesthetic procedure is always recommended. Many practitioners also recommend the use of prophylactic antibiotics, although the effectiveness of a single antibiotic injection is questionable and has not been prospectively evaluated. To minimize dart site infection, most darting needles can be sterilized prior to use. Aseptic techniques can be used during dart preparation, such as wearing sterile gloves while assembling the dart and loading it (Bush & Gray 1972).

Human Safety Concerns during Darting Procedures

Dart projectors should be considered firearms and treated with the same rules of basic gun safety to prevent accidental discharges. The ballistic properties of any dart can lead to serious injuries to people. Because darts are subject to radical changes in trajectory when they are deflected by wind, obstacles, and bouncing off animals, the operator must evaluate the position of all personnel around and particularly behind the target before the pulling trigger.

Most of the dart systems described previously are designed to automatically discharge drugs, making an accidental drug exposure likely when they hit a human. On rare occasions, darts may expel the drug prior to full needle penetration or after bouncing out of the animal's skin. In these cases, the drug can be aerosolized or sprayed onto the surface of the animal, resulting in accidental human drug exposure. Emergency plans for managing accidental human drug exposure must be in place prior to any immobilization procedures. Such plans should include access to effective emergency communication equipment such as a cellular telephone or two-way radios, knowledge of CPR, and basic first-aid procedures.

The most important safety considerations are proper planning and familiarization with the drug delivery method selected. Advanced planning for each procedure is also essential so that each person involved is cognizant of their roles and safety considerations. Prior practice and familiarization with the equipment make the operator more confident and effective in delivery of the anesthetics. Ultimately, the responsibility for the safety of an anesthetic delivery is on the anesthetists and the operator of the equipment.

Conclusions

The methods of drug delivery to nondomestic species are essential to the practice of zoo animal and wildlife anesthesia. However, these methods are often complicated and must be learned and practiced before application. Each remote delivery system has both advantages and significant limitations. Practitioners interested in obtaining equipment should familiarize themselves with all the available systems. Commercial websites often provide detailed information on specific product lines. Classes and conference lectures or wetlabs can provide valuable comparative product information and the opportunity to use several products. Additional information is also available in other books that describe the use of this equipment for specific applications (Kreeger et al. 2023; Kock & Burroughs 2012).

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6

Invertebrates

Sarah J. Wahltinez, Craig A. Harms, and Gregory A. Lewbart

Introduction

What sort of topic is invertebrate anesthesia and analgesia? A better first question might be "What exactly are invertebrates?" The invertebrates are a collection of animals, comprising more than 95% of the earth's species, unified by the lack of a single anatomical trait: the vertebral column. Ruppert et al. (2004) stated invertebrates are a group of unrelated taxa that share no universal "positive" traits.

There are currently approximately 40 recognized phyla of invertebrates (not including the protozoans). Many of these phyla are not well known to veterinary medicine, but for no better reason than they may contain few species, microscopic representatives, or have no obvious economic value. Each phylum and its members are important to the diversity and survival of the planet, even if the group is only studied by a small number of scientists. Relatively little is known about the veterinary care, and more specifically acceptable anesthesia and analgesia choices, for many of these taxa. Writing a comprehensive book chapter for all invertebrate groups would be inefficient. Consequently, we have elected to include information on the metazoan taxa encountered by veterinarians and researchers. This chapter reviews the most common anesthetic techniques for these taxa, with a focus on those species most frequently under human care as well as a review of acceptable euthanasia methods.

Invertebrates are subjects of in situ and ex situ research, are kept as pets, and are common display animals in public aquaria. Many invertebrate species (e.g., flatworms, nematodes, cephalopod and gastropod mollusks, horseshoe crabs, and various species of insects (e.g., fruit flies)) have been used in research laboratories for decades. Their related contributions have greatly increased our understanding of heavy metal and pesticide toxicity, color perception and vision, embryology, and an extensive list of diseases, including cancer, diabetes, inherited genetic disorders, multiple sclerosis, and Parkinson's disease. In zoos and public aquaria, invertebrates are attractive display animals and common inhabitants in interactive exhibits such as touch pools, butterfly houses, and invertebrate zoos. Interaction with invertebrates at touch pools in public aquaria has been shown to impart positive attitudes and changes in the knowledge of visitors (Ogle 2016).

The influence and elevated awareness of animal welfare and shifting public opinion have resulted in increased consideration for the welfare of invertebrate animals. In research, the attempts and efforts to reduce, refine, and replace the use of vertebrate species have impacted invertebrate animal models. The general perception that invertebrates are more acceptable than vertebrates in research settings is primarily due to the belief that invertebrates do not experience pain. Selecting invertebrates for research makes the process of Institutional Animal Care and Use Committee oversight very easy since there are no regulations or restrictions in the United States on invertebrate use. Despite growing concerns from different organizations and institutions, the Animal Welfare Act and Public Health Service Policy do not protect invertebrates. Some organizations, including many zoos and aquariums, require a protocol for invertebrates used in research. The United States Department of Agriculture (USDA) has an Information Resource on the Care and Use of Invertebrates (AWIC Resource Series No.8 2000) document that has numerous references for invertebrates used in research. In zoos and aquaria, standards for the care of invertebrates are increasing. The Association of Zoos and Aquariums (AZA) has published care manuals for giant Pacific octopus, Japanese spider crab, and jellyfish. The USDA has standards for nonindigenous arthropods (USDA APHIS 2002), but these guidelines are geared towards preventing the release of potentially invasive species. *The UFAW Handbook on the Care and Management of Laboratory Animals* has in its eighth edition a section on cephalopods with references

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(Hubrecht & Kirkwood 2010). Several reviews, references, and recommendations have been published on behaviors and husbandry of different invertebrate species (Anderson & Wood 2001; Fiorito et al. 2015; Smith & Berkson 2005; Wood & Anderson 2004).

The discussion about pain recognition and welfare in invertebrates is slowly moving and many changes have been initiated from the United Kingdom and other European countries (Berry et al. 2015; Cooke et al. 2019; Diggles 2019; Elwood 2019). The increased veterinary interest in invertebrate medicine will result in more research and scientific findings, leading to appropriate care for invertebrate species in clinical and laboratory settings. It is possible that selected invertebrates will soon be included in US animal welfare regulations, leading to regulatory oversight for invertebrate species in research. Cephalopod mollusks are protected in the European Union under EU Directive 2010/63/EU and in the United Kingdom, Canada, and Australia. Decapod crustaceans and cephalopod mollusks are protected in in Switzerland, Norway, and New Zealand (Smith et al. 2013). Sentience in some cephalopod mollusks and decapod crustaceans was recently reviewed with implications for animal welfare regulations (Birch et al. 2021). The criteria evaluated included (1) associative learning beyond habituation and sensitization, (2) flexible self-protective behaviors in response to injury and threat, (3) behavior demonstrating the animal values local anesthetics or analgesics when injured, (4) motivational trade-offs demonstrating balancing of threat versus opportunity for reward, (5) responses affected by potential local anesthetics or analgesics, (6) connections between nociceptors and integrative brain regions, (7) possession of integrative brain regions, and (8) possession of nociceptors. Based on these criteria, Birch et al. (2021) concluded there is very strong evidence of sentience in octopods and strong evidence for true crabs (infraorder Brachyura).

Animal welfare considerations aside, effective anesthesia can facilitate successful completion of procedures more efficiently, and often with less biological disruption than physical restraint alone, leading to better results.

Anesthesia Overview

Hypothermia, despite its prominence in the literature, is not considered anesthesia and does not provide analgesia or muscle relaxation. Hypothermia is thought to be painful and should not be used as an anesthetic, especially for surgery or other potentially painful procedures. Distress and mortalities have been reported from hypothermia in squid (Bower et al. 1999). Cardiovascular and respiratory system compromise during hypothermia, as well as consequences of rewarming, may be the leading causes of adverse outcomes.

There is a lack of evidence-based information on anesthetic monitoring of invertebrates. Respiratory and cardiovascular systems knowledge for the species should dictate anesthetic monitoring. Ruppert et al. (2004) contains relevant information on life history and physiology that can be helpful in determining anesthetic depth and monitoring invertebrates under anesthesia.

Aquatic Invertebrates

Aquatic invertebrates are commonly anesthetized by immersion in a solution containing an anesthetic, which can be considered analogous to inhalant anesthetics for vertebrates. The anesthetic water should match the water quality of the animal's environmental water as closely as possible (e.g., hardness, osmolality, pH, salinity, and temperature). Immersion anesthetic agents may be delivered as a static bath treatment for short-term procedures or via a recirculating system for longer duration procedures. Induction, maintenance, and recovery water should be well aerated.

With the exception of crustaceans, magnesium salts ($MgCl_2{\cdot}6H_2O$ and $MgSO_4{\cdot}7H_2O$) are commonly used as immersion agents for sedation, anesthesia, and euthanasia of many aquatic invertebrates. Hexahydrate magnesium chloride and heptahydrate magnesium sulfate (Epsom salts) are the compounds typically meant when $MgCl_2$ and $MgSO_4$ are referred to in invertebrate anesthesia literature. For our purposes $MgCl_2$ and $MgSO_4$ will refer to $MgCl_2{\cdot}6H_2O$ and $MgSO_4{\cdot}7H_2O$, respectively. At a 7.5% concentration (75 g/L) in distilled water, $MgCl_2{\cdot}6H_2O$ is nearly isosmotic with seawater. Thus, 7.5% stock solution can be added incrementally to seawater without altering osmotic pressure, whereas adding $MgCl_2{\cdot}6H_2O$ directly to seawater can markedly increase osmolarity, an important consideration for anesthetizing aquatic invertebrates.

Opinions differ about the ability of $MgCl_2$ to produce adequate sedation and analgesia via blocking nerve transmission and neurotransmitter release, or if it acts solely as a neuromuscular blocking agent (Clark et al. 1996). Unique aspects of invertebrate anatomy and physiology as well as routes of administration, when compared to vertebrates, seem to play a role in the observed effects; however, the issue remains unresolved for all taxa (Clark et al. 1996). Magnesium ions act centrally in suppressing neural activity in cephalopods (Messenger et al. 1985) and cephalopods have been found to lose both afferent and efferent nerve transmission, indicating true anesthesia (Butler-Struben et al. 2018). Further research is needed to evaluate the



Figure 6.1 Purple sea urchin (*Arbacia punctulata*) being observed during an anesthesia trial with MS-222. The idea of invertebrate anesthesia is a new concept for many people and was an engaging subject for this group of schoolchildren. Image by GA Lewbart.

effects of $MgCl_2$ on nerve transmission across invertebrate taxa to determine if it is a true anesthetic.

Ethanol is another frequently used immersion agent for aquatic invertebrates. Its depressive effects on the central nervous system have been well described and include inhibition of neuronal calcium and sodium channels in mollusks (Deitrich et al. 1989). Concentrations of ethanol used for anesthesia (up to 10%) are far lower than those used as a tissue preservative (70% and greater). The latter high concentrations are unsuitable for use for anesthesia or for a first- or single-step euthanasia.

Tricaine methanesulfonate (MS-222), an immersion anesthetic agent commonly used for fish, is often assumed to be a logical choice to try on aquatic invertebrates simply because of their common environment. In practice, with the exception of some echinoderms (Fig. 6.1), jellyfish (Fig. 6.2), and anemones, MS-222 is less effective for aquatic invertebrates (Butler-Struben et al. 2018; Gorges et al. 2022) or requires substantially higher concentrations (Applegate et al. 2016).

Other agents used for aquatic invertebrate anesthesia include benzocaine, eugenol/clove oil, ketamine, lidocaine, menthol, pentobarbital, 2-phenoxyethanol, propylene phenoxytol, tiletamine-zolazepam, urethane, and xylazine. Details are included with specific taxa below.



Figure 6.2 This moon jelly (*Aurelia aurita*) has been euthanized with an overdose of magnesium chloride (142 g/L for 15 minutes) and is being weighed prior to fixation in Davidson's fixative. Image by GA Lewbart.

Terrestrial Invertebrates

Terrestrial invertebrates can be anesthetized or immobilized with various gaseous and volatile agents, including chloroform, carbon dioxide, desflurane, isoflurane, and sevoflurane. These are administered in exposure chambers either commercially designed for invertebrates, adapted from small mammal chambers, or custom-made. Anesthetics may be administered via precision vaporizer into the chamber or by adding liquid anesthetic to a fibrous matrix (e.g., cotton ball, filter paper, rayon pad) within the chamber, ensuring no direct contact with the invertebrate to be anesthetized. This latter method is simpler, but less controlled, and can result in high anesthetic concentrations with greater risk for anesthetic complications. See the arachnid section for details on anesthetic chambers for terrestrial invertebrates.

Anesthesia by Taxa

Coelenterates

Anatomy, Physiology, and Natural History

Coelenterates (cnidarians) have a radially symmetric body with a single gastric opening surrounded by tentacles and derive their name from their cnidocytes, or stinging cells. The two basic body forms are called polyps and medusae, which may occur at different life stages in the same individual. Polyps are tube-shaped and attached to substrate while medusae are bell-shaped and free swimming. There are over 11,000 species of coelenterates, including anemones, corals, and jellies. Their nervous system is composed of a pair of nerve nets comprising interconnected neurons. Medusae also possess nerve rings and ganglia found along the edges of the bell (Ruppert et al. 2004).

Many coelenterates, especially those in tropical waters, have endosymbiotic tissue dinoflagellates most commonly from the genus Symbiodinium. These intracellular algae, known as zooxanthellae, allow coelenterates to thrive in oligotrophic waters by sharing products from photosynthesis in exchange for a protected environment and nutrients from the host coelenterate (Ruppert et al. 2004).

Anesthetic Agents Used and Techniques

Most reports of coelenterate anesthesia are based on relaxation or narcotization in preparation for terminal fixation to prevent contraction of polyps, therefore there is limited information about the recovery and lasting impacts of these narcotization solutions on the animals. Further research is needed to determine optimal anesthetic protocols for survival procedures in this phylum. Doses for coelenterate anesthesia are reported in Table 6.1.

Jellyfishes

Anatomy, Physiology, and Natural History

The iconic adult jellyfish is the medusa, however, there is a jellyfish developmental polyp stage (Ruppert et al. 2004).

Physical Restraint

During handling, jellyfish can be easily damaged by nets or hands, and should be submerged in water at all times. Jellyfish can be captured using bowls or plastic bags in a swirling motion to draw water into the vessel. After handling, jellyfish should be carefully inspected to ensure there is no air trapped under the bell, which can be detrimental to their health. Trapped air can be removed by gently turning jellyfish upside down and tapping the bell from below (AZA Aquatic Invertebrate TAG 2021). Some jellyfish are venomous and stings can be harmful to humans. Precautions, including wearing protective gloves, should be taken to prevent human envenomation.

Anesthetic Agents Used and Techniques

Jellyfish have been anesthetized using a menthol solution (Fuentes et al. 2011) and MS-222. Moon jellyfish immersed in MS-222 at 0.3 and 0.6 g/L had reduced response to stimuli and decreased movement with no mortality observed (Gorges et al. 2022). Medusae have also been relaxed with $MgSO_4$ iso-osmotic to seawater (Colley & Trench 1985), isotonic $MgCl_2$ (Kikinger 1992) and menthol (Park 1998), however, these animals were fixed and dehydrated for histology. To evaluate anesthetic depth, a rocking stimulus test, probe stimulus test, and bell contraction quality and body tone have been used (Gorges et al. 2022).

Sea Anemones

Anatomy, Physiology, and Natural History

Sea anemones exist as large solitary polyps and lack a medusa stage (Ruppert et al. 2004).

Physical Restraint

Sea anemone often retract their tentacles in response to disturbances, which prevents visual examination, procedures, and interpretation of histology if animals are fixed without relaxation.

Anesthetic Agents Used and Techniques

Sea anemones have been anesthetized by immersion in seawater with menthol crystals titrated until the animals were nonresponsive. This method did not appear to impact their regenerative abilities, but, other health parameters were not examined (Bossert et al. 2013). Juvenile and adult anemones have also been relaxed in $MgCl_2$ (71.4 g/L) diluted 1:6 with 1/3-strength artificial seawater for 10–15 minutes (Amiel et al. 2015). Another reported anesthetic dose is 7 g $MgCl_2$ dissolved in 100 mL of 1/3-strength artificial seawater (Stefanik et al. 2013).

Prior to fixation, anemones can be relaxed using immersion in solutions of menthol crystals (50 g of crystals in 100 mL of water), $MgCl_2$ (19 or 35–75 g/L), or $MgSO_4$ (35–75 g/L), tricaine methanesulfonate (MS-222, 200–500 mg/L) (England 1987; Haussermann 2004; Moore 1989; Morrall et al. 2000; Sebens & Paine 1978; Spano & Flores 2013). The immersion time required may depend on animal size. Menthol or a combination of menthol and $MgSO_4$ may be more effective in larger anemones (England 1987). $MgCl_2$ (60 g/L) has also been administered directly into the gastrovascular cavity immediately before immersion in fixative (Spano & Flores 2013). Since these

Table 6.1 Anesthetic drugs for coelenterates.

Coelenterates					
Order	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Rhizostomeae (jellyfish)	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	Iso-osmotic to seawater*	Immersion	*Cotylorhiza tuberculata*	Kikinger (1992)
	Magnesium sulfate ($MgSO_4 \cdot 7H_2O$)	Iso-osmotic to seawater*	Immersion	*Cassiopeia xamachana*	Colley & Trench (1985)
	Menthol	Titrated to nonresponse	Immersion	*Rhizostoma pulmo*	Fuentes et al. (2011)
	MS-222	0.3 and 0.6 g/L	Immersion	*Aurelia aurita*	Gorges et al. (2022)
Limnomedusae (freshwater jellyfish)	Menthol	Titrated to nonresponse*	Immersion	*Craspedacusta sowerbii*	Park (1998)
Actinaria (anemones)	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	60 g/L*	Directly administered to gastrovascular cavity	*Anthopleura hermaphorditica*, *Bunodactis hermafroditica*	Spano & Flores (2013)
		70 g/L	Immersion	*Nematostella vectensis*	Stefanik et al. (2013)
		41 g/L*	Immersion	*Aiptasia pallida*	Morrall et al. (2000)
		35 g/L*	Immersion	South American sea anemones	Sebens & Paine (1978)
		18.75 g/L*	Immersion	British sea anemones	Moore (1989)
		14.3 g/L	Immersion	*Nematostella vectensis*	Amiel et al. (2015)
	Magnesium sulfate ($MgSO_4 \cdot 7H_2O$)	35-40 g/L*	Immersion	Sea anemones from the tropical Red Sea and Indo-Pacific Ocean	England (1987)
	Menthol	Titrated to nonresponse	Immersion	*Nematostella vectenis*	Bossert et al. (2013)
				Chilean shallow-water sea anemones	Haussermann (2004)
				British sea anemones	Moore (1989)
		500 g/L*	Immersion	*Anthopleura hermaphorditica*, *Bunodactis hermafroditica*	Spano & Flores (2013)
	MS-222	200-500 mg/L*	Immersion	British sea anemones	Moore (1989)
Scleractinia (stony corals)	Magnesium sulfate ($MgSO_4 \cdot 7H_2O$)	Not given	Immersion	*Oulastrea crispata*	Kawaguti (1964)
	Menthol	Titrate to nonresponse	Immersion	*Galaxea fascicularis*	Agostini et al. (2008)
Octocorallia (soft corals)	Magnesium sulfate ($MgSO_4 \cdot 7H_2O$)	Titrated to nonresponse*	Immersion	Octocorals	Janes (2008)

* Not all animals were recovered, dose may need to be adjusted for anesthesia.

animals did not recover, anesthetic doses may need to be adjusted for recovery procedures.

Corals

Anatomy, Physiology, and Natural History

There are two main types of corals: stony corals (Scleractinia), which create a calcium carbonate exoskeleton (e.g., staghorn and elkhorn corals), and soft corals (Octocorallia), which lack a stony skeleton (e.g., sea fans and sea pens). Corals are very diverse and may be solitary or colonial (Ruppert et al. 2004).

Physical Restraint

Scleractinian corals often retract their polyps in response to handling, which precludes visual examination or sampling of their soft tissue.

Anesthetic Agents Used and Techniques

Menthol crystals have been used to anesthetize corals with a quick recovery (Agostini et al. 2008). Corals have been relaxed in calcium-free seawater prior to fixation (Chen et al. 2008). Due to potential physiological derangements this calcium-free method is not recommended for anesthesia. Prior to dissection for electron microscopy, corals have been relaxed using $MgSO_4$ (Kawaguti 1964). To relax soft corals, a $MgSO_4$ solution (110 g/L) has been added to seawater containing the animals in 5-mL increments every 15–20 minutes prior to fixation (Janes 2008).

Mollusks

Anatomy, Physiology, and Natural History

The mollusks are a diverse and large phylum that occupy freshwater, marine, and terrestrial environments. There are approximately 100,000 described species with high environmental and economic value. They are an important source of food, animals for pets, display, research, jewelry, artwork, and the lucrative shell-collecting hobby. Details of molluscan anatomy, physiology, and natural history can be found in a number of references, including Ruppert et al. (2004), Lewbart (2022), and any general invertebrate zoology text. Presented here are three major classes of mollusks (gastropods, cephalopods, and bivalves), with the most economically important groups discussed regarding anesthesia and analgesia. Doses for mollusk anesthesia are reported in Table 6.2.

Gastropods

Anatomy, Physiology, and Natural History

The gastropods are a large and easily recognized group that includes the abalone, nudibranchs, sea hares, slugs, and snails, among others. Most are aquatic and have a well-developed head and sensory organs, an external shell, muscular foot, and gills within a respiratory chamber. Many aquatic gastropods have an operculum that can seal the shell aperture and prevent access to the gills and other soft body parts. This behavior can impede anesthetic induction via immersion.

Physical Restraint

Gastropods are generally easy to restrain manually or with a protective container. While most gastropods are harmless to humans, members of the tropical genus Conus can inflict serious injury with small venomous "harpoons," which are modified radular teeth.

Abalones are commercially farmed and frequently require physical examination, sizing, pearl seeding, and removal from tanks for maintenance and harvesting (White et al. 1996). Research in abalones involves furthering knowledge of their ecology, genetics, and reproduction. Removing abalones is often only possible with mechanical assistance due to their ability to tightly adhere to the substrate. Forced removal may result in injury or mortality. A muscle-relaxing agent may be necessary to avoid stress and mechanical injury related to dislodging.

Anesthetic Agents Used and Techniques

Snails can be anesthetized using immersion in 5% ethanol (Flores et al. 1983) or menthol, or with inhalant agents like isoflurane (Girdlestone et al. 1989). Snail anesthesia is defined as when the body and tentacle withdrawal response to gentle stimulation is absent. A positive tentacle withdrawal reflex suggests an insufficient depth for surgery or invasive procedures (Girdlestone et al. 1989). A 10% Listerine® solution (ethanol 21.9%, menthol 0.042%) in normal *Lymnaea*, saline is commonly used to anesthetize snails (Woodall et al. 2003). Sodium pentobarbital at 400 mg/L in water has been reported to produce anesthesia with a slow onset (8 hours), good effect, and low mortality rate (Martins-Sousa et al. 2001). A combination of MS-222 and sodium pentobarbital has been described as a useful method of relaxing and anesthetizing various species of snails (Joosse & Lever 1959; Mutani 1982) with an onset time of approximately 60 minutes and long duration.

Isoflurane anesthesia for terrestrial snails requires an anesthetic chamber with fresh gas inflow and waste gas scavenging (Girdlestone et al. 1989). For pond snails, the minimum alveolar (or, more correctly, anesthetic) concentration is reported as 1.09% (Girdlestone et al. 1989). Induction is relatively fast (<10 minutes), but excitation is common. The main disadvantage of inhalant methods is the need to take the animal out of the chamber for a procedure, resulting in fluctuation of anesthetic depth and increased pollution of the working area. Furthermore, the depth of anesthesia may not be suitable for surgery.

Table 6.2 Anesthetic drugs and dosing for mollusks.

Mollusca					
Class	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Gastropoda	Benzocaine	100 mg/L	Immersion	*Haliotis iris*	Aquilina & Roberts (2000)
				Haliotis laevigata, *Haliotis rubra*	Edwards et al. (2000)
	Ethanol	3%	Immersion	*Haliotis laevigata*, *Haliotis rubra*	Edwards et al. (2000)
		5%	Immersion	*Cryptomphallus aspersa*	Flores et al. (1983)
	Isoflurane	MAC 1.09%	Inhalation	*Lymnaea stagnalis*	Girdlestone et al. (1989)
	Listerine® (ethanol 21.9%, menthol 0.042%)	10%	Immersion	*Lymnea stagnalis*	Woodall et al. (2003)
	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	50 g/L	Immersion	*Aplysia californica*	Anderson et al. (2010)
		200 g/L*	Intracoelomic injection (30 mL)	*Aplysia californica*	Junge & Ortiz (1978)
		Isotonic	Injection into foot (25% body weight)	*Aplysia californica*	Kanz et al. (1979)
	Magnesium sulfate ($MgSO_4 \cdot 7H_2O$)	40-220 g/L	Immersion	*Haliotis midae*	White et al. (1996)
	2-phenoxyethanol	1 mL/L	Immersion	*Haliotis laevigata*, *Haliotis rubra*	Edwards et al. (2000)
		0.5-3 ml/L	Immersion	*Haliotis midae*	White et al. (1996)
	Sodium pentobarbital	50 mg/L	Immersion	*Haliotis iris*	Aquilina & Roberts (2000)
		400 mg/L	Immersion	*Biomphalaria* spp.	Martins-Sousa et al. (2001)
	Sodium pentobarbital and MS-222	80 mg/L and 3 g/L	Immersion	*Lymnaea stagnalis*	
				Bulinus spp., *Lymnaea* spp., *Gyraulus* spp., *Anisus* spp.	Mutani (1982)
		120 mg/L and 3 g/L	Immersion	*Biomphalaria* spp., *Helisoma* spp.	Mutani (1982)
Cephalopoda	Ethanol	1.5–3%	Immersion	*Sepia officinalis*	Harms et al. (2006)
		2%	Immersion	*Octopus vulgaris*	Andrews & Tansey (1981)
	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	6.8 g/L	Immersion	*Sepia officinalis*	Gore et al. (2005)
		37.5 g/L	Immersion	*Sepia officinalis*, *Loligo forbesi*, *Alloteuthis subulata*, *Octopus vulgaris*, *Eleodine cirrhosa*	Messenger et al. (1985)
Bivalvia	Chloral hydrate	4 g/L	Immersion	*Ostrea edulis*	Heasman et al. (1995)
	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	35 g/L	Immersion	*Ostrea edulis*	Culloty & Mulcahy (1992)
		30–50 g/L	Immersion	*Pecten fumatus*	Heasman et al. (1995)
	Propylene phenoxytol	1–3 mL/L	Immersion	*Pinctada maxima*	Mills et al. (1997)
		2–3 mL/L	Immersion	*Pinctada albina*, *Pinctada margaritifera*	Norton et al. (1996)

* Not all animals were recovered, dose may need to be adjusted for anesthesia.
MAC, minimum anesthetic concentration.

Ketamine and propofol do not induce anesthesia and may have an excitatory effect (Woodall & McCrohan 2000), while ketamine in combination with xylazine may be toxic (Martins-Sousa et al. 2001).

Aplysia spp. sea snails are commonly anesthetized with intramuscular or intracoelomic injection of $MgCl_2$ (Junge & Ortiz 1978; Kanz et al. 1979). Induction is fast (2–5 minutes), smooth, and results in good muscle relaxation. Immersion in 50 g/L $MgCl_2$ resulted in an initial increase in activity followed by progressive sedation (loss of attachment to substrate and righting reflex) and anesthesia (immobile and nonresponsive) over the course of 35 minutes, with rapid recovery (less than 1.5 minutes) following rinsing in and return to anesthetic-free water (Anderson et al. 2010). Halothane via immersion and MS-222 via immersion and intracoelomic administration appear to be ineffective anesthetic agents in *Aplysia* spp. (Clark et al. 1996).

Protocols used in abalones for removal and research include benzocaine (100 mg/L), ethanol (3%), 2-phenoxyethanol (1 mL/L), $MgSO_4$ (40–220 g/L), and sodium pentobarbital (1 mL/L) (Aquilina & Roberts 2000; Edwards et al. 2000; White et al. 1996). Magnesium sulfate can be administered in water (4–22 g/100 mL) with the concentration depending on size of the abalone; higher doses are needed for larger animals (White et al. 1996). Induction time is fast (5–8 minutes) and recovery is usually uneventful (3–35 minutes, depending on dose and anesthesia time). Phenoxyethanol is administered at 0.5–3.0 mL/L with rapid induction (1–3 minutes) and recovery (5–20 minutes) (White et al. 1996). Nembutal (sodium pentobarbital, 1 mL/L) produces good muscle relaxation with an induction time of 15 minutes and complete recovery (Aquilina & Roberts 2000). This compound has the distinct drawback of being a controlled drug with the challenges surrounding this class of compounds. Clove oil (0.5–1.5 mL/L) and propylene phenoxytol (2.5 mL/L) are not recommended because both agents can cause high mortality (Aquilina & Roberts 2000; Edwards et al. 2000) and MS-222 (1 g/L) and benzocaine (0.1 g/L) are ineffective as muscle relaxants (Aquilina & Roberts 2000). Both MS-222 and propylene phenoxytol cause significant excitation at induction, resulting in copious mucus production and loss of pigment (Aquilina & Roberts 2000).

Recovery from any immersion anesthesia requires thorough washing of the abalone and exposure to flowing anesthesia-free seawater delivered at the optimal temperature (18°C) until muscle strength returns.

Cephalopods

Anatomy, Physiology, and Natural History

This group of predatory and specialized mollusks includes such familiar forms as the chambered nautilus, cuttlefish, octopuses, and squids. Cephalopods are exclusively marine and most have the ability for fast locomotion. They have advanced nervous systems, excellent vision and tactile senses, closed circulatory systems, and high metabolic rates. Most have an internal skeleton or shell. The exceptions to this are the octopuses with no shell and the chambered nautilus with an external shell. Cephalopods have been extensively studied in many fields and the scientific literature is filled with their contributions.

Physical Restraint

Cephalopods, when stressed, which is common under human care, often expel ink as a defense mechanism. They are generally difficult to handle, other than for a quick move or relocation, without sedation. Cloth gloves prevent cephalopod suckers from gaining purchase on hands and wrists, and allow a greater degree of control for brief manual restraint. Buckets, plastic nets, or other smooth objects may be used to capture or restrain cephalopods. It should be kept in mind that these species are "specialized escape artists" (Wood & Anderson 2004). Artificial turf lining the upper reaches of aquatic enclosures discourages climbing by octopuses.

Anesthetic Agents Used and Techniques

The two most commonly used anesthetic agents in cephalopods are ethanol and $MgCl_2$, with the latter being the preferred option. It is employed by preparing an isotonic solution of 7.5% (75 g/L) $MgCl_2$ in distilled water mixed with an equal volume of seawater (Messenger et al. 1985). Induction time is between 1.5 and 13 minutes, with a short period of hyperventilation, then a gradual increase in arm flaccidity and righting reflexes; it is typically considered to be very smooth (Messenger et al. 1985). Respiration decreases and may even cease if the anesthetic concentration is not reduced. The gills should be at least intermittently, and ideally constantly, perfused with seawater containing the anesthetic of choice. Time of recovery from $MgCl_2$ is fairly quick (1–10 minutes), but dependent on the length and type of procedure (can be up to 20 minutes after longer procedures).

Cuttlefish have been successfully anesthetized with 1.5–3% ethanol (15–30 mL/L) diluted in seawater (Harms et al. 2006). Inductions are rapid (1 minutes), especially at higher concentrations, and dilution to a lower concentration (10–15 mL/L) to decrease the risk of overdosing should be considered. Occasional transient excitement has been noticed with lower concentrations of ethanol (Harms et al. 2006). If the procedure cannot be performed with the animal submerged, anesthesia is maintained with a recirculating anesthesia system (Lewbart & Harms 1999). The anesthetic concentration of the water should be adjusted by dilution over time to the anesthetic depth desired.

For cuttlefish, a 7.5% (75 g/L) $MgCl_2$ stock solution is prepared with distilled water (Gore et al. 2005). The stock solution is mixed with a known amount of seawater to prepare an anesthetic concentration suitable for induction. A final concentration of 6.8 g/L (100 mL of the stock solution mixed with 1 L of seawater) has been reported to have an induction time of 6–12 minutes without negative side effects (Gore et al. 2005). For most cuttlefish, a total water volume of 6–8 L is commonly needed. Induction is usually smooth and without a period of excitation. Decreases in concentration via dilution may be required to adjust the depth of anesthesia.

Octopuses are anesthetized in a similar manner as above. Two commonly employed anesthetic agents are ethanol and $MgCl_2$. Ethanol (2% v/v in seawater) can produce excitement during the short induction time (increased respiratory rate, attempts to climb out of the solution, and ink ejection; Andrews & Tansey 1981). Induction time has been reported to be 4 minutes and full recovery at 2.5 minutes after removal of the anesthetic solution (Andrews & Tansey 1981). Ethanol (2%) is not effective in cold-water species (below 15°C) (Gleadall 2013).

The use of urethane has been reported (Andrews & Tansey 1981; Messenger et al. 1985; Gleadall 1991) and was routinely used in the 1970s and 1980s, but despite good anesthetic effect, the traumatic effect on the animals from excitation during induction could be severe, and there are human exposure concerns. Chloroform, chloral hydrate, and CO_2 are unsuitable anesthetic agents in cephalopods as they can lead to high mortality (Garcia-Franco 1992; Gleadall 1991).

For recovery or resuscitation, the cephalopod is placed in a container with anesthesia-free, aerated, and/or circulated seawater and anesthesia-free water should be directed over the gills for a washout effect. If spontaneous respiration is not present, gentle and slow mantle massage of the mantle/body can be used to provide a combination of circulatory and respiratory support until normal respiration returns. The tentacles remain extended and flaccid in the first phase of the recovery and will retract in response to light stimulus (e.g., pinching) with progressive awakening (Harms et al. 2006).

Cephalopods can be monitored with visualization of respiratory rate and pattern. Normal awake values for 100–800 g *Octopus vulgaris* are 26–30 breaths per minutes (Andrews & Tansey 1981). The cardiovascular system is assessed by placing a Doppler probe on the dorsal area (above the aorta) or behind the gills (above either branchial heart) to monitor blood flow and heart rate. In transparent species (especially with $MgCl_2$), the organs inside the mantle cavity can be observed. Depth of anesthesia is difficult to assess in cephalopods. Anesthetic level seems adequate when no response to tactile and surgical stimuli is present (e.g., withdrawal of appendages or movement, contraction of the skin around the eye in response to pressure on the globe, withdrawal of the animal in response to a pinch of the skin over the eye (Andrews & Tansey 1981)). Other indicators of anesthetic depth are loss of normal posture, flaccidity of the arms, and an inability to regain normal posture (Andrews & Tansey 1981). Respiration is usually spontaneous; a depression or cessation is a sign of a concerningly deep level of anesthesia.

Bivalves

Anatomy, Physiology, and Natural History

This vast and economically important group of highly adapted aquatic mollusks includes the clams, mussels, oysters, and scallops. They lack a well-developed head, are generally nonvisual (the scallops are an exception), feed by filtration utilizing the gills for food transport, and use a muscular and sometimes quite large foot for locomotion. Research on these species focuses on their importance as a human food source and as environmental indicators.

Physical Restraint

Bivalves are generally easy to handle and restrain safely. Nearly all will tightly close their calcareous valves when handled or disturbed and may require sedation or physical manipulation (prying) to open the valves, which are held fast by strong adductor muscles. This behavioral response can greatly impede anesthetic induction, particularly if the anesthetic is irritating to any degree.

Anesthetic Agents Used and Techniques

Propylene phenoxetol (1%) can be used to anesthetize oysters in a dose range from 1 to 3 mL/L. Higher doses induce a rapid and relatively deep level of anesthesia (Mills et al. 1997) and may need diluting throughout the procedure to decrease recovery time (Norton et al. 1996). Generally, concentrations of 1–2 mL/L are safe and effective. The oyster should be placed hinge down in the solution and leaning against the wall of an aerated container to facilitate monitoring. Induction time is reported between 6 and 15 minutes. Adequate anesthesia is reached when the oyster gapes wide enough to part the gill curtain and shows no responsiveness to handling (Mills et al. 1997) or soft tissue contraction to a stimulus (Norton et al. 1996). Reducing handling stress before placing oysters into the anesthesia container will improve the anesthetic effects and facilitate valve opening. Recovery time is short (less than 30 minutes), although it depends on the length of procedure, concentration of anesthetic, and temperature (Norton et al. 1996).

Magnesium chloride seems to have variable effects on oysters. Some describe little effect of $MgCl_2$ in pearl oysters (Mills et al. 1997; Norton et al. 1996), mainly due to long induction times (1–2 hours). Culloty and Mulcahy (1992)

reported good anesthetic effects, but long induction and recovery times (90 minutes) at 3.5%. The effect of $MgCl_2$ seems to be dependent on species and concentration. Chloral hydrate and MS-222 are not effective in oysters due to slow induction and recovery, and are associated with complications, including death. Some of these undesirable effects may be related to the low pH of unbuffered MS-222 (Norton et al. 1996).

In scallops, anesthesia may be required for muscle relaxation and valve opening. In general, the depth of anesthesia/relaxation is adequate when handling and stimulating the mantle tissue fails to produce valve closure. Recovery is often defined as the regained ability for valve closure in response to a stimulus (Heasman et al. 1995).

Magnesium chloride is the drug of choice in scallops due to its rapid and consistent induction and recovery. The agent is dissolved in a small volume of seawater and then added to the aerated induction container to reach a concentration of 30–50 g/L. Induction times at these concentrations are quick and in the range of 2–6 minutes. Recovery time in scallops anesthetized with $MgCl_2$ seems to be consistently short (10 minutes) regardless of concentration used or temperature (Heasman et al. 1995).

Chloral hydrate has variable effects on scallops, with significant changes in induction and recovery at different concentrations and temperatures (Heasman et al. 1995). A concentration of 4 g/L produces anesthesia in 10–25 minutes at a temperature of 24°C. Lower temperatures significantly slow induction time. Higher concentrations shorten the induction time but can result in increased mortality. Recovery time at 4 g/L is between 20 and 30 minutes, but varies widely depending on temperature and concentration. Aerated recovery water and continuously flushing with anesthetic-free seawater facilitate recovery.

Other drugs have been examined for scallop anesthesia with little success. Benzocaine causes initial hyperactivity, ethanol does not have any effect, MS-222 causes hyperactivity and hyperextension, metomidate results in shell-closure, and $MgSO_4$ leads to high mortality (Heasman et al. 1995). Giant clams (*Tridacna* sp.) have been anesthetized with propylene phenoxetol (Mills et al. 1997).

Annelids

Anatomy, Physiology, and Natural History

The annelids are a large and diverse group of segmented vermiform animals that that are divided into three classes: Polychaeta, Clitellata (earthworms and leeches), and Sipuncula (peanut worms), formerly its own phylum. Some taxonomists include the sipunculids with the polychaetes. A former class of annelids, the Branchiobdellida, which are only found as crayfish ectoparasites, is now an order in the subclass Hirudinea. All are characterized by coelomic cavity, circulatory, excretory, and nervous system segmentation. This segmentation probably evolved as a means of burrowing via peristaltic contractions (Ruppert et al. 2004). A cuticle covers the animal, and setae occur in nearly all annelids. A linear gut tube lies between the anterior mouth and posterior anus (Ruppert et al. 2004). Anesthetic agents and dosing are reported in Table 6.3.

Table 6.3 Anesthetic drugs and dosing for annelids.

Annelida					
Class	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Polychaeta	Dentol®	8%*	Immersion	Nereidid worms from the Persian Gulf	Bonyadi-Naeini et al. (2016)
	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	75 g/L	Immersion	*Parapionosyllis manca*	Lewbart & Riser (1996)
		80 g/L*	Immersion	*Eurythoe complanata*	Müller et al. (2003)
Oligochaeta	Alcohol (presumably ethanol)	5%	Immersion	*Lumbricus terrestris*	Cooper & Roch (1986)
	Ethanol	5%	Immersion	*Lumbricus terrestris*, *Eisenia foetida*	Cooper (1968); Marks & Cooper (1977)
		5%	Immersion	*Lumbricus terrestris*	Salgado et al. (2014)
Hirudinea	Benzocaine	400 mg/L	Immersion	*Hirudo medicinalis*	Cooper et al. (1986)
	Mephenesin	Saturated	Immersion	*Hirudo medicinalis*, *Glossiphonia complanata*	Tettamanti et al. (2003)
	Soda water (50%)	500 mL/L	Immersion	*Hirudo medicinalis*	Cooper et al. (1986)

* Not all animals were recovered, dose may need to be adjusted for anesthesia.

Polychaetes

Anesthetic Agents Used and Techniques

Like many marine invertebrates, polychaetes can be sedated with $MgCl_2$ via immersion. While it is likely that some species are more sensitive than others, a concentration of between 7.5% and 8.0% seems to work well for relaxation (Lewbart & Riser 1996; Müller et al. 2003). A 2016 study by Bonyadi-Naeini et al. determined that a product called Dentol® (Khoraman Laboratory, Iran), which contains 10% carvacrol, was very safe and effective for the relaxation of nereid polychaetes. Animals were placed in an 8% Dentol® solution in seawater and were relaxed in less than 1 minute. Carvacrol is an aromatic oil found in many different plants (Bonyadi-Naeini et al. 2016). Dentol® may be hard to find outside of Iran.

Oligochaetes

Anesthetic Agents Used and Techniques

Cooper and Roch (1986) anesthetized the earthworm (*Lumbricus terrestris*) with a 5% alcohol (presumably ethanol) solution for a period of 1 hour prior to tissue grafting experiments. In earlier experiments, Cooper (1968) used 5% ethanol in Rushton's Ringers solution until the worms (*L. terrestris* and *Eiesnia foetida*) were immobilized. Marks and Cooper (1977) used 5% ethanol at 23°C for *L. terrestris* and *E. foetida*, and Salgado et al. (2014) reported success using 5% ethanol for anesthetizing *L. terrestris*.

Hirudineans

Anesthetic Agents Used and Techniques

The literature on leech anesthesia is minimal. One study found that immersion of *Hirudinaria medicinalis* in 400 mg/L benzocaine adequately immobilized the animals with a recovery time of approximately 3 hours (Cooper et al. 1986). The same study found that 50% soda water (active ingredient CO_2), at a concentration of 500 mL/L, was effective following a 2-minute excitatory period. This protocol resulted in a variable recovery period of up to 4.5 hours. One article describes the use of saturated mephenesin (3-o-toloxy-1,2-propanediol) to anesthetize leeches for grafting research (Tettamanti et al. 2003).

Arachnida

Doses and drugs for anesthesia of arachnids are reported in Table 6.4.

Spiders and Scorpions

Anatomy, Physiology, and Natural History

There are over 70,000 species of arachnids, with the majority identified as spiders or mites. Most arachnids are terrestrial carnivores. Arachnids respire through invaginations of the exoskeleton into their hemocoel, either through book lungs or tracheae. Scorpions respire using four pairs of book lungs while spiders perform gas exchange through lungs and/or tracheae. Like most arthropods, spiders and scorpions have a well-developed, open circulatory system of hemolymph pumped into sinuses by a muscular tubular heart in the anterior abdomen (Ruppert et al. 2004).

Physical Restraint

Manual restraint is commonly used to handle and transport spiders, but it is advisable to wear latex or nitrile gloves, as some tarantula species are capable of shedding urticating hairs that can be quite irritating, especially to allergic individuals. Direct handling of scorpions should be kept to a minimum for the safety of both the handler and

Table 6.4 Anesthetic drugs and dosing for arachnids.

Arachnida					
Group	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Spiders and scorpions	CO_2	98%	Inhalant	*Nephila edulis*	Madsen & Vollrath (2000)
	Isoflurane	5%	Inhalant	*Heterometrus longimanus*, *Pandinus dictator*	Sheldon et al. (2019)
				Theraphosa blondi, *Grammostola rosea*	Zachariah et al. (2009)
	Sevoflurane	5%	Inhalant	*Grammostola rosea*	Zachariah et al. (2014)
Horseshoe crabs	MS-222	1 g/L	Immersion	*Limulus polyphemus*	Archibald et al. (2019)
	2-phenoxyethanol	2 mL/L	Immersion		

the animal. Clear plastic containers, and in some cases utensils like long forceps or tongs, can be used to move an animal from one place to another (Frye 2022). The primary drawbacks to manual restraint of scorpions or spiders are stress and injury to the animal and envenomation of the handler. Caution should be taken not to drop the animal or have it leap or fall to the ground.

Anesthetic Agents Used and Techniques

Inhalant anesthetic agents are most commonly and successfully used to anesthetize spiders and scorpions. All agents (desflurane, isoflurane, sevoflurane) can be used depending on cost and availability; isoflurane and sevoflurane are most commonly used for scorpions and spiders (Cooper 2001; Melidone & Mayer 2005; Pizzi & Kennedy 2022; Sheldon et al. 2019; Zachariah et al. 2009, 2014).

Several different induction chambers have been described (Cooper 2001; Melidone & Mayer 2005; Pizzi and Kennedy 2022) and used successfully for delivering inhalant anesthesia to spiders and in some cases scorpions. Ideally these chambers are commercially available invertebrate-specific with appropriate fresh gas inflow and scavenging outflow. Regular small mammal induction chambers or simple self-made clear plastic containers also work.

In containers without the use of an inflow and outflow system, a cotton swab soaked with a small amount of inhalant agent is placed into the box. The animal should be placed in a separate smaller container with ventilation pores. The smaller container holding the animal is placed into the larger box, allowing the inhalant to diffuse while ensuring that no direct animal contact with the inhalant-soaked cotton swab will occur. This method is not ideal because of the higher anesthetic agent exposure risk personnel, less control of the anesthetic amount, and higher risk of overdose (e.g., up to 32% isoflurane in air).

An induction chamber using anesthetic gas given via a vaporizer is preferred. The animal is placed in the chamber and the chamber is filled with the anesthetic gas (3–5% for isoflurane, 4–6% for sevoflurane). To decrease the filling time in larger chambers, the oxygen flow rate can be high at the beginning (1–3 L/min) and decreased to a minimum if there are no leaks in the system (300–1000 mL/min). Oxygen flow lower than 200 mL/min decreases vaporizer accuracy and may decrease the amount of anesthetic agent in the chamber due to the uptake by the animal. The amount of carbon dioxide accumulation in the chamber may increase using low fresh gas flows. An appropriate scavenging system is necessary to decrease pollution and staff exposure to anesthetic gases. With increasing anesthetic depth, the vaporizer can be adjusted by decreasing the anesthetic concentration over time.

The advantages of the chamber technique are convenience of use, low cost, and safety to the patient. The disadvantage is that the animal can only be temporarily sedated or anesthetized. For most procedures the animal is removed from the chamber, limiting the time for any procedure before the animal recovers. Repeated inductions also increase the exposure of the clinician and staff to the anesthetic gases. A chamber has been developed (Melidone & Mayer 2005) that allows the clinician to perform surgery or other manipulations on the animal without removing the animal from the chamber.

Another technique is to induce the spider in an anesthetic chamber and then place its abdomen (with the associated book lungs/tracheae) into a smaller chamber "sealed" with a latex glove. This technique has merit when a procedure must be performed on the cephalothorax or limbs (Dombrowski 2006).

Carbon dioxide, nitrogen, and hypothermia have also been used to immobilize spiders (Madsen & Vollrath 2000; Pizzi & Kennedy 2022). No reports about the amount of nitrogen used or the quality of nitrogen anesthesia could be located. Carbon dioxide gas is administered in a chamber, often producing 98% saturation. Dilution with air or oxygen is difficult, resulting in an increased risk for mortalities (Pizzi & Kennedy 2022). The side effects of CO_2 anesthesia are well recognized in vertebrates (e.g., respiratory acidosis, behavioral signs of distress), which, if also observed in invertebrates, may indicate that other anesthetic options are preferable.

Observe the spider or the scorpion for righting reflexes and other movements to assess depth of anesthesia. It may take 10–15 minutes and several attempts until full immobilization has occurred. During the procedure, leg movement in response to stimuli is a sign of insufficient depth of anesthesia. An increase in heart rate and respiratory rate may occur but is often unrecognized. Deep anesthesia can be difficult to evaluate; slow respiratory rate and heart rates are often the only way to assess a patient for excessive depth of anesthesia.

Respiratory rate is observed at the cranial lateral side of the animal. A Doppler or ultrasound machine can be used to monitor heart rate. The spider heart lies under the dorsal surface of the body. The Doppler's pinpoint-crystal head is placed over the heart area with an appropriate amount of gel. Normal heart rates are considered to be 30–70 beats per minute in large spiders and up to 200 beats per minute in smaller species.

After turning off anesthetic delivery, recovery from anesthesia is usually gradual and can take between 3 and 20 minutes depending on ambient temperature and the depth of anesthesia during the procedure. When fully awake the animal should be returned to its enclosure and

maintained at its preferred ambient temperature. Feeding after anesthesia should be delayed for 48 hours (Pizzi & Kennedy 2022).

Horseshoe Crabs

Anatomy, Physiology, and Natural History

The American horseshoe crab (*Limulus polyphemus*) is the most common of four global species and is frequently used as a laboratory animal model to study its sensory structures, the nervous system, and embryology. Horseshoe crabs have a well-developed semiclosed circulatory system composed of a tubular heart, arterial system, and sinuses. Ventilation is achieved through gill movements that pump water around the gills as well as pumping hemolymph through the gills. Horseshoe crab hemolymph contains hemocyanin, a respiratory pigment, which gives their hemolymph its characteristic blue color (Ruppert et al. 2004). The horseshoe crab's most common use and value to humans comes from *Limulus amebocyte* lysate, an extract of amoebocyte cells from the hemolymph, which is a critical component in assessing the safety of medical equipment and pharmaceuticals by detecting the presence of endotoxin (Smith & Berkson 2005; Smith 2022).

Physical Restraint

Horseshoe crabs are easily handled and restrained, although strong locomotion and righting reflexes can make examinations challenging (Smith & Berkson 2005). Holders are cautioned not to pinch their fingers between the lateral edge of the opisthosoma and the genal angle of the prosoma (Smith 2022).

Anesthetic Agents Used and Techniques

The dorsal, tubular heart of the horseshoe crab is located over the entire length of the prosoma (Spotswood & Smith 2007). The hemolymph collection site has been well described (Smith & Berkson 2005; Smith 2022) and is easy to perform. Hemolymph pH and blood gases may be measured for monitoring anesthesia (Archibald et al. 2019). Electrocardiogram (ECG) patches placed on the cephalothorax can detect heart rate. Normal awake heart rates in horseshoe crabs are reportedly 30 beats per minute at a temperature of 23°C and may vary by temperature (Redmond et al. 1982). Ultrasonography may be used to measure heart rate, as well as cardiac contractility and respiratory rate through the carapace without having to invert the animal to view the book gill excursions (Archibald et al. 2019). Resting heart rate, cardiac fractional shortening, and respiratory rate at 22.8–28°C were ~22–50 per minute, ~32–50%, and ~35–53 per minute, respectively (Archibald et al. 2019). Immersion in MS-222 at 1 g/L buffered with sodium carbonate (not bicarbonate), and 2-phenoxyethanol at 2 mL/L provided effective anesthesia with clinically useful induction and recovery times (Archibald et al. 2019). Effective buffering of MS-222 at this concentration required sodium carbonate rather than sodium bicarbonate to avoid simultaneously markedly increasing the salinity of the anesthesia water. Both MS-222 and 2-phenoxyethanol reduced cardiac contractility and respiratory rate with minimal effect on heart rate. Subjectively, 2-phenoxyethanol provided smoother anesthesia.

Crustaceans

Anatomy, Physiology, and Natural History

Crustaceans are a large group of diverse arthropods that includes an estimated 67,000 species (50,000 are marine), including barnacles, crabs, crayfish and lobsters, prawns, shrimps, and water fleas (Applehans et al. 2012). Crustaceans belong to the clade Mandibulata, which also includes insects and myriapods (centipedes and millipedes). Crustacea are aquatic mandibulate arthropods with two pairs of antennae, stalked compound eyes, biramous jointed appendages, one or more pairs of segmental excretory organs, a carapace, gills, and a free-swimming nauplius larvae. The second pair of antennae and mandibles provide the sharpest distinction from other arthropods. Martin and Davis (2001) treat the taxon Crustacea as a subphylum. Recent and compelling work has led most taxonomists to accept that insects (Hexapoda) are actually crustaceans and should be included in a combined crustacean-hexapod clade (Ahyong 2020). Several names have been proposed for this new taxon, including Crustaceomorpha, Pancrustacea, and Tetraconata (Ahyong 2020). This revision addresses the conundrum of why insects never colonized the marine environment and why crustacean success on land and in freshwater is limited. The combined group has exploited all three biomes (Ahyong 2020). In this chapter we will conform with the conventional separation of crustaceans and insects.

Physical Restraint

Some species can be manually restrained with gloved hands or with the help of utensils such as tongs or nets. Because some larger crustaceans can cause serious injury to handlers, care should be taken when manipulating or restraining these animals (e.g., some crabs and lobsters).

Anesthetic Agents Used and Techniques

Various anesthetic agents can be used on crustaceans. Doses are reported in Table 6.5. Immersion in clove oil or

Table 6.5 Anesthetic drugs and dosing for crustaceans.

Crustacea					
Order	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Decapoda	Alfaxalone	15 mg/kg*, 100 mg/kg	Intravascular injection	*Callinectes sapidus*	Minter et al. (2013)
	AQUI-S	100 mg/L	Immersion	*Macrobrachium rosenbergiii*	Coyle et al. (2005)
		40–200 mg/L*	Immersion	*Jasus edwardsii*	Robertson et al. (2018)
	Clove oil	>0.125 mL/L (induction)	Immersion	*Pseudocarcinus gigas*	Gardner (1997)
	Eugenol	>0.2 mL/L	Immersion	*Macrobrachium rosenbergiii*	Saydmohammed & Pal (2009)
	Isobutyl alcohol	1.5–7.0 mL/L*	Immersion	*Homarus americanus*	Foley et al. (1966)
	Ketamine	40–90 mg/kg	Intramuscular injection	*Orconectes virilis*	Brown et al. (1996)
		0.025–0.1 mg/kg	Intravascular injection	*Pseudocarcinus gigas*	Gardner (1997)
		20 mg/kg	Intravascular injection	*Callinectes sapidus*	Quesada et al. (2011)
	Ketamine-xylaxine	20 mg/kg each	Intravascular injection	*Callinectes sapidus*	Quesada et al. (2011)
	Lidocaine	0.4–1 mg/g	Intramuscular injection	*Orconectes virilis*	Brown et al. (1996)
		0.2 mg/g	Intravascular injection	*Callinectes sapidus*	Quesada et al. (2011)
	Procaine	25 mg/kg	Intravascular injection	*Carcinus maenas*	Oswald (1977)
	Tiletamine-zolazepam	30 mg/kg	Injection	*Callinectes sapidus*	Quesada et al. (2011)
	Xylazine	16–22 mg/kg	Intravascular injection	*Pseudocarcinus gigas*	Gardner (1997)
		20 mg/kg	Intravascular injection	*Callinectes sapidus*	Quesada et al. (2011)
		70 mg/kg	Intravascular injection	*Carcinus maenas*	Oswald (1977)

* Sedation at lower doses, anesthesia at higher doses.

isobutyl alcohol, and injections of alfaxalone, ketamine, lidocaine, tiletamine-zolazepam, and xylazine have been reported (Brown et al. 1996; Ferraro & Pressacco 1996; Foley et al. 1966; Gardner 1997; Minter et al. 2017; Oswald 1977; Quesada et al. 2011). An intravascular injection can be performed in large crabs through the coxal arthropodial membrane of a cheliped (Oswald 1977; Gardner 1997) using a small needle (25 gauge). Anesthetic immersions commonly used in other aquatic invertebrate taxa, such as MS-222, 2-phenoxyethanol and magnesium salts ($MgCl_2$ and $MgSO_4$), are generally not effective in decapod crustaceans (Coyle et al. 2005; Foley et al. 1966; Fregin & Bickmeyer 2016; Gardner 1997; Oswald 1977). Immersion in isobutyl alcohol (1.5–7.0 mL/L) results in sedation at low doses and anesthesia at high doses. The induction time and duration of effect are dose dependent (Foley et al. 1966).

Lidocaine (0.4–1 mg/g) can be injected intramuscularly into the tail and anesthesia lasts for about 5–30 minutes in crayfish, depending on the dose administered, with an average induction time of 1.5 minutes (Brown et al. 1996). Intravascular lidocaine (0.2 mg/g) lasted approximately 3 minutes in blue crabs (*Callinectes sapidus*) (Quesada et al. 2011).

Ketamine has been used in crayfish (40–90 mg/kg [μg/g]) (Brown et al. 1996), the Australian giant crab (*Pseudocarcinus gigas*) (0.025–0.1 mg/kg intravenous [IV]) (Gardner 1997), and blue crabs (Quesada et al. 2011) with variable success. Ketamine given intramuscularly to crayfish provides consistent anesthesia (induction time 1 minute) for over 10 minutes (40 μg/g) to 2 hours (>90 μg/g) without excitatory side effects during induction or recovery (Brown et al. 1996). When ketamine alone was given to the giant crab (*P. gigas*) intravascularly, a short

period of excitement occurred, but the induction time was short (15–45 seconds). The duration of anesthesia was dose dependent and lasted between 8 and 40 minutes (Gardner 1997). Intravascular injections of ketamine (20 mg/kg) in blue crabs resulted in a smooth and fast induction (<60 seconds) but the duration of anesthesia was only 3–12 minutes. The majority of crabs were categorized as having light anesthesia. Intracardiac injections of ketamine (20 mg/kg) resulted in death in four out of five crabs (Quesada et al. 2011).

Xylazine has shown good anesthetic effects in adult giant crabs when used at doses between 16 and 22 mg/kg IV (Gardner 1997) or in common shore crabs (*Carcinus maenas*) at 70 mg/kg IV (Oswald 1977). Induction seems to be smooth and fairly fast (3–5 minutes); dose dependent immobilization lasts 25–45 minutes. Side effects, including bradycardia, dysrhythmias, and extrasystoles, have been reported with high doses (70 mg/kg) (Oswald 1977). A similar short induction (30–60 seconds) was seen in blue crabs administered xylazine (20 mg/kg) IV, with a duration lasting 5–30 minutes (Quesada et al. 2011). Higher doses of xylazine (70 mg/kg) resulted in the death of blood-spotted crabs (*Portunus sanguinolentus*) (Premarathna et al. 2016). Care should be taken when using high-end doses of xylazine.

Ketamine and xylazine combined (20 mg/kg each) IV resulted in a quick induction (30–40 seconds) and lasted 5–10 minutes in blue crabs. Tiletamine-zolazepam (30 mg/kg) IV also had a quick induction (20–60 seconds) and lasted 5–7 minutes (Quesada et al. 2011). Intravascular injections of alfaxalone provide sedation (15 mg/kg) and anesthesia (100 mg/kg). Induction is rapid (<1 minute) but prolonged recoveries have been observed with higher doses (Minter et al. 2013). Intravascular injections of etomidate (16 mg/kg) were ineffective and propofol (20 mg/kg) is not recommended as it can result in limb autotomy in blue crabs. Pentobarbital (20 mg/kg) IV produced inadequate sedation in five out of six blue crabs (Quesada et al. 2011).

Procaine (25 mg/kg IV) has been used in crabs and provides good anesthesia with a very short induction time (20–30 seconds). This included a 10-second excitatory period that led to tonic contraction before paralysis. Duration was very long (2–3 hours) with slow recoveries (Oswald 1977) and may be reserved for long-term experimental procedures.

For smaller crabs, in which an intramuscular or IV injection is impractical, clove oil can be used as a bath treatment and has shown a 16-minute onset of anesthesia at a dose of >0.125 mL/L and a long recovery phase (2.5 hours). Once the animal is anesthetized, a reduction of concentration is necessary because 0.125 mL/L clove oil over a long period of time is also used for euthanasia (Gardner 1997). Freshwater prawns (*Macrobrachium rosenbergiii*) were anesthetized with immersion in eugenol and experienced a lower oxygen consumption rate at doses higher than 0.2 mL/L. Induction and recovery times were similar with immersion in eugenol and a mixture of eugenol and menthol (Saydmohammed & Pal 2009). Immersion in AQUI-S (isoeugenol; 100 mg/L) has been reported for anesthesia of the freshwater prawn (*M. rosenbergii*) (Coyle et al. 2005). Southern rock lobsters (*Jasus edwardsii*) immersed in AQUI-S (40-200 mg/L) exhibited sedation at the lower end of the dose range and anesthesia at the higher end (Robertson et al. 2018).

Crustacean heart rates can be measured by applying ECG pads with ample gel on the carapace above the heart or by Doppler flow probe (Fig. 6.3). The normal heart rate for lobsters is between 5 and 20 beats per minute with a circadian influence (higher at night) (Aguzzi et al. 2004) and 30–70 beats per minute for the shore crab (Styrishave et al. 2003), depending on pH and temperature. Anesthetic depth is evaluated in crustaceans by the relaxation of the body, the ability to withdraw extremities, and very slow withdrawal of their antennae.



Figure 6.3 This American lobster (*Homarus americanus*) has been anesthetized with eugenol immersion and is being euthanized with injectable intracardiac potassium chloride. A Doppler is being used to monitor heart rate. Within seconds of the potassium chloride administration the heart stopped beating. Image by GA Lewbart.

Analgesics and their effects are understudied in crustaceans. Morphine has been shown to decrease the response of crabs (100 mg/kg) and shrimp (91 mg/kg) to noxious stimuli; this effect is reversible with naloxone administration (Lozada et al. 1988; Maldonado & Miralto 1982; Tomsic & Maldonado 1990). However, this decreased response appears to be due primarily to sedation rather than analgesia (Barr & Elwood 2011). Ketorolac administered intracardiac was fatal to blue crabs (*C. sapidus*); consistent concentrations were observed when administered to crabs intramuscularly (0.25–0.75 mg/kg); however, in light of observed mortalities in blue crabs, use in crustaceans may be contraindicated pending studies in other species (Souza et al. 2020).

Insects

Anatomy, Physiology, and Natural History

The insects are a diverse group with nearly a million described species that some taxonomists term the Hexapoda. Insects are arthropods with three major body segments (head, thorax, and abdomen) and three pairs of legs. Most have well-developed mouthparts, keen eyesight, sensory antennae, and wings. They have an open hemolymph circulatory system and gases are exchanged through spiracles that open into a system of tracheae. Insects have been employed as research animals for many decades. *Drosophila* may be the best-known representative for genetic research studies, but other species are important contributors of information on pathogen–vector interaction in various diseases, metamorphosis and anatomy/physiology (facet eye, senses), ecology and agriculture, pharmaceutical control etc.



Figure 6.4 This fully awake Australian thorny devil stick bug (*Eurycantha calcarata*) is being given fluids as part of a hemolymph transfusion study. Insects and other terrestrial invertebrates can frequently be examined and weighed without the need for anesthesia. In cases where anesthesia is required, a number of inhalant agents have been successfully used. Image by GA Lewbart.

Physical Restraint

In most cases insects can be handled and restrained manually without risk to the animal or handler (Fig. 6.4). In some cases, gloves are recommended as a protective measure and various utensils can be employed to immobilize or restrain insects (Cooper 2022).

Anesthetic Agents Used and Techniques

Recent works have investigated the effects of isoflurane (Troup et al. 2019), sevoflurane (Chen et al. 2019), and isoflurane and sevoflurane on *Drosophila* (MacMillan et al. 2017). This latter paper found that both gas inhalants were superior to hypothermia and carbon dioxide with regards to side effects, such as reproductive compromise and juvenile mortality. No deleterious side effects were noted with sevoflurane anesthesia (MacMillan et al. 2017). Chen et al. (2019) found no mortality associated with sevoflurane but the gas did lead to an exacerbation of eye phenotype in the offspring.

Carbon dioxide remains popular for immobilizing insects in entomological research, although multiple side effects and high mortality are recognized (Nicolas & Sillans 1989; Valles & Koehler 1994; MacMillan et al. 2017). A more progressive approach is the use of volatile anesthetic agents such as isoflurane or sevoflurane. This requires a chamber apparatus to allow for appropriate delivery and scavenging of the inhalant agent (Walcourt & Ide 1998) (see the section on arachnids for further details on anesthetic chambers). Exposure to chloroform or desflurane in custom-made small glass tube induction chambers immobilized *Drosophila* larvae for survival confocal imaging (Cevik et al. 2019). Chloroform resulted in more rapid induction but slower recovery than desflurane, with less depression of heart rate and auditory response. Doses for the anesthesia of insects are reported in Table 6.6.

Hypothermia has been reported for immobilization of insects, but its use is discouraged for surgical and otherwise stressful or painful procedures (Cooper 2005; MacMillan et al. 2017).

Table 6.6 Anesthetic drugs and dosing for insects.

Insecta					
Order	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Diptera	Chloroform	30 seconds × 2	Inhalant	*Drosophila melanogaster*	Cevik et al. (2019)
	Desflurane	10 minutes × 2			Cevik et al. (2019)
	Isoflurane	ED_{50} = 0.3%*			Troup et al. (2019)
		4.6%			MacMillan et al. (2017)
	Sevoflurane	2.1%, 3%			Chen et al. (2019)
		6.7%			MacMillan et al. (2017)

* The effective dose (ED_{50}) is the concentration where half of the animals tested were immobile for longer than 10 seconds.

Nematodes

Anatomy, Physiology, and Natural History

Nematodes are one of the largest groups of invertebrates, with approximately 500,000 known species (Bodri 2022). Numerous species have been extensively used in research for plant–parasite effects, diseases, and genetics.

Caenorhabditis elegans is the most researched nematode as it is commonly used as an animal model. Its size, small and consistent number of somatic cells, and easily accessible nervous system make it an ideal research animal. *C. elegans* studies have led to scientific information about meiosis, nicotine dependence, volatile anesthetics, and genetics.

Anesthetic Agents Used and Techniques

Due to its popularity, most anesthetic agents reported for nematodes are based on *C. elegans* and anesthetic effects on the animal are well described (Bodri 2022). *C. elegans* has been anesthetized with CO_2 (Bodri 2022), 4.5% ethanol (Morgan & Sedensky 1995), propylene phenoxetol (Nelson & Riddle 1984), and numerous inhalants (chloroform, flurothyl, fluorxene, halothane, and isoflurane) (Crowder et al. 1996; Morgan & Cascorbi 1985; Morgan et al. 1990). Much higher concentrations of inhalant anesthetics are required for *C. elegans* compared to vertebrates (Zalucki and van Swinderen 2016). Crowder et al. (1996) recommend 6.5% isoflurane. The effective dose (ED_{50}, the concentration where half of the animals tested were immobile for longer than 10 seconds) values for the nine inhalant agents were established in Morgan's studies and the anesthetic chamber for these species has been described (Morgan & Cascorbi 1985; Bodri 2022). This included isoflurane with a concentration range of 5.6–7.18%, consistent with the findings of Crowder et al. (1996). Doses for the anesthesia of nematodes are reported in Table 6.7.

Echinoderms

Anatomy, Physiology, and Natural History

Echinoderms have deuterostome development, pentaradial symmetry as adults, and a calcium carbonate endoskeleton. There are approximately 7000 species divided into five classes, including sea stars and sea daisies (Asteroidea), brittle and basket stars (Ophiuroidea), sea cucumbers (Holothuroidea), sea urchins, sea biscuits, sand dollars (Echinoidea), and feather stars and sea lilies (Crinoidea) (Ruppert et al. 2004). The echinoderm nervous system is composed of a circumoral nerve ring with extending radial nerves. While the circumoral nerve ring is centrally located, it does not appear to have a coordinating function and is not a true central nervous system (Cobb 1995).

Physical Restraint

Most species of the echinoderm phylum can be handled safely and effectively without anesthesia or sedation. They are slow moving and quite hardy (one exception being the brittle stars). Certain species of sea urchins can inflict a painful "sting" with movable, sharp spines. Nets, tongs, and gloves can aid in the safe handling for physical restraint. Anesthesia should be used for invasive and potentially painful procedures.

Anesthetic Agents Used and Techniques

If echinoderms need to be anesthetized/immobilized, immersion in $MgCl_2$ or MS-222 is commonly used (Harms 2022). Doses for the anesthesia of echinoderms are reported in Table 6.8.

Brittle and Basket Stars

Anatomy, Physiology, and Natural History

Brittle stars have thin arms while basket stars have branched arms (Ruppert et al. 2004).

Table 6.7 Anesthetic drugs and dosing for nematodes.

Nematoda					
Order	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Rhabditida	Chloroform	ED_{50} = 0.52%*	Inhalant	Caenorhabditis elegans	Morgan & Cascorbi (1985)
		ED_{50} = 1.47%*	Inhalant		Morgan et al. (1990)
	Ethanol	4.5%	Immersion		Morgan & Sedensky (1995)
	Flurothyl	ED_{50} = 8.1%*	Inhalant		Morgan & Cascorbi (1985)
		ED_{50} = 14.3%*	Inhalant		Morgan et al. (1990)
	Fluorxene	ED_{50} = 10.9%*	Inhalant		Morgan & Cascorbi (1985)
		ED_{50} = 10.8%*	Inhalant		Morgan et al. (1990)
	Halothane	ED_{50} = 0.85%*	Inhalant		Morgan & Cascorbi (1985)
		ED_{50} = 3.18%*	Inhalant		Morgan et al. (1990)
		ED_{50} = 3.6%*	Inhalant		Crowder et al. (1996)
	Isoflurane	ED_{50} = 4.9%*	Inhalant		Morgan & Cascorbi (1985)
		ED_{50} = 6.5%*	Inhalant		Crowder et al. (1996)
		ED_{50} = 7.18%*	Inhalant		Morgan et al. (1990)
	Propylene phenoxetol	0.5 µL/mL for L1 larvae, 1.5 µL/mL for L2 larvae, 2.0 µL/mL for L3 larvae, 4.0 µL/mL for dauer larvae, 2.5 µL/mL for L4 larvae, and 3.0 µL/mL for adults	Agar Pad		Nelson & Riddle (1984)

* The effective dose (ED_{50}) is the concentration where half of the animals tested were immobile for longer than 10 seconds.

Table 6.8 Anesthetic drugs and dosing for echinoderms.

Echinodermata					
Class	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Ophiuroidea	MS-222	1 g/L	Immersion	*Ophiophragmus filograneus*	Dobson (1985)
	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	1:1 ratio iso-osmotic $MgCl_2$ to seawater	Immersion	*Ophiophragmus filograneus*	Dobson (1985)
	Menthol	2.5–5%*	Immersion	*Amphipholis squamata*	Costello & Henley (1971)
		Half saturation	Immersion	*Ophiophragmus filograneus*	Dobson (1985)
	2-phenoxyethanol	5%	Immersion	*Ophiophragmus filograneus*	Dobson (1985)
	Propylene phenoxetol	1 g/L*	Immersion	*Ophiophragmus filograneus*	Wilkie (1992)
Crinoidea	MS-222	1 g/L	Immersion	Not specified	Hendler (2004)
	Nitrogen	Bubbled for 10–15 minutes	Immersion	Six species of crinoids from the Marshall Islands	Zmarzly (1984)
	Propylene phenoxetol	Titrated to effect*	Immersion	*Antedon bifida*	Nichols (1960)

Table 6.8 (Continued)

Echinodermata					
Class	**Agent**	**Dose**	**Method of Administration**	**Species**	**Source**
Holothuroidea	Menthol	Not given*	Immersion	*Aslia lefevrei*	Costelloe & Keegan (1984)
	Propylene phenoxytol	2 g/L*	Immersion	*Holothuria forskali*	Van den Spiegel & Jangoux (1987)
		Saturated*	Immersion	*Stichopus badionotus*	Hill & Reinschmidt (1976)
Asteroidea	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	37.5 g/L*	Immersion	*Luidia clathrate*, *Astropecten articulatus*	McCurley & Kier (1995)
		80 g/L	Immersion	*Asterias forbesi*	Anderson (1965)
	Menthol	10 g/L*	Immersion	*Asterina pectinifera*	Saha et al. (2006)
		Not given	Immersion	Five species of asteroids from Malaysia	Pinn et al. (2014)
	MS-222	1 g/L*	Immersion	*Echinaster spinulosus*	O'Neill (1989)
		10 g/L*	Immersion	*Coscinasterias calamaria*	O'Neill (1994)
	Propylene phenoxetol	1 g/L*	Immersion	*Marthasterias glacialis*	Santos et al. (2005)
Echinoidea	Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	100 g/L	Immersion	*Strongylocentrotus droebachiensis*	Hagen (2003)
	MS-222	0.4 g/L†, 0.8 g/L	Immersion	*Arbacia punctulata*	Applegate et al. (2016)
	2-phenoxyethanol	30 g/L	Immersion	*Strongylocentrotus droebachiensis*	Hagen (2003)
	Potassium chloride (KCl)	2.5–50 g/L	Immersion	*Strongylocentrotus droebachiensis*	Hagen (2003)

* Not all animals were recovered, dose may need to be adjusted for anesthesia.
† Sedation at low dose, anesthesia at high dose.

Physical Restraint

As brittle and basket stars are fragile, they must be handled gently to prevent autotomy. Sedation or anesthesia, when possible, is recommended to prevent injury to the animal.

Anesthetic Agents Used and Techniques

MS-222 (1 g/L), $MgCl_2$ (1:1 ratio of iso-osmotic $MgCl_2$ to seawater), menthol (half saturation), and 2-phenoxyethanol (5%) have been shown to reduce or prevent arm autotomy in brittle stars (Dobson 1985). Details pertaining to anesthetic plane are not reported but the brittle stars reportedly recovered. A 2.5–5% solution of menthol in seawater has been reported for anesthesia of *Amphipholis squamata* (Costello & Henley 1971). Prior to fixation or preservation, brittle stars have been anesthetized by immersion in propylene phenoxetol (1 g/L) (Wilkie 1992).

Feather Stars and Sea Lilies

Anatomy, Physiology, and Natural History

Feather stars and sea lilies are the most ancient of the echinoderms. They are typically sessile or semisessile. Feather stars are free-swimming while sea lilies are attached to the substrate with a stalk. They are suspension feeders, collecting food using their branched arms (Ruppert et al. 2004).

Anesthetic Agents Used and Techniques

There are few reports of anesthetizing feather stars and sea lilies. They reportedly do not respond to magnesium salts. MS-222 (1 g/L) (Hendler 2004) and propylene phenoxetol titrated to effect (Nichols 1960) may be more effective. Bubbling nitrogen gas in seawater for 10–15 minutes has been reported to successfully immobilize feather stars, with the animals recovering successfully (Zmarzly 1984).

Sea Cucumbers

Anatomy, Physiology, and Natural History

Sea cucumbers are elongated and cylindrical, with a soft and leathery body wall characterized by a thick dermis. Their mouth and anus are found at opposite ends (Ruppert et al. 2004).

Anesthetic Agents Used and Techniques

Some sea cucumbers may respond less well to magnesium salts and better to propylene phenoxetol (Hendler et al. 1995). When exposed to seawater saturated with propylene phenoxetol, sea cucumbers exhibited increased activity for the first 30 minutes, began to relax after 1 hour and were fully relaxed after 2 hours. These animals recovered in running seawater. Sea cucumbers left in the propylene phenoxetol for 13 hours did not survive (Hill & Reinschmidt 1976). Another reported dose for propylene phenoxetol is 2 g/L (Van den Spiegel & Jangoux 1987), however, these sea cucumbers were dissected in a terminal procedure. Menthol crystals have also been used to anesthetize sea cucumbers (Costelloe & Keegan 1984).

Sea Stars

Anatomy, Physiology, and Natural History

Most sea star species have five arms, or rays, which extend from their central disc, but some species can have more than 40 (Ruppert et al. 2004).

Anesthetic Agents Used and Techniques

A common sea star anesthetic is $MgCl_2$. A 75 g/L $MgCl_2$ solution (75 g $MgCl_2$ in 1 L of dechlorinated freshwater) is isotonic to natural seawater (Wahltinez et al. 2021). Immersion in either an 80 g/L $MgCl_2$ solution (Anderson 1965) or a 1:1 mixture of 7.5% stock solution with seawater has been reported (McCurley & Kier 1995). Higher concentrations, however, may be needed for induction but may be hyperosmotic. Adjustments over time during maintenance of anesthesia may be accomplished by gradually diluting the anesthetic solution by administering more seawater. A wide range of MS-222 doses (Fig. 6.5) has been reported and used in a concentrated form (1–10 g/L in seawater) (O'Neill 1989, 1994). Other reported anesthetic agents are menthol (10 g/L) (Pinn et al. 2014; Saha et al. 2006) and propylene phenoxetol (1 g/L in seawater) (Santos et al. 2005). Sea star induction can be assessed by evaluating the loss of righting reaction and response to tactile stimulation of the ambulacral groove.

Sea Urchins

Anatomy, Physiology, and Natural History

Sea urchins have spherical bodies with long spines, except in the flattened "irregular" urchins like sea biscuits and sand dollars, which bury themselves in the substrate. (Ruppert et al. 2004).

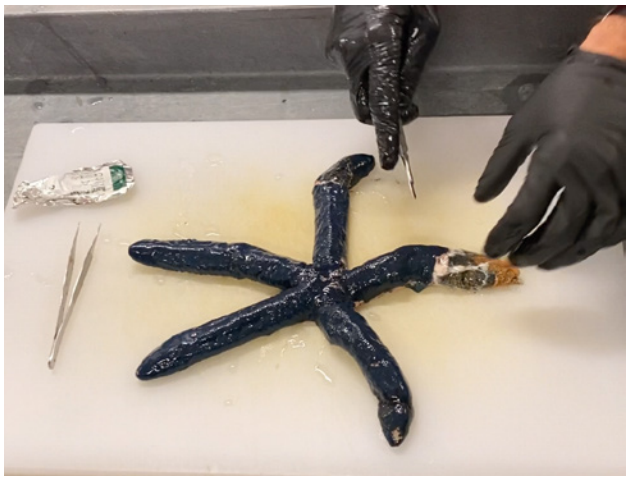


Figure 6.5 This sea star (*Linckia* spp.) has been sedated with immersion in MS-222 prior to partial amputation of a necrotic arm. Image by GA Lewbart.

Anesthetic Agents Used and Techniques

Anesthesia in sea urchins is primarily geared towards preventing spawning, preserving the commercial value of the gonad. $MgCl_2$ doses may vary by species and urchin age. A low dose of $MgCl_2$ (1.0 g/L) prevented spawning and decreased mortality in adult purple urchins (*Paracentrotus lividus*) while higher doses of 8.1–20.3 g/L were associated with increased mortality (Arafa et al. 2007). No mortality was observed in juvenile green sea urchins (*Strongylocentrotus droebachiensis*) immersed in 100 g/L $MgCl_2$ (Hagen 2003). MS-222 buffered with sodium bicarbonate was an effective sedative (0.4 g/L) and anesthetic (0.8 g/L) for sea urchins (Applegate et al. 2016). Criteria for evaluating anesthetic effects included drooping spines, loss of adhesion to a vertical surface, decreased response to tactile stimuli, and loss of righting response (Applegate et al. 2016). Other anesthetics reported for use in sea urchins are KCl (2.5-50 g/L) and 2-phenoxyethanol (30 g/L). Benzocaine (20 g/L) has been deemed unsuitable (Hagen 2003).

Pain and Analgesia

The concept that invertebrates have the capacity to feel pain is a current topic of debate. The crux of the debate may lie in the differentiation between nociception and pain. Nociception describes the neurophysiologic components leading to the sensation of pain but excludes the central perception of nociceptive input that ultimately leads to pain sensation. Pain is defined as "an unpleasant sensory and emotional experience associated with, or resembling that

associated with, actual or potential tissue damage". In humans, pain is modulated by the cerebral cortex (Xie et al. 2009). Although invertebrates do not possess a central nervous system with a well-described cortex or similar structure, a nociceptive response is present (Tobin 2004), nociceptor cells are present (Nicholls & Baylor 1968), and opioid systems have a functional role in invertebrate nociception (Kavaliers et al. 1983; Kavaliers 1988; Fiorito 1986; Saksida et al. 1993; Smith 1991; Thomas et al. 1997). No definitive answer exists, however, as to whether invertebrates perceive pain and would suffer emotional distress from it. The animals' response to chemical, electrical, and mechanical stimuli is seen by withdrawal and escape behaviors. This response is decreased or slowed when an analgesic is used (Kavaliers & Hirst 1983). It is not yet clear if this decreased response is due to a sedative effect or an analgesic effect. With the increase in pain research and animal welfare recognition, our knowledge on this complex topic will expand and these questions may be answered.

Until more information is available regarding pain perception by invertebrates, an anesthetic should be given to any animal that is subjected to a painful procedure, and the amount of stress and pain induced should be reduced through appropriate anesthetic choices.

The use of analgesic agents in invertebrate species has its own limitations since very few reports document the administration and dosing of analgesic agents, especially very small species. More importantly, there are few to no studies evaluating the effects and impact of different analgesics on the patient, receptors, anesthesia, and recovery.

More research is required in this area, but in the meantime, if possible, and if not harmful (e.g., ketorolac in blue crabs), drugs with analgesic properties should be used to anesthetize invertebrates when invasive procedures are performed. Hypothermia and CO_2 do not possess analgesic properties and may even show hyperalgesic characteristics. An inhalant agent is preferred over the latter methods. Although inhalant agents do not possess true analgesic properties, they do render mammalian patients insensible to painful stimuli when administered at sufficient doses. If a procedure is expected to be associated with significant postoperative pain, the administration of an analgesic is advisable. Knowledge concerning analgesic receptors in invertebrates, and if or how commonly used analgesics of vertebrates would apply, is sparse. Sodium channels are conserved across taxa, which makes local anesthetics (e.g., lidocaine) a promising option for invertebrate analgesia. Lidocaine injections have been shown to block afferent signal to the central nervous system and prevent behavioral responses to noxious stimuli in cephalopods, indicating analgesic properties (Butler-Struben et al. 2018; Crook 2021). Morphine does not appear to have analgesic properties in decapods (Barr & Elwood 2011).

Euthanasia

A section on invertebrates was included in the *AVMA Guidelines for the Euthanasia of Animals* for the first time in the 2013 edition, and was revised and expanded in the 2020 edition (Leary et al. 2020). Further guidance can be found in other sources (Cooper 2022; Murray 2022; Reilly 2001; Poole 1999).

Due to challenges in confirming death in many invertebrates, a two-step euthanasia protocol is recommended where the first step renders the animal nonresponsive and the second step ensures death. Acceptable first-step methods for aquatic invertebrates include immersion in clove oil, ethanol, eugenol, and magnesium salts. Acceptable first-step methods for terrestrial invertebrates include inhalant gas anesthetics delivered via an induction chamber and injection of pentobarbital-containing euthanasia solution into the circulating hemolymph. Acceptable second-step methods include immersion in fixatives such as 70% alcohol, 10% formalin, Davidson's solution, and physical methods such as boiling, freezing, and pithing. Methods that do not cause rapid death or cause stress and trauma prior to loss of response are not euthanasia. Unacceptable methods as a solo or first step for euthanasia of invertebrates include removal of aquatic animals from water or immersion of terrestrial animals in water to die by hypoxia, leaving animals in a container without aeration to die by anoxia, freezing, or immersion in a caustic chemical such as tissue fixative (Leary et al. 2020).

Despite the ongoing debate on the capacity of invertebrates to perceive pain, it is widely accepted that different species of invertebrates show various types of stress responses and react to noxious stimuli. Even if the perception of pain is not yet understood, it is our responsibility to treat every living creature with respect, assure the well-being of these animals, and decrease any stress in the best way possible (Murray 2022).

The most commonly used methods for euthanasia are terminal anesthesia followed by physical destruction of the nervous system. Physical destruction of the nervous system/primary ganglia may be added to the chemical method because death is often difficult to verify (Hackendahl & Mashima 2002). The nervous system varies in the different invertebrate species and decapitation alone may not always be a suitable method (Hackendahl & Mashima 2002). Other destructive methods may have to be implemented when doubts about the confirmation of death from an anesthetic overdose are present. More information about ideal species-specific methods of euthanasia is needed.

Specific euthanasia methods and techniques used can be adjusted for sample analyses and research goals. Horseshoe crabs can be euthanized with an injection of

1–2 mL of pentobarbital-containing euthanasia solution directly into the cardiac sinus (Smith & Berkson 2005). Sea stars have been euthanized by immersion in $MgCl_2$ (75 g/L) until they are nonresponsive followed by a physical method of quick dissection. This method allows for the isolation of high-quality RNA (Wahltinez et al. 2021). Jellyfish euthanized in an immersion of $MgCl_2$ (142 g/L) were suitable for NMR spectroscopy-based metabolomics analysis. The recommendations for cephalopods are an overdose of ethanol or $MgCl_2$ followed by brain destruction (Murray 2022; Reilly 2001; Scimeca et al. 2022). Recommended euthanasia methods for crustaceans are an overdose of ethanol or clove oil followed by destruction of ganglia (Reilly 2001). Eugenol immersion at 500 mg/L followed by intracardiac ivermectin at 5 mg/kg or KCl at 10 mmol/kg were effective methods of euthanasia in blue crabs (*C. sapidus*) (Mones et al. 2022). Injection of KCl at 13 mmol/kg at the base of the second walking leg to flood the hemolymph sinus containing the ventral nerve cord has been recommended for euthanasia of American lobsters (*Homarus americanus*) (Battison et al. 2000). Despite presumed rapid effects on the central nervous system, this method may be better applied as the second step of a two-step protocol. This method has also been applied to terrestrial arthropods, and termed "targeted hyperkalosis" to describe terminal depolarization of the thoracic ganglia leading to death (Bennie et al. 2012). Pizzi describes the immersion in 70% ethanol after general anesthesia as an acceptable euthanasia method in spiders (Pizzi 2010, 2022).

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7

Cartilaginous Fishes: Elasmobranchs and Holocephalans

Natalie D. Mylniczenko, Charlene Burns, and Tonya Clauss

Introduction

The class Chondrichthyes comprises nearly 1200 extant species worldwide (Compagno 1999) belonging to two subclasses, Elasmobranchii and Holocephalii. They are probably the most successful of all fishes based on historical endurance in the fossil records (Grogan & Lund 2004). Elasmobranchs (sharks and batoids) represent 96% of the cartilaginous fishes while the Holocephalans (chimeras and elephant fish) represent only 4% (Compagno 1999) and, as such, elasmobranchs are the primary focus in this chapter. With so many different species and such a variety of anatomical and physiological characteristics among them, immobilization and anesthesia can be challenging. Additionally, much of the information relied on for anesthesia in cartilaginous fishes has been anecdotal.

Growth of the aquatic animal medicine field has resulted in a greater breadth of clinical experience with teleost and elasmobranch fishes. This has led to some generalities that can be applied to facilitate safe and effective immobilization and anesthesia.

Decisions on whether to manually or chemically immobilize an animal should be based on the invasiveness of the procedure planned, the duration of time the animal will need to be immobilized, the experience and capabilities of the staff involved, and human and animal safety. When chemical immobilization is deemed necessary, determination of what drug or drug combination should be used depends on the level and duration of sedation or anesthesia desired, the method and feasibility of delivery of the drug, and the ability to safely support and monitor the animal through recovery.

Anatomy and Physiology

The anatomy and physiology of cartilaginous fish has been well described in detail in other texts (Carrier et al. 2004, 2011; Hamlett 1999; Oetinger & Zorzi 1995; Smith et al. 2004; Mylniczenko 2021). Overall there is notable variability in the response of elasmobranchs to handling and anesthesia, which is due to physiology and anatomy. The animal's response to a drug is dependent on many factors, including drug receptor type, tissue distribution, method of administration, body temperature, hepatic biotransformation, blood distribution, renal function, and respiratory mechanism and function. These factors, among others, explain the frequent variation of drug effect seen in elasmobranchs both within and between species. This may be due to receptor binding differences (presence or lack of receptors to a specific drug), affinity to the receptor, different physiological response to the binding, and numbers of available binding sites for a small or great response. Drugs can also bind with blood proteins or other nontarget tissue, thus altering the amount of drug available and the effect on target tissue. In elasmobranchs, albumin is not present (Krol et al. 2014), which would impact a drug that requires albumin for transport. Additionally, naturally high levels of urea may impact the functionality of drugs.

Intramuscular injections may produce inconsistent responses due to the variable density of vasculature and location of associated myotomal muscle bodies (Bernal et al. 2001; Bernal & Graham 2001; Totland et al. 1981). As with some teleosts, sharks also have red and white muscles (Fig. 7.1a). The red (myotomal) muscles are slow contracting ("slow twitch") and aerobic, whilst the more predominant white muscles require less oxygen and are faster to contract ("fast twitch"). Relative abundance makes injections into the fast twitch muscles more likely. Anesthetic injections in the red muscle may result in more rapid induction times, as has been noted in some teleosts (Williams et al. 2004). Some drugs that produce a notable response when administered intravenously may produce little to no response when delivered intramuscularly or orally (Clauss et al. 2011; Mylniczenko, pers. exp.).

Active, pelagic sharks (e.g., hammerhead [*Sphyrna mokarran*] and blacktip [*Carcharhinus limbatus*]) have a

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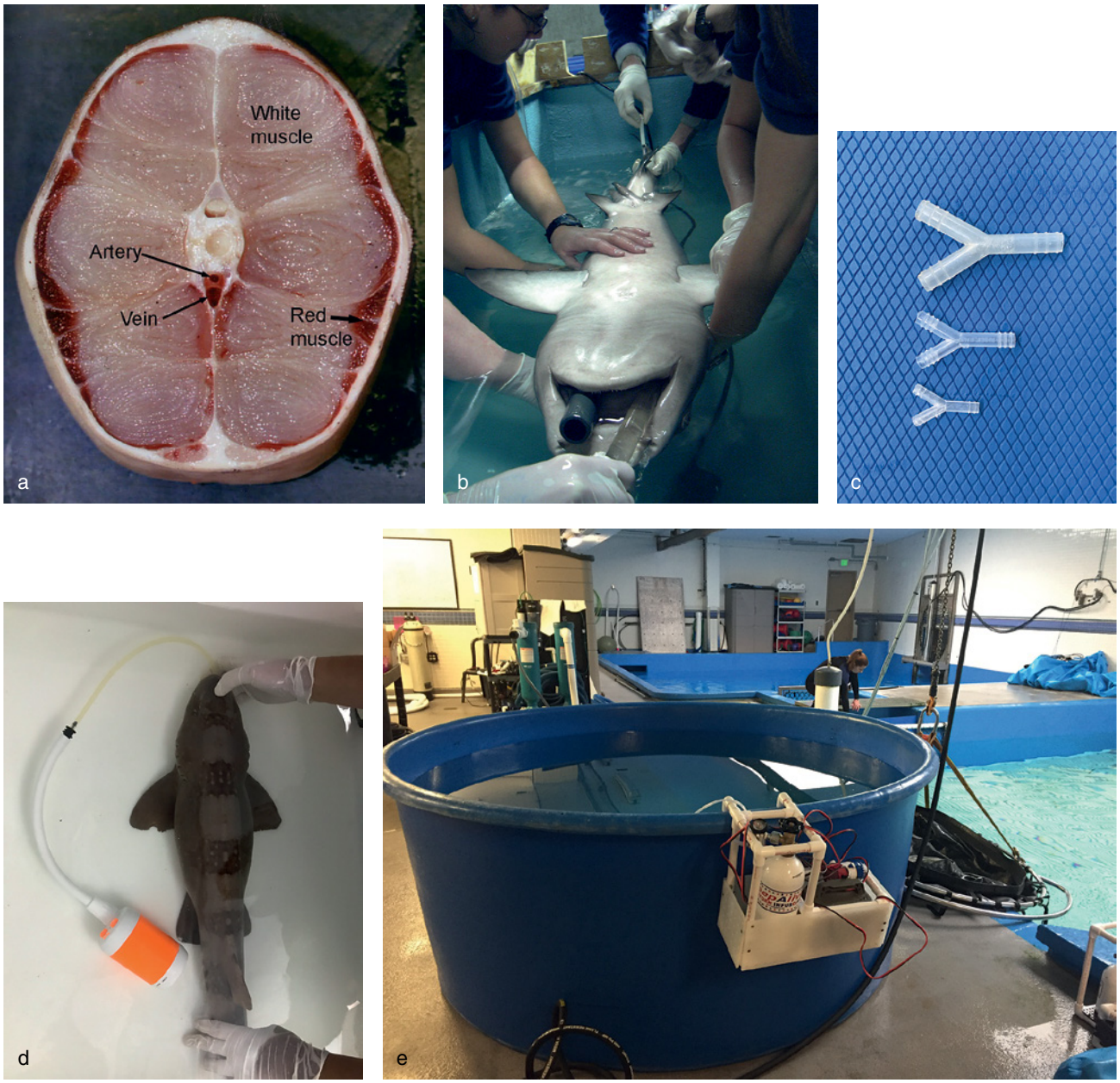


Figure 7.1 (a) Cross-section of the tail of a blacktip reef shark (*Carcharhinus melanopterus*) demonstrating the more vascular or "red" muscle in comparison to the "white" muscle. Note the location of the artery and vein in comparison to the vertebral column. (b) Assisted ventilation in a sandbar shark (*Carcharhinus plumbeus*). There is a PVC tube in place to keep the mouth open. A continuous flow pump is used to direct oxygenated water over the gills. Water flow out of the gill slits determines the appropriate positioning. (c) Variable "Y" pieces for ventilatory equipment that can distribute water flow to each gill series; these are size appropriate for smaller species. (d) Rechargeable, portable, underwater camp shower that can be used for ventilation of smaller elasmobranchs. (e) A portable oxygen tank and water-resistant battery pack to deliver oxygenated water via pump.

higher percentage of myotomal muscles (up to 22%) than less active sharks (e.g., nurse shark [*Ginglymostoma cirratum*] and epaulette [*Hemiscyllium ocellatum*]) (Bone 1999). Although more active sharks from the family Lamnidae (e.g., porbeagle [*Lamna nasus*], mako [*Isurus oxyrinchus*], white [*Carcharodon carcharias*]) and the common thresher shark from the Alopiidae family have a similar muscular plan to those previously mentioned, their myotomal framework is unique and more comparable to that of scombrid teleosts (e.g., tuna and mackerel). In these species, the red muscle is condensed into a solid piston-like muscle mass that is found closer to the vertebrae (Bernal et al. 2001; Carey et al. 1985; Graham & Dickson 2000, 2001; Graham et al. 1983; Sepulveda et al. 2005). In these highly active

elasmobranchs, the vascular supply to this red muscle is through a set of lateral vessels that give rise to a countercurrent heat exchange system (retia mirabilia). This allows conservation of metabolically derived heat, giving these sharks some endothermic abilities. The red muscle temperature may be elevated significantly above ambient (Bernal et al. 2003; Bone & Chubb 1983; Carey et al. 1982) and produce regional heterothermy. Environmental temperature may have little to no impact on the metabolic rates of these endothermic sharks. Ambient temperature, however, plays a major role in controlling the metabolic rates of the majority of elasmobranchs, which are ectothermic. Body temperature therefore must be considered as it impacts metabolic rates, determines enzyme activity, and may influence drug elimination and duration of effect.

In most studied animals, the liver metabolizes certain drugs to either active or inactive forms. Elasmobranch liver size and composition are species dependent but it is overall larger than in other animals and more lipid rich. In the normal animal, it can account for up to 23% of body weight and as much as 80% may be lipid (Holmgren & Nilsson 1999). Drug pharmacodynamics are dependent, in part, on their lipophilic or lipophobic solubility, as well as the amount of hepatic cellular exposure. This adds an additional layer of complexity to drug metabolism in elasmobranchs. Unfortunately, there is very little pharmacokinetic data in elasmobranchs, especially regarding anesthetics.

The kidney is very different to that of mammals, having a higher filtration rate (Lacy & Reale 1999) and is critical for the maintenance of the natural high osmolarity (Henderson et al. 1988) These differences may influence drug elimination rates. Like reptiles, elasmobranchs have a renal-portal system that allows blood from the caudal half of the animal to drain directly into the kidneys. Historically, injections in the caudal half of the body were avoided in reptiles and fish as theory suggested the renal portal system may enhance the nephrotoxicity or influence renal excretion of drugs. Studies in reptiles, however, found no significant difference in drug metabolism when injections were given in the fore or hind limbs, suggesting the renal portal system has little, if any, negative influence on drug metabolism (Beck et al. 1995; Holz 1999; Holz et al. 2002). Based on studies in reptiles, it is unlikely the renal portal system poses a threat to drug action or metabolism in elasmobranchs.

The basic function of the respiratory system is the exchange of gasses (oxygen and carbon dioxide). While simplistic in theory, elasmobranchs manage their metabolic exchange of these gasses differently. Elasmobranch respiration can be loosely based on their preference of habitat: pelagic (open water), intermediary, and benthic (bottom). Examples of these include (1) pelagic: black tip (*C. limbatus*) and blue shark (*Prionace glauca*); (2) intermediate: sand tiger shark (*Carcharhinus taurus*) and brown shark (*Carcharhinus plumbeus*); (3) benthic: Japanese wobbegong (*Orectolobus japonicus*) and the nurse shark (*G. cirratum*). Many pelagic elasmobranchs rely predominantly on ram ventilation, forcing water over their gills by swimming constantly. The nonpelagic animals can pump water over their gills via buccal pumping and can rest on the bottom for extended periods of time. These animals tend to have a higher tolerance for anaerobic conditions (Mylniczenko et al. 2007). Benthic animals are those that spend much of their active time on the sea bottom, while the intermediates swim more than they rest. The classifications are not strict. In general, benthic animals can buffer acidemia and/or manage hypoxemia more efficiently. This is critical because activity (such as capture) will significantly affect elasmobranch blood gasses and physiologic status. In general, there are few obligate ram ventilators in aquaria, but these animals need additional care during anesthesia and recovery to ensure adequate ventilation.

Most benthic sharks and batoids have a supplemental respiratory feature, the spiracle, located dorsally behind the eyes. This opening may serve as an alternate route for channeling water over the gills when the mouth of elasmobranchs is in contact with the sediment or substrate. It is suggested that the spiracle function is voluntary to prevent sand entry into the gills (Butler 1999). During anesthesia, ventilation may occur either via the mouth or through the spiracles. The advantage to ventilation via the mouth is flow may easily be directed over both gill sets simultaneously (Fig. 7.1b–d). Specific modifications are necessary to achieve simultaneous flow over both gill sets when water is directed through the spiracles. An example of this is a mouthpiece shaped as a "Y" (Fig. 7.1c). To facilitate a safe, portable, waterproof method of providing ventilation, a camp shower can be modified (Fig. 7.1d). Addition of oxygen pumped into the water can provide additionally ventilatory support (Fig. 7.1e).

Elasmobranchs possess a functional hypothalamic–pituitary–interrenal (HPI) axis based on the presence of adrenocorticotropic hormone (ACTH), which regulates interrenal production of 1α-hydroxycorticosterone (1α-OHB), a primary corticosteroid, which is produced only in elasmobranchs. Only recently, an assay developed for its measurement (Anderson 2012; Idler & Truscott 1966, 1967, 1968, 1969; Truscott & Idler 1968, 1972; Wheaton et al. 2018). Comparatively, cortisol is not present in elasmobranchs, while it is the primary corticosteroid in teleost fish (Skomal & Bernal 2011). Corticosterone (CS) is also found in some elasmobranch species (Rasmussen & Crow 1993; Rasmussen & Gruber 1990, 1993; Snelson et al. 1997), but 1α-OHB has been shown to be the dominant

hormone. CS assays are often not accurate and there is cross-reaction (Anderson 2012; Skomal & Bernal 2011). The hormone has a proposed mixed role in mineralocorticoid and glucocorticoid responses, thus fluid shifts and energy utilization with a stress response can alter how the animal responds to handling as well as drug absorption and distribution.

There are few studies of the role of the HPI axis in regulating the elasmobranch primary stress response. Catecholamines increase immediately after a stressor and peak after the cessation of the event (Randall & Perry 1992). Manire et al. (2007) found both a short- and long-term CS response to capture and handling in bonnethead sharks (*Sphyrna tiburo*). These reports suggest a relationship between a stressful event and the activity of the interrenal gland. The secondary stress response has been studied more than the primary response, receiving a lot of attention in the last several years (Van Rijn & Reina 2010; Frick & Reina 2009; Karsten & Rice 2004; Mandelman & Farrington 2007; Mandelmann & Skomal 2009; Marshall et al. 2012; Naples et al. 2012; Renshaw et al. 2012). New data show a correlation of 1α-OHB with the secondary stress response (Wheaton et al. 2018). This information can be very useful in assessing elasmobranchs during the timeframe of a restraint; clinical applications will be discussed later in this chapter.

In addition to the stress response, other physiological or anatomical factors that may influence the drug response include gill health, lipid content, health status, and body condition changes associated with age, season, sexual maturity, and nutrition. There are many variables that need to be considered when anesthetizing elasmobranchs.

Capture

Many elasmobranchs housed in public aquaria share large systems with mixed species. Catching these animals can be challenging and even dangerous to both the people and animals involved. Retrieving these animals may be done either by behavioral conditioning, manually using a variety of techniques, or with chemical immobilization. Regardless of the method used, minimizing distress and maintaining safety should be primary goals.

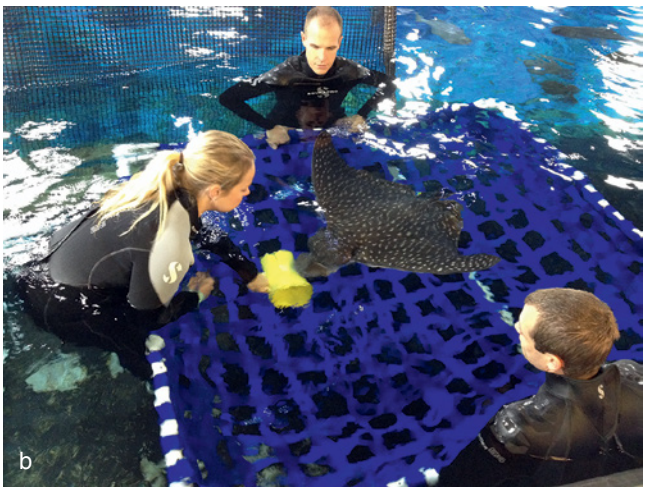
Elasmobranchs are very responsive to behavioral conditioning and training techniques. The benefits of animal training programs include enrichment, better animal control and monitoring, reduced stress during handling, implementation of advanced husbandry techniques, enhanced education programs, and positive associations between animals and caretakers (Baker 1991). Operant conditioning is a process by which a subject produces a behavior in the presence of a cue on the condition of achieving desirable outcomes or avoiding undesirable consequences. While the training of sharks and rays may be somewhat limited, several facilities have achieved impressive results through operant conditioning and behavioral modification (Fig. 7.2).

Behaviors as seemingly simple as target training or station feeding can be invaluable and can facilitate shifting to different areas of an exhibit, stretcher trainer, morphometrics, and layouts for ultrasounds (Fig. 7.3a–e) (Sabalones, pers. exp.). A useful method is to swim or direct animals into a deflated swimming pool (which is then inflated once the animal is captured) or into a chute/restraint device for induction of anesthesia (Fig. 7.3f–i). Additionally, training animals to swim onto a ramp and then into a net or directly into a net (or stretcher) facilitates examinations and treatments (Fig. 7.3c–e). Behavioral management in some of the larger elasmobranchs is arguably a necessity as manually catching and restraining can be difficult, if not impossible, and has the potential to cause significant stress and possible injury to the staff and animal(s).

When animals are not conditioned to present behaviorally for examinations or other procedures, more active capture techniques must be used and may or may not involve administration of drugs. A shark 'sock' has gained popularity at aquaria (Fig. 7.4a). A clear vinyl bag is used which has the narrow end covered with a nylon mesh and the opposite to enable water flow to be directed at the head of the shark. Divers operate the bag, one at the closed end and two at the entrance. The animal (sedated or not, species dependent) is guided into the bag and the apparatus is then brought to the procedural area (Daly et al. 2007) (Fig. 7.4a,b). Unanesthetized large batoids (e.g., bowmouth (*Rhina ancylostoma*) (Fig. 7.4c) and giant guitarfish (*Rhynchobatus djiddensis*), sawfish (Fig. 7.4d,e) and other large elasmobranchs (Fig. 7.4f) can be caught using a large box net. The square PVC frame and attached knotless net is sunk to the exhibit floor. Divers in SCUBA corral the target animal over the net and people at the surface then haul the net up rapidly. The animal may then be restrained manually or chemically. Smaller sharks such as bonnetheads and blacktips may be caught via a hoop net when they approach a feeding station.

In some cases, a net draped across the width of a tank and pushed across the length of the enclosure (much like seine netting) can be used to both encourage animals into a medical pool and to limit the overall size of the area animals need to be captured in. This technique also allows the possibility to significantly reduce the depth of the area by bringing the bottom of the net to a more comfortable depth (Fig. 7.4g,h). Disadvantages include the number of staff/divers required to execute a "catch up" as well as catching multiple animals and nontarget animals. Animals





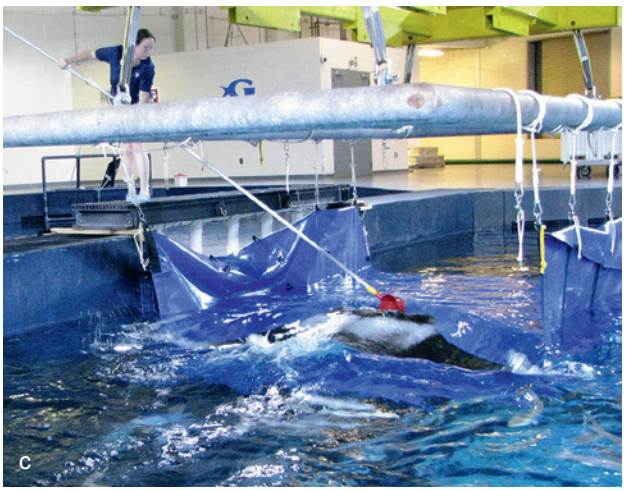


Figure 7.2 (a) A sandbar shark (*Carcharhinus plumbeus*) target feeding during a training session. (b) An eagle ray (*Aetobatus narinari*) targeting a stretcher in a training session. (c) Behaviorally conditioning a manta ray (*Manta alfredi*) to swim into and through a stretcher. Photo credit: Georgia Aquarium.

such as sawfish in these situations are difficult to manage and need to be excluded.

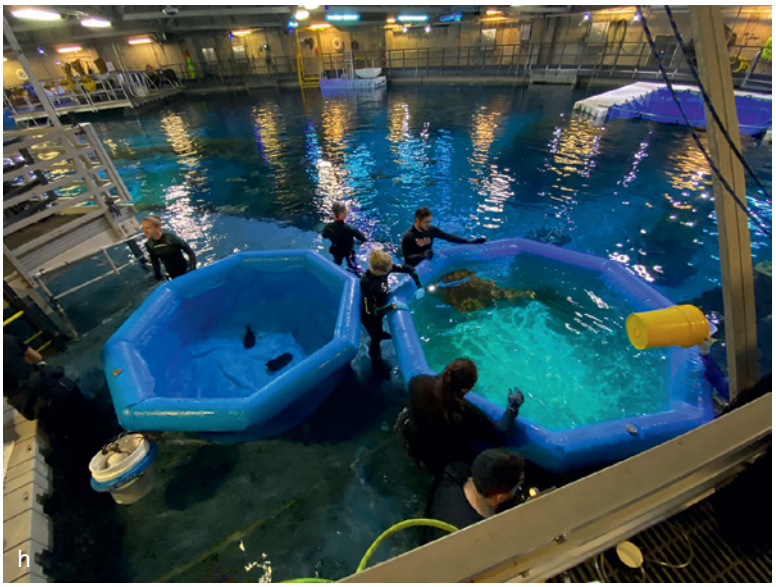
Drugs may also be used to assist in retrieving elasmobranchs from an exhibit or holding system. Immersion anesthetics are often impractical (but possible) due to tank size and the presence of other animals. However, divers may spray very concentrated immersion agents such as tricaine methanesulfonate (MS-222) or eugenol directly over the gills (into edge of mouth/face) to sedate it long enough to gain physical control. Injectable drugs may be delivered while the animal is swimming. This is usually done intramuscularly, but intravenous anesthetics have been delivered to a variety of rays and whale sharks by staff at the Okinawa Churaumi Aquarium in Okinawa, Japan (Makio, pers. comm.) and to whale sharks at the Osaka Aquarium Kaiyukan in Osaka, Japan (Takaomi, pers. comm.).

When dealing with more active or aggressive animals, diligent care must be taken when administering drugs via pole syringe, nearby darting apparatus, and especially when hand injecting. Animals when surprised, even if partially sedated, may turn around on a diver and inflict harm in their effort to ward off a threat. The speed of the animal and the trauma from their teeth or skin cannot be underestimated. Oral medications may also be delivered if the animal in question is target or station trained.

Oral doses required to sedate elasmobranchs are often quite high and the amount of drug required may be volume limiting or cause the animal to regurgitate the food item it is delivered in. As with injectable agents, the response to oral anesthetics is often unpredictable. Anesthetics and sedation will be discussed in greater detail later in this chapter.



Figure 7.3 (a) Behavioral training for individual feeding and for physical therapy in spotted eagle rays (*Aetobatus narinari*). (b) Voluntary control of a porcupine ray (Urogymnus asperrimus) to remove sutures (c) A cownose ray (*Rhinoptera bonasus*) trained to swim into a net ("ray tray") for medical procedures. (d) A cownose ray (*Rhinoptera bonasus*) being moved into a sedation pool. (e) Physical examination on a manta ray (*Manta alfredi*) in a stretcher. Photo credit: Georgia Aquarium. (f) A slightly deflated pool with a cownose ray (*Rhinoptera bonasus*) that can be inflated and used for medications, anesthesia, or observation. (g) A large enclosure option for creating smaller spaces and smaller immersion options: the pool within a pool. (h) Staged anesthesia with one pool having eugenol (Aqui-S 20E™) for induction and the other tricaine methanesulfonate (MS-222) for maintenance anesthesia. (i) A teeter totter for training large rays to target, enter the stretcher, and then tip out the opposite direction.



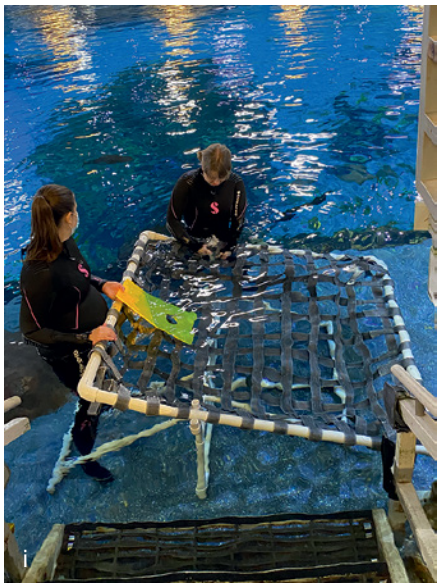


Figure 7.3 (Continued)







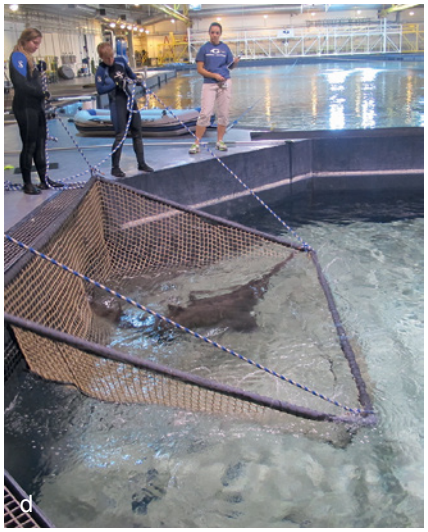


Figure 7.4 (a) A clear vinyl bag ("shark sock") with a wide round opening and a narrower distal hole, to allow for water flow, at the distal portion of the bag. This is used to guide a fish into the bag for transport to the surface of the water and further restraint. (b) Next step, with the animal in the bag and being guided up the water column. Note divers with baffles to help guide the animal. (c) Restraint of a bowmouth guitarfish (*Rhina ancylostoma*) in a partially submerged box net. Photo credit: Georgia Aquarium. (d) Retrieval of a largetooth sawfish (*Pristis microdon*) from an exhibit utilizing a boxnet. (e) SCUBA divers corral the animal over the submerged net, which is then quickly hoisted to the surface. Photo credit: Marj Awai, Georgia Aquarium. (f) A swim-through stretcher for greater hammerhead (*Sphyrna mokarran*) training and handling. (g) A metal bridge across an enclosure with a net (wall-to-wall) that extends to the depth of the tank. The bridge and net can move across the entire tank to isolate animals or push them from one end to the other. (h) The same net as in (b) with an underwater view of divers maneuvering the net over coral heads in the enclosure's bottom.

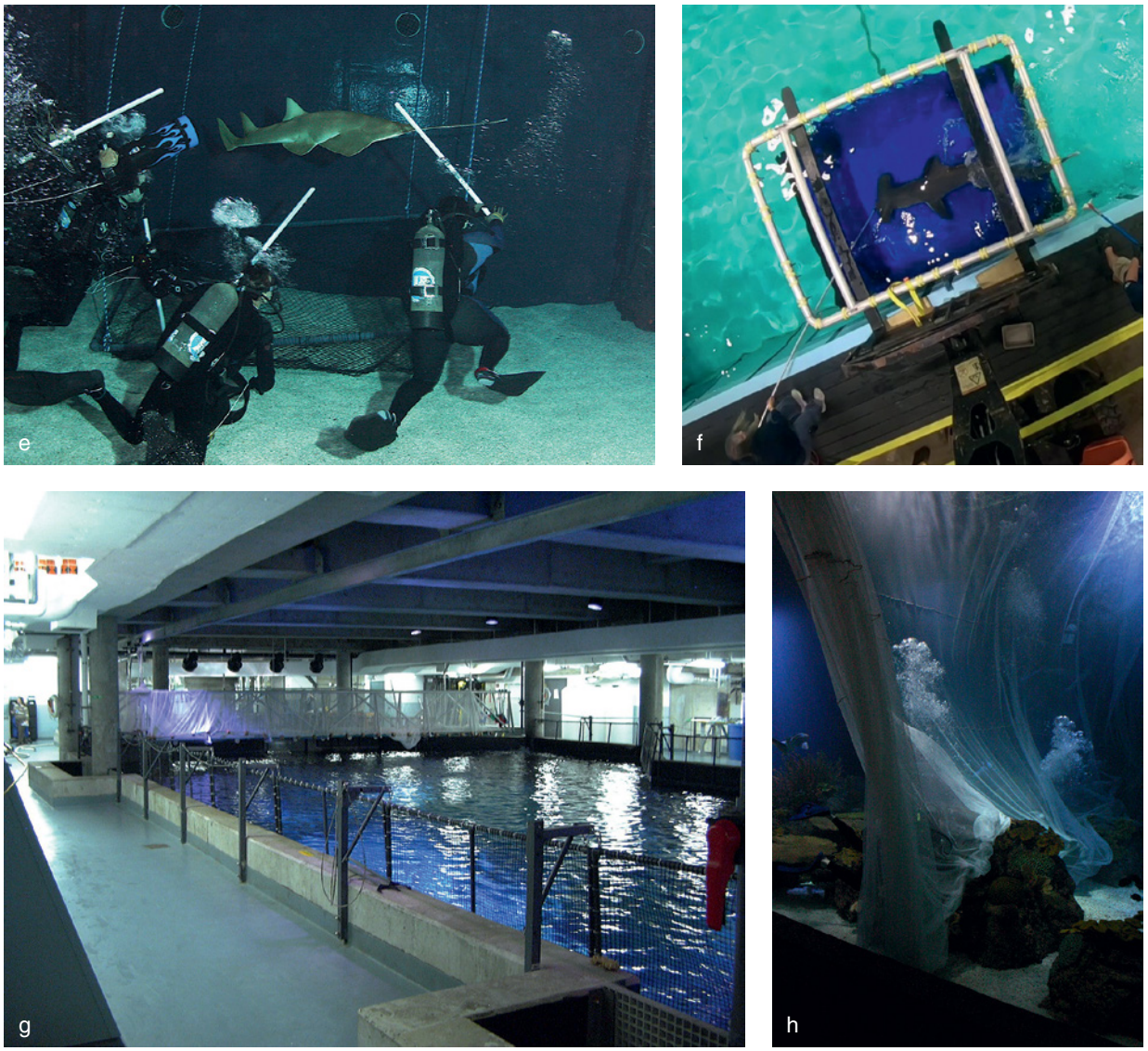


Figure 7.4 (Continued)

Physical Restraint

Tonic immobility (TI) or "hypnosis" is a defensive behavior resulting in a temporary state of "profound and reversible motor inhibition elicited by some forms of physical restraint" (Monassi et al. 1999). It is induced by placing an animal in dorsal recumbency. Once in TI, animals may exhibit either hypo- or hypertonicity and usually have a deep rhythmic respiratory pattern (Brooks et al. 2011; Kessel & Hussey 2015; Williamson et al. 2018; Mukharror et al. 2020). These animals, especially batoids, may go through a period of marked excitability during the initial catch and handling, but once in this hypnotic state, they are subdued. The level of restraint and duration of effect is highly variable between species.

When immobilized with TI, the blood pressure and heart rate of *C. melanopterus* decreased significantly. Branchial irrigation improved blood pressure in these animals, but heart rate was unchanged (Davie et al. 1993; Henningsen 1994). This indicates a vagal nerve response with the ability to have physiologic shifts based on ventilator support. Some aquaria report that pinching the dorsal fin will have a calming effect on some species, akin to reptile ocular–vagal responses, but this is anecdotal and not recommended as an initial stand-alone method of restraint. A controversial notion is that tonic mobility is appropriate as an anesthetic for surgical implantations (Kessel & Hussey 2015) but this warrants serious consideration for several reasons: no analgesia or hyperalgesia can occur and TI is frequently misunderstood and a true physiologic TI

state should be ensured (versus manual restraint). Animals should be ventilated appropriately to provide adequate oxygenation as respirations are altered. It may be that in field situations TI is chosen to allow an animal a more immediate recovery for return to the wild or that regulatory agencies will not approve the use of medications in animals being released. It is suggested that TI is "inherently a stressful experience". This is based on bloodwork changes in *Negaprion brevirostris* when they experience TI or when it is unsuccessful (Brooks et al. 2011).

Even when not utilizing manual restraint for an entire procedure, it is often necessary at the onset of a chemical immobilization. In those cases, rapid capture and restraint either by netting or by hand is recommended. Pursuing animals for prolonged periods frequently results in rapid elevations of lactate and acidemia. Only experienced staff should be involved with manual restraint of elasmobranchs. Even some of the smallest species are extremely strong, thus increasing the chances of injury to people and animals. Some additional human safety factors to consider include (1) abrasions from the placoid scales in sharks and some rays, (2) sharp teeth or crushing plates in the oral cavity, (3) barbs on stingrays, and (4) in some of the freshwater ray species, the surrounding epidermal bumps are venomous (Mylniczenko 2010). To mitigate these issues, under dangerous situations it is advisable to utilize baffles made of mesh and PVC or some other shielding device (Fig. 7.5a), to wear appropriate gloves that prevent bite and crush

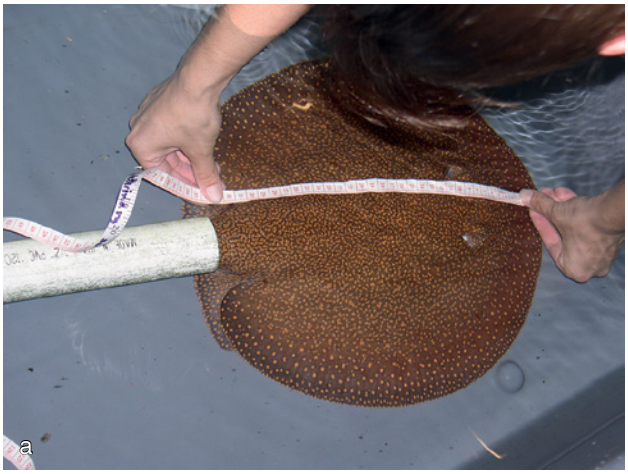






Figure 7.5 (a) A PVC safety tube placed over the tail of a freshwater stingray (family Potamotrygonidae). (b) Remote ventilation for a sand tiger shark (*Carcharhias taurus*) while recovering from anesthesia using a baffle during anesthetic recovery. (c) Remote ventilation for a brown (sandbar) shark (*Carcharhinus plumbeus*) while recovering from anesthesia in a smaller pool.

injuries (e.g., Kevlar gloves), and in some circumstances to wear suits or gloves that prevent bodily injury (e.g., chain mail suits specifically designed to work with dangerous aquatic animals) (Fig. 7.5b). Chain mail suits themselves can be very heavy and pose different safety concerns. Ideally, in case of traumatic injury, there should also be an emergency diver evacuation plan in place and access to first aid either by trained personnel or a nearby emergency response unit. A hands-off approach is possible as well, but requires more planning and facility modification (Fig. 7.5c).

Chimaerids offer unique handling challenges in that they are soft skinned and have ambient light restrictions (because they have an all-rod retina, they must minimize the amount of light that enters the retina). These animals should be handled with soft mesh or plastic nets and corralled under water as they are very sensitive to net trauma. Ideally procedures should be conducted in low light. They have a spine that precedes the first dorsal fin that contains weak venom, therefore staff should handle cautiously.

Vascular Access

Access to elasmobranchs vasculature is determined by the size and position of the animal rather than which vessel is most ideal. The largest blood vessel accessible with the animal in dorsal recumbency, in both sharks and rays, is the artery or vein that lies along the midline just ventral to the vertebral column (Figs 7.1a and 7.6a). These vessels are located by placing the needle just posterior to the base of the trailing edge of the first or second anal fins in sharks or just caudal to the vent in rays. The needle is directed anteriorly at angle of 30–90°, relative to the body, and inserted until the needle tip meets cartilage (approximately 4 cm for a 10-kg shark) to penetrate the vessel (Stoskopf et al. 1984). A lateral approach can be used as well (Fig. 7.6b). In large-bodied species and mature animals, needles may become plugged during penetration of the cartilage wall protecting the vessel. A spinal needle (with a removable stylet protecting the needle aperture) is used in these larger animals. However, longer needles may be difficult to place accurately on the midline, therefore careful threading is necessary. Abdominal vein access has also been described (Otway 2020).

There is a vascular plexus associated with the dorsal fin that is commonly referred to as the "dorsal sinus" (Fig. 7.6c). The first and second dorsal fins have this plexus and it can be found in most shark species as well as numerous batoids. The dorsal sinus is considered an access point to the secondary circulatory system, but it is a viable access port for blood collection as well as drug administration. The reader is cautioned with interpretation of blood work from this site as it does have variations compared to the central vasculature system (Mylniczenko et al. 2006). Regardless, various species have been successfully anesthetized using this route.

The pectoral fin vasculature in large sharks, such as whale sharks, as well as wing vessels in rays can be used for either blood collection or administration of intravenous drugs (Fig. 7.6c,d). The wing vessel in rays is found by palpating the ceratotrichia (cartilaginous rays) and then placing the needle in front of the cartilage, advancing the needle slowly with slight negative pressure in the syringe until a flash is obtained. The mesopterygial vessel can also be used (Westmoreland et al. 2019).

Catheterization of the ventral coccygeal vein dorsal sinus or wing veins is possible, but difficult to maintain. When successful it permits medications to be given in a direct, consistent manner over a long period of time.

Preanesthetic Considerations

Ideally, preanesthetic assessment will include a thorough history of the fish, information on water quality conditions and husbandry practices, remote observation (preferably in the original habitat), and familiarization with any unique characteristics of the species or individual. Fish often present to the clinician when they are already systemically ill. This represents an anesthetic risk, particularly since the etiology will likely be unknown until an examination is conducted.

Determining if water quality conditions may be a contributing factor in a disease process is important and evaluation prior to sedation can be helpful. If the fish has been transported to the clinician, the water quality variables of the transport vessel can be tested as well. Observation of fish in their primary habitat or even in a transport or holding vessel is useful for assessing swim patterns, posture, general appearance, and demeanor, as well as obtaining respiratory rates.

Even minimal handling can be stressful to healthy elasmobranch. A full clinical examination or blood work prior to anesthesia may therefore not be feasible or reasonable. The stress and potential trauma associated with manual restraint for diagnostics and morphometrics may be more risky than anesthetizing a fish without that information. When the body weight cannot be safely obtained prior to anesthesia, other methods exist for estimation, such as the length-to-weight ratio data for some species. When this information is not available, blind estimates may have to be made if oral or injectable anesthetics are used. However, this may greatly affect the quality and depth of the anesthesia. If this is the case, a weight and fork length should be taken once the animal is in hand and documented for future work.



Figure 7.6 (a) Collection of blood from a ventral tail vessel in a bonnethead shark (*Sphyrna tiburo*). (b) Collection of blood from a lateral approach to the ventral tail vessel in a sand tiger shark (*Carcharhias taurus*). (c) Collection of blood from the dorsal sinus in a vessel in a sand tiger shark (*Carcharhias taurus*). (d) Collection of blood from the wing vessel in an eagle ray (*Aetobatus narinari*). (e) Underwater collection of blood from the pectoral fin vasculature of a whale shark (*Rhincodon typus*) under behavioral control using a specialized feeding technique. Photo credit: Georgia Aquarium.

As with most other animals, it is preferable that elasmobranchs be fasted prior to anesthesia so the anesthetic water and/or the procedure container are not fouled if regurgitation or elimination occurs. Caretakers should be instructed to bring additional water with them that may be used if the transport water is fouled and/or for recovery from anesthesia. Care should be taken to monitor water parameters such as temperature, pH, and dissolved oxygen of both the procedure water and recovery/clean water to maintain original habitat parameters.

Once an animal is removed from its primary habitat, all actions associated with transport, handling, and anesthesia should be swift and precise to minimize the stress response. Ideally, a preanesthetic meeting is conducted to ensure animal and human safety by outlining the goals of the capture, procedure, and recovery process as well as identifying the responsibilities for each person who is partaking in the event. Thorough preparation prior to an anesthetic procedure is essential in providing fish with the best opportunity for a full recovery.

Chemical Immobilization

The use of chemical restraint can provide a safer, less stressful procedure for the fish and staff involved. Minimization of movement and the ability to perform procedures with an elasmobranch out of the water often reduces handling time. Some diagnostic techniques and procedures cannot be adequately performed when animal movement occurs (e.g., magnetic resonance imaging, computed tomography, standard radiography) and thus chemical immobilization is essential. The authors have compiled cited and anecdotal dosages of the anesthetics used in various species of elasmobranchs (Table 7.1). Anesthetics may be delivered via immersion (inhalation), injection or per os.

Immersion (Inhalation) Anesthesia

Waterborne or immersion anesthesia is still the most widely used method for sedating or anesthetizing elasmobranchs and holocephalans. The chemical in aqueous solution is ventilated by the fish, passes into the blood via the gills and is delivered to the central nervous system. An extensive discussion of immersion anesthetics, including delivery techniques, mechanisms of action, metabolism, and clearance as well as advantages and disadvantages can be found in Chapter 8. The same principles used in bony fish also apply to elasmobranchs and holocephalans.

Immersion anesthetics are most commonly administered with the elasmobranch submerged in a specified concentration of the drug. Depending on clinician preference, a higher concentration of a drug may be used to induce anesthesia with a lower concentration being used to maintain the preferred plane of anesthesia. For balanced anesthesia, the authors use Aqui-S 20e™ as an induction agent and then move the animal to MS-222; this allows both drugs to be used at low doses with better recoveries than either drug alone. These chemicals have the advantage of being relatively safe to deliver and the concentration can be modified by addition or dilution of the solution. One disadvantage of immersion medications is the large amount of drug needed when immobilizing animals in large bodies of water. As previously mentioned, some waterborne anesthetics may be delivered in high concentration via direct administration to the gills. Gilbert and Kritzler (1960) anesthetized large sharks and rays with MS-222 (1 g/L) delivered through a hand pump sprayer while animals were free swimming. Care must be taken with this approach as some of these larger specimens are predatory and delivery requires the anesthetist to be in very close proximity to the mouth of the animal.

An alternative that facilitates the use of immersion anesthetics is training or conditioning the animal to shift into smaller bodies of water such as secondary systems or smaller containers. An example of the latter is an inflatable pool submerged, filled with tank water, and partially deflated in the main tank (Fig. 7.3f–h). Air is then added to the rim to fully inflate the pool once the animal is in the body of the pool. In large elasmobranchs, even after an animal is moved to a smaller container, the volume of drug needed for adequate immobilization can still be great. The technique of applying high concentrations of the anesthetic over the gills via the gill slits or through the spiracles, if present, can further reduce the volume of drug needed (Fig. 7.7).

Tricaine Methanesulfonate (MS-222, TMS)

This water-soluble, benzocaine derivative is used at a range of 50–150 mg/L to anesthetize both sharks and batoids (Larid & Oswald 1975). The concentration is varied with the species and procedures performed. If delivering via a hand pump, even higher concentrations will likely be necessary for induction (1–2 g/L). The drug is acidic and requires buffering. Sodium bicarbonate is the most used buffering agent and is usually mixed at a ratio of 2 parts buffer to 1 part drug based on the weight of the anesthetic. With that being said, recent studies have shown that sodium carbonate demonstrates a greater buffering capacity in a shorter time interval (N. Mylniczenko, pers. exp.; Waxman et al. 2021). Doses that exceeded this ratio resulted in blood gas abnormalities and clouding of the water. When the same anesthetic water is used to anesthetize multiple animals, it is wise to monitor the pH, oxygen, and carbon dioxide as shifts may occur. The authors recommend monitoring water quality or changing water after every third animal.

A direct linear relationship exists between MS-222 concentration and time to muscular relaxation (Dunn & Koester 1990). Levels of sedation and anesthesia (stages) have been described (Stoskopf 1986; Smith 1992). A wide variety of elasmobranch species will achieve a surgical plane of anesthesia (i.e., stage 3) using MS-222 (75–95 mg/L), but species-specific responses are common

Table 7.1 Anesthetic and immobilization drugs used in elasmobranchs.

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Acroteriobatus annulatus	Sandshark, lesser	Etorphine (M99) + midazolam		IM					No effect	Penning (2012)
Acroteriobatus annulatus	Sandshark, lesser	Medetomidine	0.1 mg/kg	IM		0.0.13			Fair	Penning (2012)
Acroteriobatus annulatus	Sandshark, lesser	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM		0.0.5			Fair to good	Penning (2012)
Aetobatus narinari	Eagle stingray, spotted (whitespotted)	Alfaxalone-alphadolone (Saffan)	0.35 mL/kg	IM	54	0.0.1			Tranquilization only achieved the deepest state within 1 hour with disorientation, slowed swimming, bumping into tank walls, net avoidance	Harvey et al. (1988)
Aetobatus narinari	Eagle stingray, spotted (whitespotted)	Eugenol (AquiS-20E)	15–25 mg/L	Immersion	2–94	10.9.0	Juvenile-adult	25	Typical recovery after a 30 minutes procedure on a healthy animal can be up to 30 minutes. Dilution after induction improves recovery speed.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Aetobatus narinari	Eagle stingray, spotted (whitespotted)	Medetomidine	0.1 mg/kg	IM	10–15	0.0.1			Good	Penning (2012)
Aetobatus narinari	Eagle stingray, spotted (whitespotted)	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM						Penning et al. (2017)
Aetobatus narinari	Eagle stingray, spotted (whitespotted)	Midazolam hydrochloride	4.6 mg/kg + 4.9 mg/kg	Oral		0.1.0	Adult		No effect first dose, supplemental dose mild sedation 15 minutes later	N.D. Mylniczenko (pers. exp.)
Aetobatus narinari	Eagle stingray, spotted (whitespotted)	MS-222 (Tricaine methanesulfonate)	40–75 mg/L	Immersion	2–94	10.9.0	Juvenile-adult	25	Juvenile specimens adequately sedated 40–65 mg/L, large females 50 mg/L	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Aetobatus ocellatus	Eagle stingray, ocellated	Eugenol (AquiS-20E)	15–75 mg/L	Immersion	2–75	4.8.7	Juvenile-adult	25	20–30 mg/L used to calm animal quicker, then dilute for longer procedure. Quick treatments can be done at high doses 75 mg/L for <5 minutes. Cardiac effects noted via U/S for long procedures.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Aetobatus ocellatus	Eagle stingray, ocellated	Eugenol (AquiS-20E) => MS-222	40–65 mg/L => 40–50 mg/L	Immersion	2–75	4.8.7	Juvenile-adult	25	AquiS-20e for induction within 5 minutes, then move to MS222 for maintanence for balanced anesthesia and short recovery time	C.M. Burns & N.D. Mylniczenko (Personal experience)
Aetobatus ocellatus	Eagle stingray, ocellated	MS-222 (Tricaine methanesulfonate)	45–80 mg/L, 100–125 mg/L	Immersion	2–75	4.8.7	Juvenile-adult	25	Up to 80 mg/L is used in routine or diagnostic examinations, for treatments or blood draws higher doses can be used for <10 minutes	C.M. Burns & N.D. Mylniczenko (Personal experience)
Atelomycterus marmoratus	Catshark, coral	Eugenol (AquiS-20E)	25–50 mg/L	Immersion	0.1–0.5	0.1.0	Juvenile-adult	25	High dose 50 mg/L can be used for short term (<10-minute) treatments or blood collection. Quick recovery.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Atelomycterus marmoratus	Catshark, coral	MS-222 (Tricaine methanesulfonate)	110 mg/L -> 75 mg/L	Immersion	0.1–0.5	0.1.0	Juvenile-adult	25	With frequent sedations, the patient needed increased doses for rapid induciton, but then dilution for longer duration procedures	C.M. Burns & N.D. Mylniczenko (Personal experience)
Atelomycterus marmoratus	Catshark, coral	MS-222 (Tricaine methanesulfonate)	60 mg/L	Immersion	0.1–0.5	0.1.0	Juvenile-adult	25	Varied with individuals, when animals were sedated more frequently concentration levels increased	C.M. Burns & N.D. Mylniczenko (Personal experience)
Atelomycterus marmoratus	Catshark, coral	MS-222 + propofol	150 mg/L + 1.5 mg/L	Immersion		0.0.6		21–24	Surgical plane of anesthesia	Levendosky (2020)
Bathytoshia lata	Brown (roughtail) stingray	Alfaxalone-alphadolone (Saffan)	0.2–0.3 mL/kg	IM	15	0.0.2			Deepest state within 1 hour: partial loss of equilibrium, settling or rising to surface, allowed netting but still responsive to touch	Harvey et al. (1988)

Bathytoshia lata (Dasyatis centroura)	Brown (roughtail) stingray	Alfaxalone-alphadolone (Saffan)	0.85 mL/kg	IM	18	0.0.1			Deepest state within 1 hour: disorientation, slowing of swimming, bumping into tank walls, net avoidance	Harvey et al. (1988)
Carcharhinus acronotus	Blacknose shark	Medetomidine + ketamine	70–100 µg/kg + 5.5–8.8 mg/kg	IM					Variable effects but did not achieve more than light sedation without supplementation of the same drugs. One animal death.	N.D. Mylniczenko (pers. exp.)
Carcharhinus acronotus	Blacknose shark	Medetomidine + ketamine	59.2–70.4 µg/kg + 2.8 mg/kg	IM		0.0.3	Juvenile	25.5	Mild to heavy sedation	M.A. Stamper (pers. exp.)
Carcharhinus albimarginatus	Silvertip shark	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM						Penning et al. (2017)
Carcharhinus brevipinna	Spinner shark	Medetomidine + butorphanol	0.1 mg/kg + 0.065 mg/kg	IM		0.0.5			Good, one later died (kidney)	Penning (2012)
Carcharhinus falciformis	Silky shark	MS-222 (Tricaine methanesulfonate)	100 mg/L	Immersion	9.5				Fair	N.D. Mylniczenko (pers. exp.)
Carcharhinus leucas	Bull shark	Medetomidine	0.1 mg/kg	IM		0.0.2	Adult		Excellent	Penning (2012)
Carcharhinus leucas	Bull shark	Medetomidine	200 µg/kg	IM	3.85		Subadult-adult	25	Stopped swimming, apnea, did not recover	M. Yanagisawa (pers. comm.)
Carcharhinus leucas	Bull shark	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM						Penning et al. (2017)
Carcharhinus leucas	Bull shark	Medetomidine + ketamine		IM		0.0.2			Poor	Penning (2012)
Carcharhinus leucas	Bull shark	Medetomidine + ketamine	100 µg/kg + 5 mg/kg	IM	4.0		1 year	25	Slow swimming, recovered but died the subsequent day	M. Yanagisawa (pers. comm.)
Carcharhinus leucas	Bull shark	Medetomidine + ketamine	150 µg/kg + 7.5 mg/kg	IM	3.9		1 year	25	Slow swimming, recovered but died the subsequent day	M. Yanagisawa (pers. comm.)
Carcharhinus leucas	Bull shark	Medetomidine + ketamine	200 µg/kg + 10 mg/kg	IM	–		1 year	25	Stopped swimming, apnea, did not recover	M. Yanagisawa (pers. comm.)
Carcharhinus limbatus	Blacktip shark	Alfaxalone-alphadolone (Saffan)	0.4 mL/kg	IM	21	0.0.1			Deepest state within 1 hour, partial loss of equilibrium, settling or rising to surface, allowed netting but still responsive to touch	Harvey et al. (1988)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Carcharhinus melanopterus	Blacktip reef shark	Eugenol (AquiS-20E)	30 mg/L =>70 mg/L MS222	Immersion	21.5	0.1.0	Adult	25	Good induction, good maintenance for endoscopic examination	N.D. Mylniczenko (pers. exp.)
Carcharhinus melanopterus	Blacktip reef shark	Midazolam hydrochloride	0.05–0.1 mg/kg	IM					Used as a premedication administered immediately after netting appeared to decrease stress or hyperexcitability during induction	N.D. Mylniczenko (pers. exp.)
Carcharhinus melanopterus	Blacktip reef shark	MS-222 (Tricaine methanesulfonate)	125 mg/L => 100–50 mg/L	Immersion		15.3.0		24–25.7	Induction -> maintenance dose. High dose induction around transport, then switched to manageable transport for examination to the low dose. Usually 100 to 50 mg/L	Naples et al. (2012)
Carcharhinus melanopterus	Blacktip reef shark	Propofol	2.5 mg/kg	IV	22.6	0.0.1	Adult		Pregnant; good plane at 4 minutes; 50 minutes swimming	Clauss & Hatcher (pers. comm.)
Carcharhinus melanopterus	Blacktip reef shark	Propofol	3 mg/kg	IV dorsal sinus	17.5	0.0.1	Adult		<1 minute initial effect; 40–60 minutes recovery; uteroscopy	Clauss & Hatcher (pers. comm.)
Carcharhinus plumbeus	Sandbar shark (brown)	Atipamezole	0.4 mg/kg	IM	30–70	0.3.0				C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	Atipamezole	33, 36 mg/kg						12–30 minutes recovery	Lécu et al. (2017)
Carcharhinus plumbeus	Sandbar shark (brown)	Atipamezole + naltrexone	0.6 mg/kg + 0.15 mg/kg	IM	30–70	0.3.0				C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	Dexmedetomidine + ketamine	0.03 mg/kg + 2 mg/kg	IM		0.1.0	3 years		Added saline to make 1 mL; mass removal	Boylan (pers. comm.)
Carcharhinus plumbeus	Sandbar shark (brown)	Dexmedetomidine + ketamine + midazolam	0.036 mg/kg + 7 mg/kg+ 0.5 mg/kg	IM	21				Able to swim animal into a net	Boylan (pers. comm.)
Carcharhinus plumbeus	Sandbar shark (brown)	Diazepam	1.2–1.6mg/kg	PO		0.0.1			Followed by MS222 staged anesthesia	N.D. Mylniczenko (pers. exp.)

Carcharhinus plumbeus	Sandbar shark (brown)	Etomidate	40 mg + 40 mg 15 min later	IM	~45	1.0.0	Adult	23–27	Procedure for diagnostics; induced TI at 29 minutes	Lécu et al. (2011)
Carcharhinus plumbeus	Sandbar shark (brown)	Eugenol	30 mg/L	Immersion	40	0.0.1		27	Induction 14 minutes, stage 3 anesthesia. Prolonged recovery 240 minutes.	Lécu et al. (2017)
Carcharhinus plumbeus	Sandbar shark (brown)	Eugenol (AquiS-20E)	10 mg/L	Immersion	30–70	0.3.0	Adult	25	Used at a low dose to transport animal short distance (<30 minutes), animal had periodic episodes of sitting on bottom	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	Eugenol (AquiS-20E) => MS-222	10 mg/L => 60 mg/L	Immersion	70.00	0.1.0	Adult	25	Low dose for transport ~30 minutes, then examination in MS-222, quick recovery	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	Eugenol 99%	30 mg/L	Immersion	40	1.0.0	Adult	23–27	Added with ethanol (1:8 ratio), Hook removal; stage II at 5 minutes, stage III at 10 minutes	Lécu et al. (2011)
Carcharhinus plumbeus	Sandbar shark (brown)	Ketamine + medetomidine	(2.76–4 mg/kg) + (25.4–34.5 µg/kg)	IM	12.4–15.7	4.1.0			One animal died 3 weeks after sedation suspected related to presedation muscle exertion	Lécu et al. (2017)
Carcharhinus plumbeus	Sandbar shark (brown)	Ketamine + xylazine	(10–25 mg/kg) + 6 mg/kg	IM	45–80	2.2.3			Stage 1 - plane 1 anesthesia, additional doses required to maintain sedation	Lécu et al. (2017)
Carcharhinus plumbeus	Sandbar shark (brown)	Medetomidine + ketamine	80 µg/kg + 4.8–5.3 mg/kg	IM	30–70	0.3.0	Adult	25	One attempt: sedated but reactive, enough to restrain, second attempt partial sedation for manual restrained, third attempt required additional supplements for safe restraint	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	Medetomidine + ketamine + butorphanol	0.1 mg/kg + (4.0–4.5 mg/kg) + (0.07–1.0 mg/kg)	IM	30–70	0.3.0	Adult	25	Only notes from one sedation: partial sedation to baffle into net for restraint for further immersion sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	Medetomidine + ketamine + midazolam => MS-222	mg/kg + mg/kg + 2.25 mg/kg => mg/L	IM => immersion		0.1.0	Adult	25	Fair induction to move into immersion for further sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Carcharhinus plumbeus	Sandbar shark (brown)	Midazolam hydrochloride	0.05–0.1 mg/kg	IM					Premedication administered immediately after netting as animals became larger and more difficult to handle to decrease stress during induction	N.D. Mylniczenko (pers. exp.)
Carcharhinus plumbeus	Sandbar shark (brown)	MS-222 (Tricaine methanesulfonate)	50–100 mg/L	Immersion	30–70	0.3.0	Adult	25	Dilute with long procedures	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharhinus plumbeus	Sandbar shark (brown)	MS-222 (Tricaine methanesulfonate)	125 mg/L -> 50–100 mg/L	Immersion				24–25.5	High dose induction a round transport, then switched to a manageable transport for examination to the low dose. Usually 100 to 50 mg/L.	N.D. Mylniczenko (pers. exp.)
Carcharhinus plumbeus	Sandbar shark (brown)	Etomidate	10 mg/L	Immersion					Induced stage II anesthesia in approximately 2–4 minutes	Stoskopf (1986)
Carcharhinus plumbeus	Sandbar shark (brown)	Metomidate hydrochloride	10 mg/L	Immersion		1	Adult		Induced stage II anesthesia in approximately 2–4 minutes; 20 mg/L reduced induction time but not deeper sedation	Stoskopf (1986)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Atipamezole	0.3–0.4 mg/kg	IM	70–121	1.1.0				C. Innis (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Atipamezole	120 mg/kg						1–4 minutes recovery	Lécu et al. (2017)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Atipamezole	5xs medetomidine dose	1/2 IV + 1/2 IM		0.0.4	Adult		Swam away 18 minutes after reversal, had no obvious post-immobilization sedation and resumed feeding within 24 hours of recovery	Snyder et al. (1998)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Atipamezole + doxapram	5xs medetomidine dose + 100 mg	IM + IV					Although both sharks resumed swimming, appeared to have incomplete reversal in that each remained sedated for several days and did not eat for 8–18 days following the immobilization	Snyder et al. (1998)

Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Atipamezole + naltrexone	0.5 mg/kg + 0.1 mg/kg	IM	70–120	2.2.0			C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Dexmedetomidine + ketamine => MS-222	0.03 mg/mL + 3 mg/L + 12.5 g/L	IM, spray to gills		1.0.0		Induction for transport, spray to gills when needed	J.M. Cavin & C. Innis (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Dexmedetomidine + ketamine => MS-222	0.05 mg/kg + 10 mg/kg => 90–70 mg/L	IM, immersion		1.0.0		Induction, maintenance; plan to reduce to 70 mg/L MS-222	J.M. Cavin & C. Innis (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Dexmedetomidine + ketamine => MS-222	0.03 mg/kg + 3.3mg/kg => 70–90 mg/L	IM, immersion		0.1.1		Rapid induction ~11 minutes, minute resp.; maintenance increased to 90 for one animal	J.M. Cavin & C. Innis (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Dexmedetomidine => MS-222	0.03 mg/kg => 50 mg/L	IM		0.1.1		Good sedation - removed from tank after 20 minutes => transport bin	J.M. Cavin & C. Innis (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Diazepam	0.1 mg/kg	IM			Adult	High individual variability. 20 minutes for induction to allow fin manipulation. If not sfficient sedation (after 30 minutes) 20% more drug was indicated. 5-hour duration.	McEwan (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Doxapram	100 mg	IV					Snyder et al. (1998)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Etomidate	1.2–1.6 mg/kg (high dose)	IM	76.5–87.5	1.2.0	Adult	More rapid and deeper level of sedation at the higher dosage, stage 2 - plane 2: slowed, came to a complete stop and did not struggle when handled. Sharks were caught immediately following administration of anesthetic.	Lécu et al. (2017)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Etomidate	0.38–0.53 mg/kg (low dose)	IM	52–77	2.2.0	Adult	Light sedation, stage 1 - plane 1. Sharks were caught immediately following administration of anesthetic.	Lécu et al. (2017)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Ketamine	10 mg/kg	IM	158.00					Tuttle (2008)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Ketamine + xylazine	15 mg/kg + 6 mg/kg	IM	200	0.2.0			For capture and transport, stage 1 - plane 1 anesthetic level, additional doses required to maintain sedation	Lécu et al. (2017)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine	0.1–0.16 mg/kg	IM	70–120	2.2.0	Adult	25	Mild to heavy sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine	0.1 mg/kg	IM		0.0.6			Good to excellent	Penning (2012)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine + butorphanol	0.1 mg/kg + 0.3 mg/kg	IM	160	1.0.0	Adult		4 minutes after injection, increased sedation. Able to guide shark for transport after 12 minutes. Sternal recumbency and ideal for transport in 20 minutes.	Larson (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine + butorphanol	0.1mg/kg + 1.0 mg/kg	IM		0.0.5			Excellent, one later died (kidney)	Penning (2012)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine + ketamine	50–100 μg/kg + 4.4–7.0 mg/kg	IM	70–120	2.2.0	Adult	25		C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine + ketamine	60.0–80.0 μg/kg + 5–10 mg/kg	IM		0.0.4	Adult	21–22	Smooth, deep narcosis within 4–18 minutes. Animals had scoliosis and lordosis; one animal was euthanized for medical reasons; not recovered.	Snyder et al. (1998)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Medetomidine + ketamine + butorphanol => MS-222	0.1 mg/kg + 5.2 mg/kg + 0.08 mg/kg => 25 mg/L	IM	70–120	2.2.0	Adult	25		C.M. Burns & N.D. Mylniczenko (Personal experience)

Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	MS-222 (Tricaine methanesulfonate)	50–80 mg/L	Immersion	70–120	3.2.0	Adult	25	Often higher dose for induction then diluting to maintanence	C.M. Burns & N.D. Mylniczenko (Personal experience)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	MS-222 (Tricaine methanesulfonate)	12.5 g/L	Spray to gills		1.0.0			Used at various times when needed	J.M. Cavin & C. Innis (pers. comm.)
Carcharias taurus	Sand tiger shark (grey nurse, ragged tooth)	Propofol	2.56–3.77 mg/kg	IV dorsal sinus	85–116.5		Adult		4–6 minutes adequate plane; 2–4 hours swimming	Clauss & Hatcher (pers. comm.)
Carcharinus obscurus	Dusky shark	Medetomidine	0.1 mg/kg	IM		0.0.6			Good, two later died	Penning (2012)
Carcharinus obscurus	Dusky shark	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM		0.0.2			Good	Penning (2012)
Cephaloscyllium ventriosum	Swellshark	MS-222 (Tricaine methanesulfonate)	100–125 mg/L=> 50 mg/L	Immersion		18		14	Induction high dose induction a round transport, then switched to a manageable transport for examination to the low dose. Usually 100 to 50 mg/L.	Naples et al. (2012)
Chiloscyllium plagiosum	Bamboo shark, whitespotted	Butorphanol	0.2 mg/kg	IV	1.6–3.0	0.2.0	Adult	25	0.2 mg/kg provided ~30 minutes of increased sedation during surgical/ invasive procedures in combination of MS-222 immersion	C.M. Burns & N.D. Mylniczenko (Personal experience)
Chiloscyllium plagiosum	Bamboo shark, whitespotted	Eugenol (AquiS-20E) => MS-222	30 mg/L => 55–65 mg/L	Immersion	2.5	0.1.0	Adult	25	AquiS-20e induction within 5 minutes then move to MS-222	C.M. Burns & N.D. Mylniczenko (Personal experience)
Chiloscyllium plagiosum	Bamboo shark, whitespotted	Medetomidine + ketamine	60 µg/kg + 3.0 mg/kg	IM						M.A. Stamper (pers. exp.)
Chiloscyllium punctatum	Bamboo shark, brownbanded	2-Phenoxyethanol (2PE)	200, 300–350, 400 mg/L	Immersion	2.3–3.9			26.1–26.9	Light sedation to deep narcosis, surgical anesthesia	M. Yanagisawa (pers. comm.)
Chiloscyllium punctatum	Bamboo shark, brownbanded	Butorphanol	0.2–0.5 mg/kg	IV	0.8–1.5	0.2.0	Subadult-adult	25	0.2 mg/kg provided ~30 minutes of increased sedation during surgical/ invasive procedures in combination of MS-222 immersion	C.M. Burns & N.D. Mylniczenko (Personal experience)
Chiloscyllium punctatum	Bamboo shark, brownbanded	Eugenol (AquiS-20E)	25 mg/L, 50–60 mg/L	Immersion	0.8–1.5	0.2.0	Subadult-adult	25	Sedation for treatments, increased dose for endoscopy	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Chiloscyllium punctatum	Bamboo shark, brownbanded	Eugenol (AquiS-20E) => MS-222	30–50 mg/L => 45–100 mg/L	Immersion	0.8–1.5	0.2.0	Subadult-adult	25	AquiS-20e induction within 5 minutes then move to MS-222	C.M. Burns & N.D. Mylniczenko (Personal experience)
Chiloscyllium punctatum	Bamboo shark, brownbanded	Medetomidine + ketamine	(100–400 μg/kg) + (5–20 mg/kg)	IM	2.3–5.0			20–26.7	Varying doses provided increasesd anesthetic plane	M. Yanagisawa (pers. comm.)
Chiloscyllium punctatum	Bamboo shark, brownbanded	Medetomidine + midazolam hydrochloride + butorphanol	0.1 mg/kg + 1 mg/kg + 1 mg/kg	IM + IV		0.0.4	Adult		No response from IM doses, IV dosages produced light sedation that allowed handling and minor procedures (transponder, blood draws, pin prick to evaluate)	N.D. Mylniczenko (pers. exp.)
Chiloscyllium punctatum	Bamboo shark, brownbanded	Propofol	2.5, 4.0, 5.0 mg/kg	IV	4.86 -5.1			22.0–25.0	2.5–4.0 mg/kg provided adequate stages of anesthesia, 5.0 mg/kg animal became apneic	M. Yanagisawa (pers. comm.)
Chiloscyllium punctatum	Bamboo shark, brownbanded	Propofol + fentanyl citrate	(2.0–2.5 mg/kg) + (1.5–5.0 μg/kg)	IV	3.6–4			21–29	Provided apporiate levels of anesthesia	M. Yanagisawa (pers. comm.)
Chiloscyllium spp.	Bamboo shark sp.	2-Phenoxyethanol (2PE)	0.02 mL/L	Immersion		0.0.1			Sedated for radiographs	Larson (pers. comm.)
Chiloscyllium spp.	Bamboo shark sp.	MS-222 (Tricaine methanesulfonate)	50–100 mg/L	Immersion	0.17–3.0	1.7.0	Juvenile-adult	25		C.M. Burns & N.D. Mylniczenko (Personal experience)
Chiloscyllium spp.	Bamboo shark sp.	Tiletamine + zolazepam (Telazol)	5, 10, 15, and 20 mg/kg	IV, IM		0.0.8			Increased the duration of apnea with increased dosages. 15 mg/kg provided complete immobilization within 15 minutes lasting up to an hour with the least amount respiratory depression.	Adams & Krol (2015)

Dasyatidae spp.	Miscellaneous species	MS-222 (Tricaine methanesulfonate)	50–80 mg/L	Immersion	2.5–57	38.115.15	Subadult-adult	25–28	Average to good, typical dose around 60 mg/L	C.M. Burns & N.D. Mylniczenko (Personal experience)
Elasmobranchii	Miscellaneous species	2-Phenoxyethanol (2PE)	0.15 mL/L	Immersion					Suggested for group/tank sedation. Higher concentrations of 2-PE did not appear to have negative effects, but animals showed a more rapid and deeper sedation.	Vaughan et al. (2008); Penning (2012); Penning et al. (2017)
Elasmobranchii	Miscellaneous species	Atipamezole	5:1 ratio of atipamezole: medetomidine	IV						Lécu et al. (2017)
Elasmobranchii	Tiger shark	Atipamezole + naltrexone	0.5 mg/kg + 10 mg/kg	IM					Animals were typically left alone to recover. After 10–20 minutes, the elasmobranch was generally able to move, breathe and swim unaided.	Penning et al. (2017)
Elasmobranchii	Miscellaneous species	Eugenol	2–5 mg/L	Immersion					Used for mild sedation of elasmobranches during transport	Lécu et al. (2017)
Elasmobranchii	Miscellaneous species	Eugenol	20–40 mg/L	Immersion						Lécu et al. (2017)
Elasmobranchii	Miscellaneous species	Naltrexone	0.14–1.3 mg/kg	IV					Reversal	Clauss & Hatcher (pers. comm.)
Galeocerdo cuvier	Tiger shark	Medetomidine	0.1 mg/kg	IM		0.0.1			Excellent	Penning (2012)
Galeocerdo cuvier	Tiger shark	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM						Penning et al. (2017)
Galeocerdo cuvier	Tiger shark	Medetomidine + ketamine	100 µg/kg + 5 mg/kg	IM	250	0.0.1	Adult		15–20 minutes for induction; able to guide into PVC sock in 1 hour	Penning (2012)
Ginglymostoma cirratum	Nurse shark	Dexmedetomidine + ketamine => MS-222	0.05 mg/kg + ~9 mg/kg => 90 mg/L	IM		0.1.0			Induction, maintenance	J.M. Cavin & C. Innis (pers. comm.)
Ginglymostoma cirratum	Nurse shark	Dexmedetomidine + MS-222	0.03 mg/kg + 20 g/L	IM		0.1.0			Induction; minimal sedation after 30 minutes; 20 minutes of spraying gills in tank before sedation	J.M. Cavin & C. Innis (pers. comm.)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Ginglymostoma cirratum	Nurse shark	Medetomidine + ketamine	70–100 µg/kg + 8–10 mg/kg	IM		15	Adult		Poor to mild sedation; often ketamine was repeated at 5 mg/kg doses and medetomidine at 30 µg/kg	Kilbourn (pers. comm.)
Ginglymostoma cirratum	Nurse shark	Medetomidine + ketamine	75 µg/kg + 7.5 mg/kg	IM	20		Juvenile		No comments available	Mulican (pers. comm.)
Ginglymostoma cirratum	Nurse shark	Medetomidine + ketamine	90 µg/kg + 9.0 mg/kg	IM	68		Adult			M.T. Walsh (pers. comm.)
Ginglymostoma cirratum	Nurse shark	MS-222 (Tricaine methanesulfonate)	20 g/L	Spray to gills		0.1.0			5 minutes of spraying in stretcher	J.M. Cavin & C. Innis (pers. comm.)
Ginglymostoma cirratum	Nurse shark	Quinoline salts	0.075–0.1 mM	Immersion	4.0/21.0/4.5	1.2.0			Blood levels reached fairly constant value within 15 minutes	Brown et al. (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	10 mg/L	ICe	2–10				1 hour slowed activity, gilling, rights and swims	Walker (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	40 mg/L	ICe	2–10				25 minutes to anesthesia, gilling; 50 minutes loss of gilling; 7 hours return of gilling; 30 hours rights; 42 hours slowed activity	Walker (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	20 mg/L	IM	2–10				5 minutes slowed activity; 20 minutes weak gilling and swimming	Walker (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	40 mg/L	IM	2–10				2 minutes to anesthesia, weak gilling; 2 hours return of gilling; 24 hours rights and swims	Walker (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	60 mg/L	IP	2–10				3 minutes to anesthesia, gilling lost; 42 hours weak gilling; 54 hours rights and swims slowly	Walker (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	10 mg/L	IV	2–10				1 minute to anesthesia loss of gilling; 20 minutes return of gilling; 3 hour weakly rights	Walker (1972)
Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	20 mg/L	IV	2–10				1 minute to anesthesia loss of gilling; 3 hours return of gilling; 5 hours weakly rights	Walker (1972)

Ginglymostoma cirratum	Nurse shark	Sodium pentobarbital	60 mg/L	IV	2–10				Died	Walker (1972)
Hemiscyllium ocellatum	Epaulette shark	Tiletamine + zolazepam (Telazol)	20 mg/kg	IM		U	Adult		Allowed some manipulation (rolling over) but could not perform invasive procedures	Kilbourn (pers. comm.)
Hemiscyllium spp.	Carpet shark spp.	MS-222 (Tricaine methanesulfonate)	60–80 mg/L	Immersion	0.01–1.3	3.0.0	Juvenile-adult	25	Adequate sedation/anesthesia	C.M. Burns & N.D. Mylniczenko (Personal experience)
Heterodontus franscisci	Horn shark	MS-222 (Tricaine methanesulfonate)	125 mg/L => 100 mg/L	Immersion		1.1.1			Induction => maintenance	Naples et al. (2012)
Heterodontus portusjascksoni	Port Jackson shark	MS-222 (Tricaine methanesulfonate)	60–75 mg/L	Immersion	0.4–2.0	1.1.0	Juvenile-adult	25	Good anesthesia	C.M. Burns & N.D. Mylniczenko (Personal experience)
Himantura granulata	Whipray, mangrove	MS-222 (Tricaine methanesulfonate)	125 mg/L	Immersion		2.2.0				N.D. Mylniczenko (pers. exp.)
Himantura spp.	Miscellaneous species	MS-222 (Tricaine methanesulfonate)	50–75 mg/L	Immersion		0.0.6		25	Surgical anesthesia	C.M. Burns & N.D. Mylniczenko (Personal experience)
Himantura uarnak	Honeycomb stingray (reticulate whipray, leopard)	Eugenol (AquiS-20E)	15 mg/L	Immersion		0.0.2		25	Provided mild sedation for 30 minutes	C.M. Burns & N.D. Mylniczenko (Personal experience)
Hydrolagus colliei	Ratfish, spotted	MS-222 (Tricaine methanesulfonate)	125 mg/L => 100 mg/L	Immersion		2.2.0			Induction => maintenance	N.D. Mylniczenko (pers. exp.)
Hypanus americanus	Southern stingray	Atipamazole + flumazenil + naltrexone	(0.2–0.26 mg/kg) + 0.1 mg/kg + (0.2–0.3 mg/kg)	IV		0.5.0	Adult		Appeared to reduce sedative effects	Neiffer (Personal experience)
Hypanus americanus	Southern stingray	Atipamazole, atipamazole + flumazenil	0.42 mg/kg => 0.42 mg/kg + 0.1 mg/kg	IM, IV		0.1.0	Adult		Reversal with atipamazole IM, additional reversals supplemented IV 1 hour later	Neiffer (Personal experience)
Hypanus americanus	Southern stingray	Butorphanol	1.0 mg/kg	IV		0.1.0	Adult	25	Give IV during surgery, good effects	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Hypanus americanus	Southern stingray	Eugenol (AquiS-20E)	10–18 mg/L	Immersion		6.0.0	Subadult-adult	25–28	Adults can be maintained for extended period on 12–15 mg/L	C.M. Burns & N.D. Mylniczenko (Personal experience)
Hypanus americanus	Southern stingray	Guaifenisin	10–40 mg/kg	IV	20–25	0.5.0	Adult		Initial induction with MS222, then increased sedation with increasing dosage of guaifenisin to stage 2; notable period of asystole at onset of injection with rapid return to normal rhythm	Rosenberg et al. (2013)
Hypanus americanus	Southern stingray	Medetomidine + midazolam hydrochloride + butorphanol	0.05 mg/kg + 0.4 mg/kg + 0.4 mg/kg	IV		0.5.0	Adult		20 minute induction, highly variable responses	Neiffer et al. (2009)
Hypanus sabinus	Atlantic stingray	MS-222 + propofol	100 mg/L + 1.0 mg/L	Immersion		0.0.6		21–24	Surgical plane of anesthesia	M. Levendosky (2020)
Mobula hypostoma	Mobula (lesser devil ray)	AquiS-20E + midazolam	10 mg/L + 0.25 mg/kg	Immersion		0.1.0	Adult	25	Light anesthesia. Reversed flumazenil.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Mobula hypostoma	Mobula (lesser devil ray)	Butorphanol	0.2–0.6 mg/L	IV		0.1.0	Adult	25	Good response q20 minutes for coelomic surgery	C.M. Burns & N.D. Mylniczenko (Personal experience)
Mobula hypostoma	Mobula (lesser devil ray)	Eugenol (AquiS-20E)	10–19 mg/L	Immersion		0.4.0	Adult	25	Up to 19 mg/L with dilution over time	C.M. Burns & N.D. Mylniczenko (Personal experience)
Mobula hypostoma	Mobula (lesser devil ray)	Eugenol (AquiS-20E) => MS-222	15 => 60 mg/L	Immersion		0.4.0	Adult	25	Induction => maintenance, better recovery	C.M. Burns & N.D. Mylniczenko (Personal experience)
Mobula hypostoma	Mobula (lesser devil ray)	Flumazenil	0.025 mg/kg	IM					Seemingly appropriate dose	C.M. Burns & N.D. Mylniczenko (Personal experience)

Mobula hypostoma	Mobula (lesser devil ray)	MS-222 (Tricaine methanesulfonate)	50–125 mg/L	Immersion		2.4.0	Adult	25	Induced stage II anesthesia in approximately 2–4 minutes; 20 mg/L reduced induction time but not reliable depth of sedation. Rapid recovery.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Mustelus californicus	Smoothhound, gray	Eugenol (AquiS-20E)	35–55 mg/L	Immersion		0.0.3		20.1 ± 1.36	Anesthetic induction time twice as long and recovery time approximately three times as long as finfish species. Elasmobranch species exhibited a prolonged induction, with more of an excitement phase. One animal aborted pups at 24 hours.	Silbernagel & Yochem (2016)
Nebrius ferrugineus	Tawny nurse shark	Midazolam hydrochloride + propofol	0.75 mg/kg + 1.0 mg/kg	IM + IV					Stage 2, plane 2	M. Yanagisawa (pers. comm.)
Nebrius ferrugineus	Tawny nurse shark	Propofol	1.0–1.5 mg/kg	IV	7.25–10.8			28.6	Stage 2, plane 2 - stage 3, plane 1	M. Yanagisawa (pers. comm.)
Negaprion brevirostris	Lemon shark	Medetomidine + ketamine	90 µg/kg + 4.5 mg/kg	IM			Adult	26	Both animals blanched after drug adminstration; noted leakage from injection sites, undetermined amount, became recombant after handling	M.T. Walsh (pers. comm.)
Negaprion brevirostris	Lemon shark	Quinoline salts	0.075–0.15 mM	Immersion	5.7–7.0	4.1.0	Juvenile	26.5	Blood levels reached fairly constant value within 15 minutes, quickly produced anesthesia; drug enters brain rapidly	Brown et al. (1972)
Notorynchus cepedianus	Sevengill shark, broadnose	Ketamine	80 mg/kg	IM	29	1			5 minutes to first effects, then 45 minutes to slow swimming, 60 minutes easily caught in net and then moved to net	Vogelnest et al. (1994)
Orectobus maculatus	Spotted wobbegong	Eugenol	30 mg/L	Immersion	7.0–9.0	0.0.2		24.2–26.0	Good sedation	Lécu et al. (2017)
Orectolobus japonicus	Wobbegong, Japanese	MS-222 (Tricaine methanesulfonate)	125 mg/L => 100 mg/L	Immersion		0.0.3			Induction => maintenance	Naples et al. (2012)
Orectolobus japonicus	Wobbegong, Japanese	Propofol	2.2 mg/kg	IV		0.0.1			Spontaneous gill movement ceased at 3 minutes, returned at 55 minutes. Spontaneous movement at 148 minutes, full recovery at 153 minutes.	Larson (pers. comm.)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Pastinachus sephen	Cowtail stingray	MS-222 (Tricaine methanesulfonate)	65–75 mg/L	Immersion	0.53–0.67	1.0.0	Adult	25	Good sedation, diluted when necessary to improve anesthetic plane	C.M. Burns & N.D. Mylniczenko (Personal experience)
Potamotrygon motoro	Freshwater stingray	Ketamine	50 mg/kg	PO	0.093–0.1	4		(75–78 F)	Stage 2 at 10 minutes: loss of equilibrium, very slow swimming, decreased opercular movement, loss of muscle tone	Raines & Clancy (2009)
Potamotrygon motoro,	Freshwater stingray	Ketamine	20, 50 mg/kg	Oral	93–100 g	6		75–78 F	Induced a hypnotic sedation (stage 2) at 30 minutes	Raines & Clancy (2009)
Potamotrygon spp.	Freshwater stingray	Alfaxalone => MS222	0.11 mL/L	Immersion	39.5–103.6 g	0.0.8	Juvenile		Rapid induction (2 minutes) for MS-222 and 2.5 minutes for alfaxalone. Surgical anesthesia. Recovery 12 minutes for MS-222 and 24 minutes for alfaxalone.	Beckman et al. (2016)
Potamotrygon spp.	Freshwater stingray	MS-222 (Tricaine methanesulfonate)	125 mg/L	Immersion		4.2.0			Good sedation - removed from tank after 20 minutes => transport bin	N.D. Mylniczenko (pers. exp.)
Potamotrygon spp.	Freshwater stingray	MS-222 => alfaxalone	Not stated	Immersion	39.5–103.6 g	0.0.8	Juvenile		Rapid induction (2 minutes) for MS-222 and 2.5 minutes for alfaxalone. Surgical anesthesia. Recovery 12 minutes for MS-222 and 24 minutes for alfaxalone.	Beckman et al. (2016)
Potamotrygon wallacei (novel sp.)	Freshwater stingray	EOLA (*Lippia alba,* essential oil)	150, 175, 200 and 225 mg/L	Immersion	109.5 ± 30.7 g	0.0.48		26.01 ± 0.5	Recommendation over eugenol 200 mg/L EOLA (this was 'homemade' cultivated from plants at university)	de Lima (2021)
Potamotrygon wallacei (novel sp.)	Freshwater stingray	Eugenol oil	75, 100, 125 and 150 mg/L	Immersion	109.5 ± 30.7 g	0.0.48		26.01 ± 0.5	Highest concentration caused moderate to severe histological changes in the gills	de Lima (2021)

Pristis microdon	Sawfish, largetooth	2-Phenoxyethanol (2PE)	0.1–0.17 mL/L	Immersion		0.0.6			0.1 ml/L not adequate for transport; 0.145 ml/L markedly sedate, full recovery 90 minutes later	Larson (pers. comm.)
Pristis microdon	Sawfish, largetooth	Eugenol	20–30 mg/L	Immersion	11	0.0.1		24.5	Good sedation	Lécu et al. (2017)
Pristis microdon	Sawfish, largetooth	Propofol	2.0–3.0 mg/kg	IV dorsal sinus	64.7–112.5	0.0.6	Adult		2–8 minutes initial effect; 45–63 minutes full recovery; good for animal moves, examination, debridement of wounds	Clauss & Hatcher (pers. comm.)
Pristis zijsron	Sawfish, longcomb	Diazepam	0.4 mg/kg	PO					Premedication 1 hour prior to any attempted handling because the animal was considered dangerous to handlers	N.D. Mylniczenko (pers. exp.)
Pristis zijsron	Sawfish, longcomb	MS-222 (Tricaine methanesulfonate)	125 mg/L => 100 mg/L	Immersion		0.1.0			Induction => maintenance	N.D. Mylniczenko (pers. exp.)
Raja binoculata	Skate, big	Alfaxalone-alphadolone (Saffan)	0.25 mL/kg	IM	50	0.0.1			Deepest state within 1 hour: partial loss of equilibrium, settling or rising to surface, allowed netting but still responsive to touch	Harvey et al. (1988)
Raja erinacea	Skate, little	2-Phenoxyethanol (2PE)	0.11 mL/L	Immersion		0.0.1			Deep sedation for minor surgical procedure. Excellent sedation, fast recovery.	Larson (pers. comm.)
Rhina ancylostoma	Guitarfish, bowmouth (sharkray, mudskate)	Eugenol	30 mg/L	Immersion	17	0.0.1		24.6	Good sedation	Lécu et al. (2017)
Rhina ancylostoma	Guitarfish, bowmouth (sharkray, mudskate)	Eugenol (AquiS-20E)	15–30 mg/L	Immersion	48	1.1.0	Subadult-adult	25	Did not become sedate enough until 30 mg/L, recovery in 15 minutes	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhina ancylostoma	Guitarfish, bowmouth (sharkray, mudskate)	MS-222 (Tricaine methanesulfonate)	100–125 mg/L, 65–75 mg/L	Immersion	24–76	2.2.0	Juvenile-adult	25	Induction dose 125 mg/L, with maintenance dose of 65 mg/L. Recovery time ~30 minutes.	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Rhina ancylostoma	Guitarfish, bowmouth (sharkray, mudskate)	Propofol	2.22 mg/kg	IV		0.0.1			No comments	Larson (pers. comm.)
Rhincodon typus	Whale shark	Midazolam hydrochloride	3.0 mg/kg	IM	1500			29.9	Stage 2, plane 2 (animal in poor condition)	M. Yanagisawa (pers. comm.)
Rhincodon typus	Whale shark	Midazolam hydrochloride + propofol	6.0 mg/kg + 1.5 mg/kg	IM + IV	1300			28.9	Midazolam = slow swimming; propofol = stopped swimming. Stage 3, planes 2–4	M. Yanagisawa (pers. comm.)
Rhinobatos cemiculus	Guitarfish, blackchin	Eugenol	35 mg/L	Immersion	20–21	0.0.4		25–26	Good sedation	Lécu et al. (2017)
Rhinobatus lentiginosus	Guitarfish, Atlantic	Butorphanol	0.2, 0.6 mg/kg	IV		1.1.0	Adult	25	Used in conjunction with immersion anesthesia for a better surgical plane during more invasive procedures (0.2 mg/kg given q30 minutes, 0.6 mg/kg given once)	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinobatus lentiginosus	Guitarfish, Atlantic	Eugenol (AquiS-20E)	30 mg/L	Immersion		1.1.0	Adult	25	Good sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinobatus lentiginosus	Guitarfish, Atlantic	Eugenol (AquiS-20E) => MS-222	25–30 mg/L -> 50–60 mg/L	Immersion		1.1.0	Adult	25	Induction in AquiS20e, maintenance in MS222. Fin movement still occurs but animals were in a surgical plane of anesthesia.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinobatus lentiginosus	Guitarfish, Atlantic	MS-222 (Tricaine methanesulfonate)	60–80 mg/L	Immersion		1.1.0	Adult	25	Blood pH levels tend to decrease on MS222 alone	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinobatus typus	Guitarfish, giant shovelnose	Eugenol (AquiS-20E)	15–17 mg/L	Immersion		2.0.0	Juvenile-subadult	25	Mild sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)

Rhinobatus typus	Guitarfish, giant shovelnose	MS-222 (Tricaine methanesulfonate)	60–70 mg/L	Immersion		2.2.0	Adult	25	Mild to heavy sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinoptera bonasus	Cownose stingray	2-Phenoxyethanol (2PE)	0.2 mL/L	Immersion		0.0.2			Sedated for ultrasound	Larson (pers. comm.)
Rhinoptera bonasus	Cownose stingray	Butorphanol	0.2–1.0 mg/kg	IV		1.2.0	Adult	25	Supplemental dosing IV during surgical procedures, allows reduction of general anesthesia	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinoptera bonasus	Cownose stingray	Eugenol	25–75 mg/L in 50% ethanol	Immersion			Adult		Deep sedation not achieved at 25 mg/l. Recovery longer than with MS-222.	Grusha (2005)
Rhinoptera bonasus	Cownose stingray	Eugenol (AquiS-20E)	50–80 mg/L	Immersion	2–26		Juvenile-adult	25	Rapid induction for short procedures. Can be a "high" dose induction before placing in MS-222. Doses of 15–17 mg/L >30 minutes have prolonged induction and recovery.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhinoptera bonasus	Cownose stingray	MS-222 (Tricaine methanesulfonate)	50–150 mg/L	Immersion	2–26	0.0.38	Juvenile-adult	25	For short procedures, such as a barb trim or blood collection, can tolerate a dosage up to 125 mg/L. For longer procedures start with 150 mg/dL of MS-222 and move to 50–70 mg/L.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Rhynchobatus djiddensis	Guitarfish, giant	Medetomidine + butorphanol	0.1 mg/kg + 1.0 mg/kg	IM						Penning et al. (2017)
Sphyrna lewini	Hammerhead, scalloped	Etomidate + medetomidine	0.79 mg/kg + 1.3 µg/kg	IV	7.8	0.1.0			Quick recovery. Effects were short-lived.	Lécu et al. (2017)
Sphyrna lewini	Hammerhead, scalloped	Etomidate + medetomidine	1.3 mg/kg + 50 µg/kg	IM, IV	4	0.1.0			Rapid sedation with both IM and IV. Effects were short-lived.	Lécu et al. (2017)
Sphyrna lewini	Hammerhead, scalloped	Eugenol (AquiS-20E)	10 mg/L	Immersion	2.8–22	0.4.0	Juvenile	25	Used for transport (<30 minutes) with mild overt sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Sphyrna lewini	Hammerhead, scalloped	Eugenol (AquiS-20E)	55–75mg/L	Immersion		0.4.0		25	Recommend dilution after 15 minutes to a low dose 10 mg/L or switch to MS222. Excellent for induction and reduction of secondary stressors.	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna lewini	Hammerhead, scalloped	Eugenol (AquiS-20E) => MS-222	55–95 mg/L => 50–70 mg/L	Immersion	2.8–8.4	0.4.0	Juvenile	25	Good sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna lewini	Hammerhead, scalloped	MS-222 (Tricaine methanesulfonate)	150 mg/L => 40–65 mg/L	Immersion	2.8–8.3	0.4.0	Juvenile	25	At high dose of 150 mg/L animals very reactive, even lower doses result in significant excitatory phase; switch to eugenol for induction and then MS222 50–65 mg/L	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna tiburo	Bonnethead shark (shovelhead)	Eugenol (AquiS-20E)	100 mg/L	Immersion	0.5	0.0.3	Juvenile	25	Used for quick treatments <10 minutes (assist feeding, injections, etc.)	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna tiburo	Bonnethead shark (shovelhead)	Eugenol (AquiS-20E)	60 mg/L => 15 mg/L	Immersion	1.0–6.0	0.4.0	Adult	25	High dose, low dose recommended in this species	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna tiburo	Bonnethead shark (shovelhead)	Eugenol (AquiS-20E) => MS-222	50–60 mg/L -> 50–60 mg/L	Immersion	1.0–6.0	0.6.0	Adult	25	High dose, low dose recommended in this species	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna tiburo	Bonnethead shark (shovelhead)	MS-222 (Tricaine methanesulfonate)	100–125 mg/L -> 50–60 mg/L	Immersion	1.0–6.0	0.15.1	Adult	25	High dose, low dose recommended in this species; Aquis20E provided better induction	C.M. Burns & N.D. Mylniczenko (Personal experience)
Sphyrna tiburo	Bonnethead shark (shovelhead)	Propofol	4.0–5.0 mg/kg	IV dorsal sinus	1.4–4.65	4.9.0	Adult		1–3 minutes initial effect; 48–64 minutes swimming	Clauss & Hatcher (pers. comm.)

Squalus acanthias	Dogfish, spiny (spurdog)	Alfaxalone-alphadolone (Saffan)	0.3–0.5 mL/kg	IM	3/2	0.0.2			Deepest state within 1 hour: disorientation, slowing of swimming, bumping into tank walls, net avoidance	Harvey et al. (1988)
Squalus acanthias	Dogfish, spiny (spurdog)	Alfaxalone-alphadolone (Saffan)	1.5 mL/kg	IM	4	0.0.2			Deepest state within 1 hour: complete loss of equilibrium and cessation of swimming, no response to touch, marked depression of ventillation	Harvey et al. (1988)
Squalus acanthias	Dogfish, spiny (spurdog)	Azaperone	4 mg/kg	Spray to gills	1–5	10.11.0			Ideal for capture and confinement; still exhibit normal swimming	Latas (1987)
Squalus acanthias	Dogfish, spiny (spurdog)	Eugenol	120 mg/L	Immersion		0.0.1		9	Euthanasia: the lethal dose was triple concentration of eugenol to reach stage stage 4 anesthesia, cardiac arrest	Lécu et al. (2017)
Squalus acanthias	Dogfish, spiny (spurdog)	Hexobarbital	20 mg/kg	IV					Recovery of righting reflex - 3 hours	Adamson & Guarino (1972)
Squalus acanthias	Dogfish, spiny (spurdog)	Medetomidine + ketamine	200 µg/kg + 4 mg/kg	IM		0.0.15			Adequate for sedation, not for surgical anesthesia	Marancik et al. (2011)
Squalus acanthias	Dogfish, spiny (spurdog)	Metomidate hydrochloride	30 mg/kg	IM	3	0.0.1			Deepest state within 1 hour: disorientation, slowing of swimming, bumping into tank walls, net avoidance	Harvey et al. (1988)
Squalus acanthias	Dogfish, spiny (spurdog)	Propofol	5 mg/kg	IV		0.0.15			Good for surgical anesthesia	Marancik et al. (2011)
Squalus acanthias	Dogfish, spiny (spurdog)	Sodium pentobarbital	20 mg/kg	IV					Recovery of righting reflex - 6–8 hours	Adamson & Guarino (1972)
Squalus acanthias	Dogfish, spiny (spurdog)	Thiopental	20 mg/kg	IV					Recovery of righting reflex - 3 hours	Adamson & Guarino (1972)
Squatina californica	Angel shark	MS-222 (Tricaine methanesulfonate)	80–100 mg/L	Immersion				10–14	No comments	Ezcurra (pers. comm.)
Stegostoma tigrinum (fasciatum)	Zebra shark (sometimes leopard shark)	Midazolam hydrochloride + propofol	1.5 mg/kg + 1.0 mg/kg	IM + IV					Stage 2, plane 2	M. Yanagisawa (pers. comm.)
Stegostoma tigrinum (fasciatum)	Zebra shark (sometimes leopard shark)	MS-222 (Tricaine methanesulfonate)	50–80 mg/L	Immersion	3.0–7.6	1.1.0	Juvenile-adult	25	In this species some minimally invasive procedures can be performed without sedation using TI/stretcher	C.M. Burns & N.D. Mylniczenko (Personal experience)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Stegostoma tigrinum (fasciatum)	Zebra shark (sometimes leopard shark)	MS-222 (Tricaine methanesulfonate)	100–125 mg/L => 50–100 mg/L	Immersion		3.4.0			Induction => maintenance. High dose induction a round transport, then switched to a manageable transport for examination to the low dose. Usually 100 to 50 mg/L	Naples et al. (2012)
Taeniura lymma	Ribbontail stingray (bluespotted)	Butorphanol	0.2 mg/kg	IM						N.D. Mylniczenko (pers. exp.)
Taeniura meyeni	Round ribbontail stingray ray (blotched fantail ray)	Eugenol (AquiS-20E)	15–20 mg/L	Immersion	92	0.0.1	Adult	25	Mild sedation - light anesthesia, using AquiS-20E in this species did not show any benefit over MS-222	C.M. Burns & N.D. Mylniczenko (Personal experience)
Taeniura meyeni	Round ribbontail stingray ray (blotched fantail ray)	MS-222 (Tricaine methanesulfonate)	50–80 mg/L	Immersion	2–267	0.2.14	Newborn-adult	25	Younger rays need higher dose 65–80 mg/L, adults 50–65 mg/L	C.M. Burns & N.D. Mylniczenko (Personal experience)
Taeniura meyeni	Round ribbontail stingray ray (blotched fantail ray)	Propofol	3 mg/kg	IV	57		Adult		2 minutes initial effect; hook removal from esophagus; additional 1.5 mg/kg at 36 minutes due to movement; 88 minutes recovery	Clauss & Hatcher (pers. comm.)
Torpedo californica	Electric ray, Pacific	MS-222 (Tricaine methanesulfonate)	80–100 mg/L	Immersion	0.5			10–14	No comments	Ezcurra (pers. comm.)
Triaenodon obesus	Whitetip reef shark	Medetomidine + ketamine	90 μg/kg + 4.5 mg/kg	IM			Juvenile	27	Animal was abnormal; infection and scoliosis; stopped gilling unless touched	M.T. Walsh (pers. comm.)
Triaenodon obesus	Whitetip reef shark	MS-222 (Tricaine methanesulfonate)	100–125 mg/L => 50–100 mg/L	Immersion		0.0.7		24–25.6	High dose induction a round transport, then switched to a manageable transport for examination to the low dose. Usually 100 to 50 mg/L	Naples et al. (2012)

Triakis semifasciata	Leopard shark	Eugenol (AquiS-20E)	35–55 mg/L	Immersion		0.0.2		20.1 ± 1.36	Anesthetic induction time twice as long and recovery time approximately three times as long as finfish species. Elasmobranch species exhibited a prolonged induction, with more of an excitement phase. One animal aborted pups at 24 hours.	Silbernagel & Yochem (2016)
Triakis semifasciata	Leopard shark	Ketamine + xylazine	7, 15, 20 mg/kg + 3, 6, 10 mg/kg	IM	447.5 ± 1.2 g	2.6.0			No effects were seen at lower doses. Ketamine at 20 mg/kg and Xylazine at 10 mg/kg induced sedation within 5–9 minutes. Atipamezole was not used and recovery occurred at 10–18 minutes after sedation was induced.	Lécu et al. (2017)
Triakis semifasciata	Leopard shark	Midazolam hydrochloride	0.2 mg/kg	IM		2.0.0			No effect	C.M. Burns & N.D. Mylniczenko (Personal experience)
Triakis semifasciata	Leopard shark	MS-222 (Tricaine methanesulfonate)	45–100 mg/L	Immersion	4.6–9.0	4.4.0	Adult	25	Single anesthetic doses have been used up to 100 mg/L, however improved responses to anesthesia using high induction of 100 mg/L then titrating it down	C.M. Burns & N.D. Mylniczenko (Personal experience)
Triakis semifasciata	Leopard shark	MS-222 (Tricaine methanesulfonate)	100–125 mg/L => 50–100 mg/L	Immersion				14	High dose induction a round transport, then switched to a manageable transport for examination to the low dose. Usually 100 to 50mg/L	Naples et al. (2012)
Triakis semifasciata	Leopard shark	MS-222 (Tricaine methanesulfonate)	150 mg/L to 75 mg/L	Immersion				19	Comparative study with propofol 2.5 mg/L for I-stats/lactates	
Triakis semifasciata	Leopard shark	Propofol	2.5 mg/L	IV		0.0.1		18	2 minutes initial effect; hook removal from esophagus; additional 1.5 mg/kg at 36 minutes due to movement; 88 minutes recovery	
Triakis semifasciata	Leopard shark	Xylazine	6, 12, 18 mg/kg	IM	0.310–1.350	1.5.0			No anesthetic effect was noted at any dose	Lécu et al. (2017)

(*Continued*)

Table 7.1 (Continued)

Species	Common Name	Drug	Dose or Dosage	Route of Administration	Body Weight (kg, unless stated otherwise)	Sedations	Age Class	Water Temperature (°C)	Comments	Reference
Trygonorrhina fasciata	Fiddler ray, eastern	MS-222 (Tricaine methanesulfonate)	90 mg/L	Immersion					Blood and morphometrics	Clauss & Hatcher (pers. comm.)
Urobatis halleri	Haller's round stingray	MS-222 (Tricaine methanesulfonate)	60–70 mg/L	Immersion	0.3–1.2	0.0.2			Slightly light to good	N.D. Mylniczenko (pers. exp.)
Urobatis jamaicensis	Yellow stingray	Butorphanol	0.5 mg/kg	IV	2	1.0.0	Adult	25	IV during surgical procedure q30minutes	C.M. Burns & N.D. Mylniczenko (Personal experience)
Urobatis jamaicensis	Yellow stingray	Eugenol (AquiS-20E)	15 mg/L	Immersion	2	1.0.0	Adult	25	Good sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Urobatis jamaicensis	Yellow stingray	MS-222 (Tricaine methanesulfonate)	50–80 mg/L	Immersion	0.5–2.0	2.2.0	Subadult-adult	25	Good sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)
Urogymnus asperrimus	Procupine ray	Butorphanol	0.2–0.3 mg/L	IV	63	0.1.0	Adult	25	IV immediately when placed in anesthetic bath provided a better plane of anesthesia in 70 mg/L for 30 minutes without prolonged recovery	C.M. Burns & N.D. Mylniczenko (Personal experience)
Urogymnus asperrimus	Porcupine ray	MS-222 (Tricaine methanesulfonate)	70–90 mg/L	Immersion	23–63	0.1.0	Adult	25	Species induction can be erratic, high dose and dilution recommend or a longer wait for induction at lower doses	C.M. Burns & N.D. Mylniczenko (Personal experience)
Urotrygon chilensis	Chilean stingray (thorny or blotched roundray)	Eugenol (AquiS-20E)	15–30 mg/L	Immersion	0.08–0.60	0.3.0	Juvenile-adult	25	Mild to heavy sedation, at higher doses <10 minutes and then dilute	C.M. Burns & N.D. Mylniczenko (Personal experience)
Urotrygon chilensis	Chilean stingray (thorny or blotched roundray)	Eugenol (AquiS-20E) => MS-222	25–30 mg/L, 55 mg/L	Immersion	0.15–0.60	0.3.0	Adult	25	Heavy sedation	C.M. Burns & N.D. Mylniczenko (Personal experience)

Urotrygon chilensis	Chilean stingray (thorny or blotched roundray)	MS-222 (Tricaine methanesulfonate)	50–70 mg/L	Immersion	0.08–0.60	0.3.0	Juvenile-adult	25	Mild sedation to light anesthesia	C.M. Burns & N.D. Mylniczenko (Personal experience)
Zapteryx brevirostris	Guitarfish, lesser	Eugenol (K-Dent)	21.25, 42.5, 85, 170 mg/L	Immersion	541.16 ± 119.18 g	11.10.0	Adult	25 ± 2	K-Dent is a dental product; according to the author 21.25 mg/L never achieved an anesthetic rating of >2, caused prolonged hyperexcitability, 42.5 was ok for procedure but took longer for sedation, 85 was ideal and 170 mf/L was excessive with prolonged recovery	Takatsuka et al. (2018)
Mustelus henlei	Smoothhound, brown	Xylazine	40 mg/kg	IM		0.0.6			No anesthetic effect noted at 1, 2, 3, 24, and 48 hours	Lécu et al. (2017)

ICe, Intracoelomic; IM, intramuscular; IP, Intraperitoneal; IV, intravenous; PO, per os.

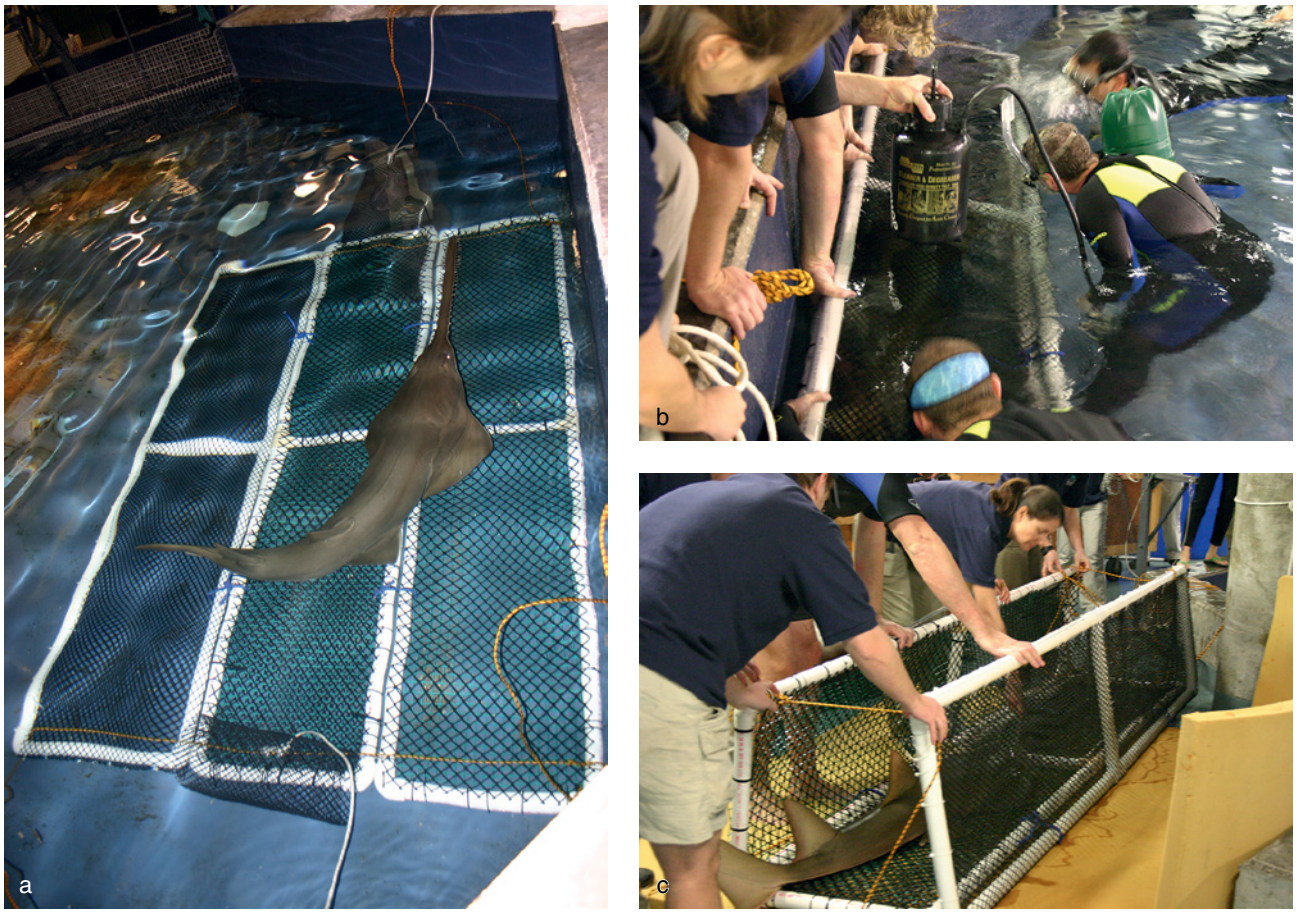


Figure 7.7 (a) Target training a green sawfish (*Pristis zijsron*) to swim over a foldable restraint device. (b) The same animal, within the folded restraint device, now in the shape of a prism with the animal's head at the far end of the photo. Divers are administering high-dose MS-222 over the gills of the animal through the device. (c) The same animal, fully anesthetized and pulled from the water, ready for examination.

(Dunn & Koester 1990). Some species of sharks have been anesthetized using a low concentration (50 mg/L) as a "preanesthetic" (sedative-type) dose followed by higher concentrations (≤85 mg/L) for maintenance anesthesia (Davis, pers. comm.). The "preanesthetic" concentration appears to reduce the excitement phase and lowers the maintenance level of MS-222. Conversely, the authors typically prefer high-dose induction (150 mg/L), especially in pelagic animals, with removal to a lower maintenance dose (50–75 mg/L). This regimen has resulted in rapid anesthesia, decreased excitement phase, better blood gas measurements, and better planes of anesthesia. Higher than 150 mg/L MS-222 will cause physical irritation to the patient.

Gilbert & Wood (1957) describe a field technique of bringing large lemon sharks (*Negaprion brevirostris*) up to the water surface with a hook and line and then applying a high concentration of MS-222 (1 g/L) with a pump handsprayer. Effects were noted within 15 seconds and the animals were anesthetized within 1 minute. It is recommended that the patient's head remain out of the water and only buffered MS-222 be applied to the gills if utilizing this technique.

MS-222 anesthesia is the preferred anesthetic for holocephalans. In the authors' experience, 80–110 mg/L buffered MS-222 provides excellent anesthesia and good recovery. There is one report of *Hydrolagus collier* being anesthetized at 0.1% MS-222 (1000 mg/L) for research purposes (Lovejoy et al. 1993).

Eugenol (Clove Oil and Aqui-S 20E™)

The active ingredient in clove oil is the phenolic compound eugenol. It is commercially available, inexpensive, and has a distinct odor of clove. Aqui-S™ (isoeugenol) is commercially produced by Aqui™ New Zealand Ltd and is not commercially available in the United States. Aqui-S 20E™ (10% eugenol) is available under an Investigation

New Animal Drug program with the Aquatic Animal Drug Approval Partnership (purchased through Aquatactics Fish Health, Kirkland, WA, USA). It is water dispersible, has a neutral pH, and reduces excitation/irritability in fish during induction. The authors favor this as an immersion drug for shorter procedures and for induction for longer procedures.

The use of eugenol and isoeugenol is useful in fractious elasmobranchs or those prone to acidemia, resulting in less frenzied swimming. Once induced, moving the patient to a low dose of MS-222 provides excellent balanced anesthesia. Disadvantages include longer induction times and if kept in it for periods greater than 15 minutes, longer recoveries. Doses used are available in Table 7.1.

Clove oil (25–50 mg/L) has been used to anesthetize epaulette sharks (*H. ocellatum*) and shovelnose rays (*Rhinobatus typus*) without complication (Grusha 2005). Controlled studies with cownose rays (*R. bonasus*) using eugenol (25, 50, and 75 mg/L) dissolved in 50% ethanol, as well as MS-222 (100 mg/L), showed similar effects for all treatment groups (Grusha 2005). The animals anesthetized with 25 mg/L eugenol, however, did not reach a plane of deep sedation. Recovery times were generally longer for the animals anesthetized with 50 and 75 mg/L eugenol compared with the rays anesthetized with MS-222. In a study with southern stingrays (*D. americana*), eugenol (20 mg/L), isoeugenol (15.7 mg/L), and MS-222 (55–65 mg/L) were compared. Minor variations were noted, but overall, all the agents provided adequate anesthesia for short-term immobilizations and minor procedures (Neiffer et al. 2009). MS-222 is considered a good induction agent as the excitatory phase is muted and induction is rapid. Once induced, moving the patient to a low dose of MS-222 provides excellent balanced anesthesia.

Disadvantages with eugenol/isoeugenol include dose-dependent longer induction times and longer recoveries if animals are maintained in it for periods greater than 15 minutes. Doses used are available in (Table 7.1). Lécu et al. (2011, 2017) used 20–40 mg/L in multiple species with good success. They also use 2–5 mg/L for transport. Since a high concentration of eugenol was used in their trials (99%) they diluted it in ethanol at 1:8 and vigorously shook the mixture for dispersal. In *Zapteryx brevirostris,* 85.0 mg/L was elected the best dose in a range from 21 to 170 mg/L) (Takatsuka et al. 2018).

2-Phenoxyethanol

2-phenoxyethanol (2-PE), a glycol ether, is a clear or straw-colored oily liquid. It has a faintly aromatic odor and is moderately water-soluble. 2-PE was used initially in aquaculture to treat ichthyophonus and other fungal, bacterial, and parasitic diseases. 2-PE has been widely used for sedation, particularly in fish transportation, as well as for general anesthesia (Ross 2001). One advantage is that it causes no pH change when added to seawater.

At uShaka Marine World in Durban, South Africa, 2-PE was mixed with dechlorinated seawater in plastic containers and poured directly into the water of two marine systems in an effort to translocate all of the teleost and elasmobranch fishes to new exhibits. Concentration increments of 0.05 mL/L were added every 30 minutes to the shark tank to a final concentration of 0.150 mL/L. Excitation events were recorded and the fishes were removed according to their effective induction to anesthesia based on loss of equilibrium. No excitation was noted in the eight sand tiger sharks (*C. taurus*), but excitation was noted at 0.100 mL/L in the two Zambezi sharks (*C. leucas*). Members of both species were guided into stretchers at the first signs of anesthesia to prevent physical injury due to collision with walls or viewing windows. Anesthesia at 0.150 mL/L lasted 70 minutes in both species. All sharks recovered well (Vaughan et al. 2008).

According to Oswald (1978), 2-PE may cause hypoventilation and it has poor analgesic properties. Sustained regular exposure can cause a neurophysiological syndrome in some individuals, thus staff handling 2-PE are advised to wear personal protective gear such as gloves and masks. Consequently, frequent use in elasmobranchs warrants caution as it is unknown if similar effects can occur. In the authors' experience, smaller sharks can be lightly sedated with an apparent wide safety margin for prolonged procedures (although doses are highly variable). However, for pelagic animals, induction length and quality of induction do not provide an advantage compared to other drugs already discussed. In general, at the doses tried, deep sedation is not achieved.

Metomidate and Etomidate

Etomidate and metomidate are GABA agonists and reportedly provide a more rapid induction and recovery than MS-222. Etomidate is more effective in alkaline water and higher water temperature, but is not affected by total hardness. In adult sandbar sharks (*C. plumbeus*), 10 mg/L of either drug induced stage II anesthesia in approximately 2–4 minutes. This stage was characterized by an absence of response to positional changes, decreased respiratory rate to approximately normal, total loss of equilibrium, no righting response, decreased muscle tone, some response to strong tactile and vibrational stimuli, and adequate restraint for external sampling (e.g., gill biopsy). Increasing

the dose to 20 mg/L reduced induction time to ≤1 minute, but anesthetic depth was more difficult to control.

Although etomidate is considerably more potent than metomidate in freshwater teleosts, this difference was not observed in sandbar sharks. Recovery from stage II plane 2 took approximately 3–5 minutes for metomidate. Recovery from deeper planes was considerably prolonged (>1 hour), speculated to be due to decreased cardiac output (Stoskopf 1986). Overall there were no advantages with immersion of either of these drugs when compared to other available water-miscible products.

Propofol

Immersion propofol has been tested in the Atlantic stingray (*H. sabinus*) and coral catshark (*A. marmoratus*) with 1 and 1.5 mg/L considered to provide surgical planes of anesthesia (Levendosky 2020).

Gas Anesthetics for Immersion Anesthesia

Halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) is an inhalation anesthetic typically used in air-breathing animals, including previous use in humans. Dunn & Koester (1990) used halothane (1.5% for induction, then 0.5–0.8% for maintenance) in nitrous oxide (100–200 mL/min) and oxygen (200–300 mL/min) for anesthesia of guitarfish (*Rhinobatas* sp.) and skates (*Raja* sp.). A precision vaporizer was used to add halothane to a mixture of nitrous oxide and oxygen that was then introduced into the water through an aerator. This combination provides easy control of anesthetic depth, shorter recovery, and a very high survival rate. A major disadvantage is contamination of the working environment room with halothane and nitrous oxide. Isoflurane (1-chloro-2,2,2-trifluoroethyl difluoromethyl ether) and sevoflurane (fluoromethyl 2,2,2-trifluoro-1-(trifluoromethyl) ethyl ether) can presumably be used in the same manner. The advantages and disadvantages of isoflurane and sevoflurane are similar to those noted for halothane and hence use of anesthetics requiring gas vaporizers is not common practice in aquatic medicine.

Gas Narcosis (Oxygen, Carbon Dioxide, Nitrogen)

Narcosis is defined as "a reversible state of arrested activity ... resulting from exposure to a xenobiotic", and narcosis and anesthesia are often used interchangeably. Most popularly, oxygen is used for "sedation" in aquaria, but its use is largely anecdotal with scant available references. As such, the border between oxygen narcosis and oxygen toxicity is not established for fish. Oxygen narcosis is used for transport or minor procedures. Hyperoxygenated (>100%, where *generally* 100% = 10 mg/dL, 120% = 11 g/dL, 140% = 13 mg/dL, etc. at 17°C; Kaill & Frey 1973) water is flushed across the gills via a power head or ventilation system. Reported signs of oxygen sedation or narcosis include decreased respiratory effort, behavioral changes including subdued activity, slower rate to recovery, and, in some cases, loss of equilibrium (Stamper, pers. exp.). Since the oxygen is not provided under pressure, supersaturation ("gas bubble disease") does not occur.

Prolonged exposure to elevated oxygen will depress ventilation and produce hypercapnia (likely the cause of narcosis) and potentially life-threatening acidemia (Spotte 1992). The use of oxygen narcosis for immobilization should therefore be limited in duration and monitoring of blood gas variables is recommended. Hyperoxygenation, even in short bursts, can also result in elevated plasma cortisol levels (Sundh et al. 2009). Chronic exposure in fish also increased the permeability of cell membranes and pathogen susceptibility (Sundh et al. 2009). Oxygen toxicity, when administration of oxygen levels exceeds biotransformation and clearance, can occur (Manning 2002). Consequently, the positive and negative aspects of hyperoxygenation must be considered in balance.

Other gasses can also cause narcosis. Carbon dioxide anesthesia is described in teleosts (Oberg et al. 2015) but not elasmobranchs. While CO_2 has some advantages (availability, inexpensive, no tissue residues) its capacity to be toxic, cause acidosis, and result in sudden death make it less ideal. Elevation of CO_2 (as with long procedures and transports) can cause sedation, although dosing and oxygen supplementation will mitigate some of those effects.

Injectable Anesthesia

Injectable anesthetics are an alternative when waterborne anesthesia is impractical due to large water volume or, as mentioned previously, when sedation is necessary to safely capture animals from complex primary exhibits. The popularity of injectable anesthesia has grown as more controlled studies offer clinicians a better understanding of the effects the drugs may have on various species. Intramuscular (IM) delivery is the most common, but intravenous (IV) and intracoelomic (ICe) administration are used in some situations.

IM delivery is typically achieved by hand injection, pole syringe, Hawaiian sling (Chapter 9), or remotely through either an underwater laser aimed dart gun (Fig. 7.8) (Aquadart; Harvey et al. 1988; Runnells & Mylniczenko 2014) or other similar remote injection devices. Additionally, the standard zoo air-charged pistols and rifles have been used from the surface with the tip of the barrel underwater aimed



Figure 7.8 An underwater dart system with laser apparatus (AQUADART; Harvey et al. 1988). See Chapter 9 for modified dart and pole syringe options.

at the patient. This method requires practice to achieve appropriate placement and discharge of the dart.

A "home-made set-up" is described for immobilizing large fishes and may prove useful for large elasmobranchs as well (Garcia-Parraga et al. 2007). When setting up a dart on a pole or extension, an air-charged dart as used in regular zoo practice is placed against a barrier at the caudal end. This is then attached to a sturdy pole (Chapter 9).

Whether an animal is free swimming or manually restrained, IM injections should be delivered quickly, ensuring reduced contact or handling time. This in turn reduces the chance of injury to the animal and people involved. The safety precautions taken when injecting free-swimming animals are described above. The challenges of underwater darting include judgment of distance, refraction from the facemask (making targeting less accurate), and getting a full discharge of darts under water (reduces gas pressure in the dart), making it less reliable than on land. With the above-mentioned laser-aimed dart gun these issues are eliminated.

As mentioned previously, many sharks have both red and white muscle (Fig. 7.1). The red, oxidative myotomal muscles usually comprise less than 10% of the body mass and consist of relatively small, well-vascularized, myoglobin-rich fibers. White myotomal muscles comprise approximately 50% of body mass and consist of less-vascularized, myoglobin-poor fibers. In fishes other than the scombrids, lamnid sharks, and the common thresher shark, the red muscle usually occurs as a relatively thin layer directly beneath the skin, gradually becoming more abundant in the posterior regions of the body (Greer-Walker & Pull 1975). Injection into different muscles will theoretically affect drug absorption. Some of the variability in response to IM drugs within a species may be due to this anatomical variation in blood supply. Skeletomuscular movement helps blood circulate (Gruber & Keyes 1981) and has a direct impact on IM drugs. Animals that are sedentary may not adequately absorb the drug through their muscles. There is also a limit to the amount of drug that can be injected in one muscle body. In rays, the musculature and cartilaginous fin rays prevent retention of high volumes.

An elasmobranch's protective denticles and epidermis make needle penetration of the integument difficult and often require the use of a heavy needle (20–22 gauge in small species, 16–18 gauge in larger species) for IM injections. Unfortunately, shark skin does not have a great degree of contractibility and muscle is at a positive resting potential. Injection site leakage is a problem. To minimize leakage, use small volumes and angle the needle either anteriorly or posteriorly to deposit the drug away from the injection site. If remotely injected darts are used to administer a drug, the dart should be left in the animal until it has become sedated, thus preventing drug leakage. Barbed or collared needles can be used. In some situations, bone wax (mix of beeswax and isopropyl palmitate), Ilex® skin protectant paste or other water-insoluble substances may be used to cover or plug the injection site when the needle is removed.

The recommended site for IM injection in a shark and elongated batoids (sawfish, guitarfish) is the dorsal saddle (Fig. 7.9). This area surrounds the first dorsal fin and extends laterally to just above the lateral line, from the posterior gill slit caudal to a point halfway between the first



Figure 7.9 Intramuscular injection into the dorsal saddle just ventrolateral to the first dorsal fin in a giant guitarfish (*Rhynchobatus djiddensis*). Photo credit: Georgia Aquarium.

and second dorsal fins (Stoskopf et al. 1984). In "flat" rays, there is adequate area for muscular injection throughout the disc, but the coelom should be avoided. Since the wings are rich with vessels, pulling back on the plunger prior to injection is indicated. IV injection is the most reliable anesthetic delivery route, providing more rapid induction and often a shorter duration of effect. Locations for vascular access are described above. Walker (1972) calculated a circulation time of 1–2 minutes for indigo cyanine green injected in the caudal tail vein of nurse sharks (*G. cirratum*). Slow circulation in elasmobranchs may delay the onset of effect of an IV drug when compared to onset times of other classes of animals. The main disadvantage with IV administration is most animals must be appropriately restrained for drug delivery. Some exceptions were previously described in which a diver swims next to an animal while administering a drug via the vasculature associated with the dorsal or pectoral fins.

ICe (into the body cavity) injection is an additional option. It requires drugs to pass through the serosal membranes of the coelomic cavity organs, making the anesthetic induction time erratic. Needle insertion at an acute angle directed anteriorly to the pelvic girdle on the right side of the abdominal wall minimizes the possibility of puncturing any internal organs, particularly the liver, which is easily damaged. In addition to unpredictable induction times and the possibility of organ puncture, other disadvantages of ICe administration include the risk of peritonitis as well as the need to place an animal in dorsal recumbency to administer the injection. The coelom is considered excretory in function (Donnelly et al. 2019) and coelomic fluid can be expelled via the coelomic pores, so volume is important to consider and can be limiting.

Injectable Anesthetics in Batoids

There are few reports on batoid injectable anesthesia, but procedures using a combination of midazolam, medetomidine, and butorphanol were successful in producing sedation adequate for minimally invasive procedures (Neiffer, pers. comm., 2011). The protocol included initial immersion in isoeugenol (15.7 ppm), followed by midazolam (0.2–0.3 mg/kg IV), medetomidine (0.035–0.05 mg/kg IV), and butorphanol (0.2–0.3 mg/kg IV) and immediate transfer to isoeugenol-free saltwater for the remainder of the anesthetic event. Recovery was complete after administration of reversal with flumazenil (0.01 mg/kg IV), atipamezole (0.228 mg/kg IV), and naltrexone (0.280 mg/kg IV). IV propofol has also been used successfully in sawfish (*Pristis microdon* and *zijsron*), cownose rays (*Rhinoptera bonasus*), and round ribbontail rays (*Taeniura meyeni*). Delivery can be via the caudal tail vein, a wing vessel, or a dorsal fin sinus of the sawfish. Dose ranges for batoids are 2.0–4.0 mg/kg and produce intermittent apnea, mild coloration changes, and expected shifts in acid-base balance. Recovery times correlate to anesthetic doses and subsequent planes of anesthesia. The longest recorded return to normal swimming in a ray was 88 minutes; this animal received two doses of propofol during a lengthy procedure to remove an embedded circle hook (Clauss, pers. comm.). An alternative in cases where anesthesia is long or depth of anesthesia needs to be increased, an elasmobranch can be placed into a low-dose immersion anesthetic for maintenance anesthesia after injectables are used. Such an example is described later using MS-222 and guaifenesin in southern stingrays.

Acepromazine

Intrasinus administration of acepromazine (0.5 and 4 mg/kg), a phenothiazine derivative, in *S. tiburo* resulted in no clinical responses (Clauss, pers. exp.).

Alfaxalone

Alfaxalone has become available again since the last publication of this chapter, but there are no reported uses. There is one abstract available (Beckman et al. 2016) on its use in Potamotrygon rays, with few details.

Historically, alfaxalone-alfadolone (Alfathesin®), a steroid anesthetic (no longer marketed in the United States), was used in the piked dogfish (1.5 mL/kg), the brown ray (*Raja miraletus*, 0.2–0.3 mL/kg), the skate (*Dipturus batis*, 0.2 mL/kg), the blacktip shark (*C. limbatus*, 0.4 mL/kg), and the spotted eagle ray (*Aetobatus narinari*, 0.3 mL/kg) (Harvey et al. 1988). The anesthetic response was highly variable, from minimal effect in the eagle ray to immobilization in the dogfish.

Azaperone

Azaperone, a butyrophenone, reduces response to environmental stimuli without motor impairment or sedation. Preliminary studies in piked dogfish (*Squalus acanthias*) showed the most efficacious application of azaperone is directly over the gills rather than by injection. No effect was noted when animals were injected with the drug IM. However, an effect was observed when the drug (4 mg/kg) was deposited on the gill filaments and the animal held out of water for several seconds (Latas 1987). At 4 hours, drugged animals, compared to control animals, showed no flight response. Blood glucose levels were unaffected. Tranquilized animals were more likely to feed compared to control animals, which exhibited several days of anorexia

after blood collection. They could negotiate tank walls and returned to normal behavior within 24 hours. The advantages of using azaperone include uninterrupted swimming patterns, normal gill ventilation, and normal cardiovascular function (Latas 1987).

When administered intrasinus (via the first dorsal fin sinus) to *S. tiburo*, a range of responses were seen. These include variable induction times (10–40 minutes), ability to handle animals, and highly varied recovery times. At the higher dosages, bottom settling was noted as well as a slow, coordinated swim pattern with obstacle avoidance. If given IM, there were no responses at 12 mg/kg, but higher dosages were not tried (volume limiting) (Clauss, pers. exp.).

Butorphanol Tartrate

Butorphanol is a systemic partial opiate agonist/antagonist used or tested as an analgesic and in combination with other injectable anesthetics (see table 8.1, Davis et al. 2006). The authors (Burns & Mylniczenko) have found that an IV dose of 0.2 mg/kg periprocedurally and perioperatively is a very useful adjunct for analgesia and for improved depth of anesthesia for short durations (~20–30 minutes). The positive effects included lower anesthetic immersion doses, cessation of movement during computed tomography scans, and elimination of reaction under surgery. Higher dosages (0.4–0.6 mg/kg) subjectively had a longer duration of obvious effects (40–50 minutes).

Carfentanil Citrate

Carfentanil citrate, an ultra-potent opioid, failed to achieve any effect in a nurse (*G. cirratum*) and a lemon shark (*Negaprion brevirostris*) at a high dosage (compared to mammals) of 0.25 mg/kg (Stoskopf 1986, 1993). This lack of response seems unusual as sharks do possess μ opioid-like receptors and peptides (Li et al. 1986; Lorenz et al. 1986). It is conceivable that as with amphibians (Wright & Whitaker 2001) the amount of receptor binding required is much higher than that reported for other animals.

Chloral Hydrate

Chloral hydrate is a hypnotic sedative whose mechanism of action is not well understood. When given intrasinus to bonnethead sharks (*S. tiburo*) at 60–80 mg/kg, reactions were variable from intermittent incoordination with little obstacle avoidance to settling on the bottom and tolerance of handling. Additionally, the drug caused minor skin reaction at the injection site (Clauss, pers. exp.).

Detomidine Hydrochloride

Dormosedan® (detomidine hydrochloride) is an alpha-2 agonist. Two trials using relatively high amounts of detomidine (115 μg/kg IM)/ketamine (4.5 mg/kg IM) in a single bull shark (*Carcharhinus leucas*) showed little effect (Stamper, pers. exp.).

Dexmedetomidine

This alpha-2 agonist gained more popularity when medetomidine could only be purchased at compounding pharmacies in concentrated form. It has been used in *C. plumbeus*, *C. taurus*, *S. tiburo*, and *G. cirratum* at dosages of 0.03 mg/kg either alone or in combination with ketamine 0.025–0.1 mg/kg IM (Gaskins & Boylan 2019).

Diazepam

Diazepam in sand tiger sharks (*C. taurus*) at a dosage of 0.1 mg/kg IM provided satisfactory sedation in one institution, but more research is indicated to define dosages (McEwan, pers. comm., 2011). The authors feel diazepam does not provide sufficient sedation at multiple dosages, but can be used for mild tranquilization in some species to facilitate capture and restraint.

Etomidate

Etomidate (0.4–1.3 mg/kg IM) has been used as an induction agent for *C. taurus* and *C. plumbeus* by either darting or pole syringe. The higher dosages resulted in more rapid induction and easier handling. The drug formulation is very thick and can result in leakage from the injection site. Anesthetic effects were noted as variable, but resulted in animals that would allow manual restraint (Lécu, pers. comm., 2017).

Guaifenesin

The mechanism of action of guaifenesin is unknown, but it is believed to depress or block nerve impulse transmission and has sedative qualities. It is commonly used for continuous-rate infusions in hoofstock species to maintain muscle relaxation and offer rapid recoveries. Guaifenisin IV was used in southern stingrays after a 5–10-minute induction in buffered MS-222 (50 ppm), which was enough to allow the animal to be turned over for IV administration of the drug (Rosenberg et al. 2013). The drug was given as a bolus at dosages of 10–40 mg/kg to observe effects in hopes of identifying a continuous-rate infusion dose for longer procedures. At the low

dosages, this drug provided very little effect and only showed sedation (stage 2) at the higher dosages, with rapid recoveries at all dosages. The only negative effect was a brief cessation of cardiac rhythm and asystole (identified by continual observance via ultrasound), which rapidly returned to a normal rhythm. One other institution has used the drug (20 mg/kg) for treatment of a suspected muscular condition and showed minor sedative effects as well (Rosenberg et al. 2013).

Haloperidol

Haloperidol lactate is a neuroleptic butyrophenone used as a tranquilizer in mammals. It is used to facilitate the transport of flighty animals and to decrease stress. Its calming effects make it a possible desirable drug for elasmobranchs. During trials in bonnethead sharks (*S. tiburo*) using the lactate form (2–10 mg/kg) intrasinus, only one animal out of five showed a response (incoordination and hyperexcitability) at the higher dosage. There was also considerable skin reaction to the drug. In general, haloperidol was not considered successful for sedation or adequate tranquilization at the dosages tested (Clauss, pers. exp.). The use of haloperidol decanoate has not been documented in elasmobranchs.

Ketamine Hydrochloride

Ketamine hydrochloride is an analgesic and cataleptic cyclohexamine. Ketamine provides good peripheral analgesia (pain relief) in mammals through suppression of dorsal horn cell activity in the spinal cord, but provides little visceral analgesia. It has been used as a single anesthetic at very high doses (50–80 mg/kg) in elasmobranchs. Seizure-like muscle spasms due to spinal reflex firing have occasionally been noted (Stoskopf 1993). Recovery is often prolonged and animals are disoriented for long periods of time. For these reasons it is preferably used in combination with other anesthetics.

Medetomidine

Medetomidine, an alpha-2 agonist, is available only via compounding at 10 and 40 mg/mL concentrations. It has been used in combination with ketamine in several shark species, including sand tiger shark (*C. taurus*), blacknose shark (*Carcharhinus acronotus*), sandbar shark (*Carcharhinus plumbeus*), and nurse shark (*G. cirratum*), to ameliorate muscle spasms that can occur with ketamine alone (Snyder et al. 1998; Tuttle & Dunn 2003). See medetomidine in multiple combinations (below and Table 7.1) for effects.

Midazolam

As a benzodiazepine receptor agonist, midazolam can result in sedation and anxiolytic activity. When used at dosages of 1–5 mg/kg IM as a sole agent in *S. tiburo, C. melanopterus*, and *C. plagiosum*, the authors have not found the drug to be useful. However, when used in combination with other drugs, induction times did seem to decrease as did the physical excitement phase (Mylniczenko, pers. exp.). When administered intrasinus in *S tiburo*, there was notable hyperexcitability and ataxia at 4–5 mg/kg in two animals, while at 8 mg/kg death occurred in one animal (Clauss, pers. exp.). In whale sharks, *Rhincodon typus*, 4.5 mg/kg IV or IM, was efficacious for sedation. It is also efficacious in manta rays (*M. birostris*) at 0.50–2.5 mg/kg IV or IM (Ueda et al. 2017). The same group also found that propofol at 1.5 mg/kg IV after the midazolam provided good general anesthesia.

Propofol

Propofol is a sedative-hypnotic that has been used in multiple species (Table 7.1). Dosage range is typically 1.0–5.0 mg/kg IV at a slow to moderate infusion rate to achieve a surgical anesthetic level within 5–10 minutes (Claus, pers. exp.). Apnea is more profound in shark species than batoids, but consistent, spontaneous respiration and righting responses usually return within 60–90 minutes. Ventilatory support should always be provided when using propofol in elasmobranchs. When administered in *S. tiburo* at 2.5 mg/kg intrasinus, slight incoordination was noted but no anesthesia. At 5 mg/kg, however, induction was rapid, a surgical plane of anesthesia was achieved, and marked respiratory suppression occurred. These bonnet heads returned to gilling >35 minutes post induction. The animals returned to swimming >65 minutes after induction. Additional work with *S. tiburo* suggests that 4.0 mg/kg is an ideal dose for moderate anesthesia for 45–60 minutes (Clauss, pers. exp.). In the spiny dogfish (*S. acanthias*) a minimum of 5 mg/kg IV was necessary to achieve a surgical plane of anesthesia (Cavin et al. 2007). With blacktip sharks (*C. limbatus*) 2.5–3.0 mg/kg delivered intrasinus resulted in rapid induction (<1 minute) and a surgical plane of anesthesia with persistent shallow, irregular spontaneous ventilation. Sharks returned to normal gilling 35–45 minutes post induction and to normal swimming in 55–75 minutes (Cavin et al. 2007; Clauss, pers. exp.). Propofol administered IV in batoids and sharks produces reliable, dose-dependent anesthesia and recoveries. The disadvantage is the IV delivery requires the animal to be in hand or for a diver to administer it underwater.

Sodium Pentobarbital

Sodium pentobarbital (10 mg/kg) produced satisfactory general surgical anesthesia in nurse sharks (*G. cirratum*) when administered rapidly IV (Walker 1972). Slow injection resulted in an erratic response. Intraperitoneal absorption was slow and response was variable, while IM injection resulted in only slightly improved response. Serum half-life was approximately 15 seconds with a second half-life of several days due to an inability of the animals to excrete the drug through their gills or kidneys. An anesthetic IV dose (10 mg/kg) resulted in loss of ventilatory movements (gilling) within 1 minute. Gilling returned after 10 minutes and a weak righting response was observed at 3 hours. A higher IV dose (20 mg/kg) resulted in a rapid loss of gilling that did not return by 3 hours. A weak righting response was only observed after 5 hours. A high IV dose (60 mg/kg) resulted in death. Larger, more active sharks require smaller doses per kilogram than smaller, sedentary specimens. For example, sandbar and bull sharks dosed at 6 mg/kg IV responded similarly to the nurse shark dosed at 10 mg/kg IV (Walker 1972).

Tiletamine/Zolazepam

Tiletamine/zolazepam (12 mg/kg) administered to a lemon (*Negaprion brevirostris*) and a sand tiger (*C. taurus*) shark produced irritability, rapid swimming, and unrestrained biting (Stoskopf 1986, 1993). Dosages of 5–20 mg/kg IM in *C. plagiosum* showed very little response even at the high dosage (some animals permitted being turned over for a few seconds) (Kilborne, unpubl. data) but a different study using the same dosage trials in *C. plagiosum* and *C. punctatum* (Adams & Krol 2015) showed that when administered IV, 15 mg/kg showed complete immobilization, but there was variability in anesthetic depth and prolonged apnea.

Xylazine

Xylazine in boney fish (teleosts) is a convulsant and causes major changes in the electrocardiogram (Oswald 1978). Used in combination with ketamine (12 mg/kg), xylazine (6 mg/kg) in sand tiger shark (*C. taurus*), lemon shark (*Negaprion brevirostris*), sandbar shark (*C. plumbeus*), and nurse shark (*Ginglymostoma cirratum*) variably ameliorated the muscle spasms that can occur with ketamine alone (Stoskopf 1993). Yohimbine hydrochloride administered IV to a nurse shark immobilized with xylazine/ketamine caused arousal (Stoskopf 1986). Lécu et al. (2017) noted no anesthetic effect at any dose of xylazine administered up to 50 mg/kg even with the addition of ketamine.

Injectable Anesthetic Combinations

Balanced anesthesia involves drug combinations, for example combinations of IM xylazine (6–7.5 mg/kg) and ketamine (12–16.5 mg/kg) have been used to produce light to moderate anesthesia in multiple species (Stoskopf 1986; Andrews & Jones 1990). Current practice, however, favors medetomidine and ketamine at varying dosages (Table 7.1) with dosages ranging from 90 to 100 μg/kg medetomidine and 4 to 5 mg/kg ketamine. Usually initial effects take 20–40 minutes, but results can be erratic. The effects vary from complete anesthesia with recumbency (some within 5 minutes), animals showing partial signs with no recumbency (despite additional dosing), and animals showing almost no sedative effects. There also appears to be a great variation between species in their responses to similar dosages under the same conditions. Additionally, recoveries are highly variable, with reports of immediate recoveries to some deaths several days later. Anorexia is a common complaint post procedure.

Penning and team have successfully used medetomidine and butorphanol for multiple procedures in several elasmobranchs. Medetomidine (0.1 mg/kg IM) and butorphanol (0.65 mg/kg IM) proved very successful with several *Carcharinus* species. Moderate success was achieved with giant guitarfish (*R. djiddensis*) by increasing the butorphanol dosage to 1 mg/kg. Inductions started at approximately 20 minutes, but animals were not handled until 45 minutes, which was considered a minimum time to avoid stimulation for successful sedation. The animals were then guided into a plastic sock (described above) and transported. In some instances, the sharks lay on the bottom of the tank, while others continued to glide very slowly. Reversals were given for rapid and full recoveries. The team noted that the addition of ketamine seemed to increase the frequency of phantom biting or biting at the stimulating activities. In these situations, they offered a bite stick for the animal to hold onto (Penning, pers. comm.).

In bamboo sharks (*C. plagiosum*), midazolam (1–5 mg/kg), medetomidine (80–90 μg/kg), and butorphanol (0.5–1 mg/kg) had little to no effect IM, but minor sedative effects IV. With the latter route the animals tolerated being turned over and stayed dorsally recumbent for several seconds to several minutes (Mylniczenko, pers. exp.).

Oral

Oral sedation of elasmobranchs is not widely practiced and is rarely reported (Raines & Clancy 2009; Clauss et al. 2011), in part because few feasible, effective options exist. Oral administration holds potential for the management of

animals in large aquaria and for improving the capture of animals for further immobilization if reliable medications can be identified.

In one study, four ocellated river stingrays (*Potamotrygon motoro*) were offered ketamine-injected earthworms at a dosage of 20 mg/kg; within 15 minutes the animals were easily netted and placed into dorsal recumbency, but did not reach anesthetic depths. In a different study, multiple sedatives were used with bonnethead sharks (*S. tiburo*), comparing oral (via capsule in food) and IV injectable drugs (Clauss, pers. exp.). The oral drugs produced little effect, even at doses considered high for other species. These drugs included chloral hydrate (no sedative response at 300 mg/kg), ketamine (no sedative response at 30 mg/kg), and haloperidol lactate (no sedative response at dosages up to 50 mg/kg). Haloperidol showed no sedative effects at 10 mg/kg in *Triakis semifasciata,* but did show behavioral modifying effects (decreased stereotypy) (Mylniczenko, pers. exp.). The authors have also used diazepam at dosages from 1 to 40 mg/kg (most in the 1–10 mg/kg range) with variable anxiolytic effects or appetite stimulation effects. There were no overt sedative effects in a variety of species: sawfish (*Pristis zijsron*), brown sharks (*C. plumbeus*), blacktip reef shark (*C. melanopterus*), leopard shark (*Triakis semifasciata*), blotched fantail ray (*Taeniura meyeni*), bowmouth (*Rhina ancylostoma*), and whale sharks (*Rhincodon typus*). More research is indicated to evaluate the usefulness of oral sedation in elasmobranchs.

Reversal Agents and Nonspecific "Reversal" Drugs

Atipamezole is a potent, selective alpha-2 reversal agent, exhibiting activity at both central and peripheral receptor sites. It has been developed specifically as an antidote to medetomidine and is able to reverse behavioral, cardiovascular, gastrointestinal, neurochemical, and hypothermic sedative effects (Swann 1993). It also reverses dexmedetomidine and detomidine. An IM dose is usually dependent on the dose of the anesthetic drug, for example five times the medetomidine dose and 10 times the dexmedetomidine dose (Gaskins & Boylan 2019). Yohimbine is a historical alpha-2 reversal agent that is still on the market and less expensive than atipamezole. Dosages of 0.125 mg/kg can be used successfully to reverse the effects of ketamine–xylazine combinations.

Naltrexone is an opioid reversal agent (Grimm & Lamont 2007). Reversal is typical after 10–20 minutes and the elasmobranchs were generally able to move, respire, and swim unaided (Penning et al. 2017).

Doxapram hydrochloride, while not a reversal, has been used to facilitate recovery in elasmobranchs. It has been noted to produce dramatic arousal and stimulation in anesthetized elasmobranchs and should be used with caution because animals can become extremely excited and dangerous (Stoskopf 1986).

Monitoring

In captive animals, a quiet environment without predatory tank mates should be used for anesthetic induction and maintenance. Several baseline physiological variables should be monitored. Ventilation rates are recorded if the animal is actively pumping water through the gills and not ram-ventilating. Gill ventilation rate and rhythm can be monitored visually. Caudal fin strokes are measured to determine the onset of drug effect; this activity is usually the first to be reduced throughout anesthetic procedures. When an animal becomes ventrally recumbent, the righting reflex, respiration, and heart rate should be closely monitored. If respiration becomes erratic, slows significantly, or ceases, the animal must be manually ventilated by directing water flow over the gills.

Although animals may appear to be ventilating well in some anesthetic situations, bradycardia and an increased resistance to gill capillary flow (as erythrocytes accumulate within the capillary bed and become swollen) has been noted to cause hypoxemia (Tyler & Hawkins 1981), therefore the authors strongly advise assisted ventilation even with voluntary gill movement and equate this with a good standard of practice.

Ventilatory effectiveness is best assessed with periodic blood gas analysis to determine pH, bicarbonate, and lactate levels. Large changes in blood chemistry can occur during the stress of capture and handling of elasmobranch fishes (Naples et al. 2012; Frick & Reina 2009; Mandelmann & Skomel 2009). Respiratory, metabolic, and lactic acidemia are common. In elasmobranchs, lactic acid is produced in large quantities during hypoventilation and/or muscle exertion; the resultant acidemia is usually corrected by hydrogen ions buffering or through gill excretion (a much slower process), therefore lactate levels will continue to rise in elasmobranchs for up to 12 hours after the inciting event (Piiper & Baumgarten 1969). Experiments with larger spotted dogfish (*Scyliorhinus stellaris*) indicated arterial partial pressure of carbon dioxide ($PaCO_2$) was increased immediately after exercise, but returned to baseline within 1 hour. The pH gradually decreased, reaching a minimum in the second hour and returned to baseline within 8 hours. Lactate concentrations increased slowly to very high levels, reaching a maximum of 220 mg% within 6–8 hours after exercise (Piiper & Baumgarten 1969). The

pH may therefore correct itself in an animal that has sufficient buffering capacity, but this is largely determined by the animal's respiratory mode and method of oxygen metabolism (Piiper & Baumgarten 1969; Cliff & Thurman 1984; Manire et al. 2001; Chapman & Renshaw 2009; Frick & Reina 2009). Benthic animals tolerate and correct acidemia more readily than pelagic animals.

Handheld analyzers offer rapid analysis at poolside or on a boat, and some automatically adjust calculations for lower body temperature. If they do not, then correction for ambient water temperature is necessary or, alternately, evaluation or trends should be followed rather than actual values. The pH is a critical variable to monitor. For the authors, animals with corrected values under 7.0 indicated an animal in crisis that needs attention (ventilatory and/or chemical), even when chemical restraint is not utilized. Lactate levels are useful for anticipating problems that may occur later or for evaluating handling/anesthetic events; repeated increasing lactate levels suggest a continued problem. These values vary by species and by method of restraint. Under circumstances of continued pH decline and/or lactate elevation, the authors have treated animals with fluids solely or in combination with sodium bicarbonate and/or acetate therapy. Adjustments to ventilation may also be warranted with consideration to direction over gills, flow rate, and oxygen saturation of the water).

Another factor to consider when evaluating blood gas variables is the location used for blood collection. In larger specimens, the dorsal sinus was historically used for blood collection due to ease of access. However, several variables have been shown to be inaccurate for the animal's baseline state in samples from this location. Not only is hematocrit lower at this site compared to the tail (Mylniczenko et al. 2006), but blood gas values are also different. The pH and lactate are not accurate or "real time" when measured in blood samples collected from the dorsal sinus (Naples et al. 2012). Blood collected from the ventral tail vein can be a mixed venous–arterial sample due to the close proximity of the vasculature. The collected sample from the tail is likely to be arterial if the needle tip is moved just off the cartilage as the vessel abuts the vertebrae.

Heart rate is monitored using either a Doppler flow detection probe (Fig. 7.10a) or ultrasound (Fig. 7.10b) placed over the heart, which is located along the ventral midline just cranial to the pectoral girdle. The heart rate will vary between species and in response to stress and temperature. Most unanesthetized fish will have a heart rate between 30 and 70 beats per minute, depending on animal size, species, and condition (Lewbart 2001). In addition to heart rate, the contraction quality and rhythm are important to examine. Changes such as weak contractions and dysrhythmias may indicate the animal is doing poorly under anesthesia. Dilution of immersion drugs or recovery should be considered. If contractions appear to be weak, evaluation of the animal's calcium is warranted, particularly ionized calcium, which can be monitored with a handheld analyzer. Normally, this value is greater than the readable limit of some portable units (>2.5 mmol/L). If it is reading below this value, and the animal has weak contractions, then the animal should be recovered and/or calcium administered to manage the relatively lower calcium levels (Mylniczenko, pers. exp.).



Figure 7.10 Heart rate can be monitored using either a Doppler flow probe (7.10a) or ultrasound probe (7.10b) placed directly over the heart.

Anesthetic stages in elasmobranchs are like mammals and teleost fish (Chapter 9; Stoskopf 1986). Stages are gauged by activity, reactivity to stimuli, equilibrium, muscle tone, respiratory rate, and heart rate (Ross & Ross 1999). The period between respiratory and cardiac arrest, however, is greater because the respiratory capillaries can exchange oxygen and carbon dioxide when water flow over the gills is maintained via assisted ventilation. Stages of anesthesia are highly variable between animals (both intra- and interspecies) and between drugs.

As a reminder, during an immobilization procedure, it is also important to monitor and control the water quality of the anesthesia or restraint system as poor or altered water parameters may negatively impact the animal(s) involved. Temperature fluctuations may occur easily if the water volume is small and should be controlled as hyper- or hypothermia can impact metabolism and recovery. Dissolved oxygen should be maintained close to 100% and may require the addition of supplemental air stones with or without supplemental oxygen. Any fouling of the system by the patient can lead to an excess of nitrogenous waste. Waterborne anesthetics, in particular MS-222, can lower the pH of the water and thus may require buffering.

Recovery Considerations and Postanesthetic Challenges

All safety precautions exercised for induction and maintenance should continue to be a priority during recovery from anesthesia. When recovering an animal from an anesthetic event, an isolated environment is preferable (Fig. 7.11a). Ideally the recovery container or tank will be easily accessible for the staff, but will also be large enough to allow the animal space to swim as it progresses through stages of recovery. Water in recovery containers should be well aerated and maintained at an appropriate dissolved oxygen level (100–120%, 10–12 mg/dL). The water flow should be aimed toward the fish's mouth if the animal is respiring spontaneously but still sedated from anesthesia. Assisted ventilation directly over the gills may be necessary if the fish is not respiring (Fig. 7.11b) or the respiration rate continues to be slow or irregular. It is not recommended to pull the fish forward through the water with its mouth open. In the authors' experience, this method is inferior to the use of a ventilation system, indicated by differences in the quality of blood gas results.

Careful observation is important, and staff should be readily available to intervene if the fish becomes distressed or the recovery process halts. It is important to have experienced personnel involved when making judgment calls on the release of a recuperated animal. If an animal is released too early it may not be able to maneuver appropriately in the water column, and it may swim briefly and then fall to the bottom of the recovery pool. Although this is not considered a respiratory issue with buccopharyngeal breathers, it can be problematic with pelagic animals; the animal must be retrieved and continue to be supported through recovery. As a fish recovers from anesthesia, the respiratory rate should return to normal and the rhythm should become more consistent. Muscle tone and fin movements should return, followed by progressively better coordination.

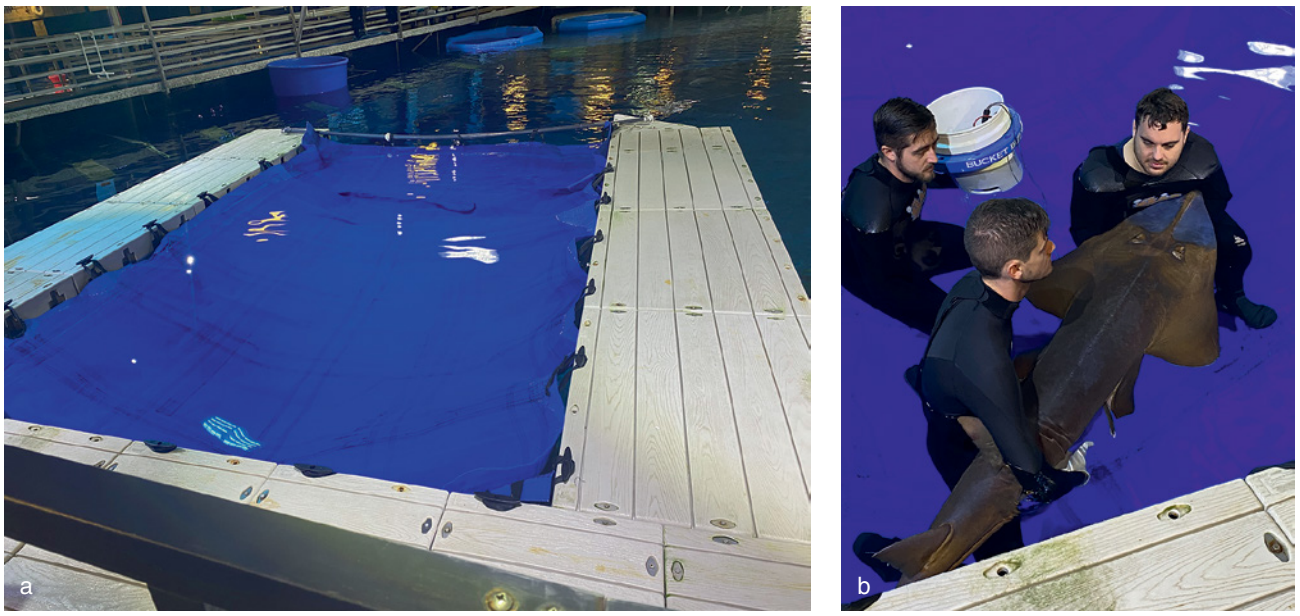


Figure 7.11 (a) Floating docks and tarp to create a recovery and isolation area in a large aquarium system. (b) Recovery of a shovelnose guitarfish (*Rhinobatus productus*) using the tarped area and a floating bucket for maintaining ventilatory equipment safely. The ventilation is being provided ventrally, out of the view of the photograph.

Recovery from immersion anesthesia begins when the fish is placed in anesthesia-free water. During the recovery process, the water in the tank may need to be changed as anesthetics and their metabolites may be excreted from the fish into the water and potentially reabsorbed, although this is rarely indicated. The same process is theoretically possible with oral or parenteral drugs as they too may be excreted into the water and reabsorbed. Recovery from oral or parenteral anesthetics technically begins after the drug is administered and fully metabolized. Faster recovery in some cases is facilitated by administering reversal agents. However, there is no reversal for some drugs and in those situations it is up to the fish to fully metabolize and clear the drug(s) for full recovery to occur. Recovery time from oral and parenteral agents is dependent on the route of administration, rate of metabolism, use of reversal agents, health status of the patient, and species. Extended recovery periods may occur with excessive anesthetic dosages, medically compromised animals, long procedures, or for unknown pharmacokinetic reasons.

Prolonged recoveries and other unpredictable scenarios can also be attributed to the immensely variable responses to anesthesia, as extrapolation of doses is challenging. At the New England Aquarium, two sand tiger sharks (*C. taurus*) anesthetized with dexmedetomidine (0.03 mg/kg) and ketamine (3.0 mg/kg), followed by MS-222 (70–90 mg/L) immersion, had markedly different recovery times. Even after reversal with atipamezole, one shark began to swim 6 hours after reversal and returned to the exhibit tank. The other shark did not begin to swim until 24 hours after reversal (Cavin & Innis, pers. comm.). At the Living Seas with Nemo and Friends® (Walt Disney World, Orlando, FL, USA) highly variable responses to a similar drug combination were noted and ranged from no response to rapid induction, with recoveries that were also highly variable. This included a quick return to normal to exhibition of abnormal behavior, including swim gait abnormalities, anorexia, and prolonged lethargy for up to 7 days in the same species.

Recovery or resuscitation attempts should not be abandoned prematurely in apneic fish as respiratory arrest may precede cardiac arrest by extended periods of time. In the authors' experience, anesthetics such as propofol may produce respiratory arrest for periods in excess of 30 minutes followed by full recovery when the sharks are artificially ventilated. Fifteen bonnethead sharks (*S. tiburo*) at the Georgia Aquarium were anesthetized with propofol (4.0–5.0 mg/kg) administered into the first dorsal sinus. Spontaneous respirations ceased within 3–5 minutes. The sharks were artificially ventilated with a submersible pump and vitals monitored closely as well as blood gasses. Gilling resumed in all 15 animals within 36–52 minutes after propofol administration. Fish with persistent apnea or bradypnea that also experience bradycardia, abnormal blood gases, or other physiological challenges may be given doxapram. The authors have observed positive responses to doxapram (5 mg/kg IV, IM, intracoelomic or over the gills) in several cases of respiratory arrest. Caution should be used when administering doxapram as it may cause hyperexcitability, especially in sharks.

In some situations, it may be necessary to provide supportive care and/or emergency drugs such as atropine, corticosteroids, fluids, or other therapeutics. In cases of shock or physiological collapse, corticosteroids such as methylprednisolone, prednisolone, or dexamethasone may be given with the caveat that it is unknown if steroid therapy is effective in elasmobranchs. In the authors' experience, corticosteroid administration has been subjectively helpful in many cases and no adverse effects have been noted.

Emergency fluid therapy should take into account the animal's osmotic balance as well as any imbalances or deficiencies that may be present. Elasmobranchs are hyperosmotic to their environment with urea, NaCl, and trimethylamine oxide being the major osmoregulatory plasma components (Olson 1999). Elasmobranch Ringers solutions should be used and recipes are available (Mylniczenko & Clauss 2017). Thorough summaries on the osmoregulation of elasmobranchs as it is currently understood can be found in the literature (Hammerschlag 2006; Anderson et al. 2007). Greenwell et al. (2003) provide an overview of the clinical implications involved with elasmobranch osmoregulation, including additional guidelines on the principles of fluid administration. The fluids are ideally administered through a needle or catheter placed in the caudal vein or the dorsal sinus, but may also be administered intracoelomically or orally. No rates of fluid administration have been published based on scientific studies, but the authors use maintenance doses of 7–10 mL/kg. Some elasmobranchs appear to respond to oral freshwater administration at 1–3% of body weight in less severe situations. When metabolic acidemia occurs, if the fish is unable to compensate and does not respond to increased oxygen supplementation and fluid therapy, it may be beneficial to administer an alkalinizing agent such as sodium bicarbonate or sodium acetate. Care should be taken not to overcorrect, causing an alkalemia or electrolyte imbalance. In these cases, monitoring with a point-of-care analyzer is extremely helpful and can guide clinical decisions.

As with other classes of animals, administration of emergency medications varies by case and should be governed by individual animal needs. Table 7.2 lists emergency and supportive care therapeutics the authors have used that have been valuable when working with elasmobranchs and holocephalans.

Table 7.2 Drugs used for emergency and supportive care in elasmobranchs.

Drug	Dosage	Route	Indication
Atropine	0.1 mg/kg	IV, IM, IP	Bradycardia, arrythmia, organophosphate poisoning
Glycopyrrolate	0.01 mg/kg	IV, IM	Bradycardia, arrythmia
Epinephrine	0.2 mL/kg	IV, IM, IP	Bradycardia, cardiac arrest
Doxapram	2–10 mg/kg	IV, IM, over gills; may cause hyperexcitability	Apnea, respiratory arrest
Erythropoietin	100–150 u/kg	IM	Anemia
Furosemide	2 mg/kg	IV, IM, IP	Excessive coelomic fluid, generalized edema
Dexamethasone	1 mg/kg	IV, IM, IP	Stress, shock, trauma
Methyl-prednisolone acetate	30 mg/kg initial, 15 mg/kg subsequent dosage		
Midazolam	0.5 mg/kg	IV, IM	Seizures
Diazepam	1–2 mg/kg		
Calcium gluconate	50–150 mg/kg	IV, IP	Muscle fasiculations, tetany, dysrhythmias, decreased myocardial contractility
Calcium lactate/calcium glycerophosphate	10 mg/kg	IV, IM, IP	
Iron dextran	10 mg/kg	IM	
Sodium bicarbonate	1 mEq/kg	IV, IM, IP	Acidosis
Sodium acetate	1 mEq/kg diluted ~ 1:10 with fluids	IV, IP	
Hank's balanced salt solution + 8 g/L NaCl and 21 g/L urea	5–10 mL/kg	IV, ICe, PO	Dehydration, shock, fluid loss, hypovolemia, hypotension
0.9% NaCl + 8 g/l NaCl and 21 g/l urea	5–10 mL/kg		
Blood transfusion	Blood: up to 10 mL/kg Heparin : 1 mL (1:1000 IU/mL) per 10 mL of blood	IV	Shock, anemia, hypovolemia

ICe, intracoelomic; IM, intramuscular; IP, Intraperitoneal; IV, intravenous; PO, per os.

Field Immobilization

Immobilization of elasmobranchs in the field has been in practice for many years. Live-release biological assessments and subsequent tagging and tracking provide valuable information on factors such as the population dynamics, spatial patterns, foraging behavior, and health status of free-ranging animals. These activities have become increasingly common practice as scientists try to understand the causes and significance of changing or declining populations and relationships to ocean health.

Generally, animals are manually restrained after hook and line, long-line, or trawl net capture, but other techniques may be employed as warranted. In these situations, naïve animals are being placed under the rigors of extreme exercise and are particularly vulnerable to exertional rhabdomyolysis, hypoxemia and lactic acidemia, hook and handling trauma. and stomach eversion. Pelagic (ram-ventilating) species are especially susceptible to stress and exhaustion. and can have a poor chance of survival, but this is highly species dependent (Mandelman & Skomal 2008). The location of release may also have an impact on survivability. Predatory fish, including other elasmobranchs, may take the opportunity to predate a tired, recently released animal, particularly if the area has been chummed to attract additional specimens for capture. Often, however, there is no control over the matter as the animals are mainly caught and released in open water. Capture–release scenarios that result in the least impact to the animal are imperative.

Experienced handlers are required as the space on a boat or dock is limited, areas on deck are potentially unstable or wet, and animals are strong and often very agitated (see previous comments in this chapter about manual restraint

and safety). If the animals are out of the water for any length of time, it is advised that they are safely ventilated with the water they were just pulled from. If animals are to be maintained in live wells, consider the time in the well, volume of water, oxygen delivery to the water, swim-glide pattern (usually nonexistent under these circumstances), and number of animals in the well (more animals means more consumption of oxygen, crowding, and excretion of biological end products).

In some scenarios with animals too large to be hauled onto the deck, they must be restrained in the water along the side of the boat or dock (Fig. 7.12). Under these circumstances, even more expertise and potentially specialized equipment is important for human and animal safety. When capture and immobilization involves extremely large specimens, such as white sharks, whale sharks or manta rays, specialized watercraft is also necessary.

It is rare to use anesthesia for field immobilization procedures for several reasons: speed, efficiency, space, and, most importantly, regulations governing using drugs in potential food fish (Aquatic Animal Drug Approval Partnership 2010). It is important to note that if elasmobranchs are to be retained under managed care for extended periods of time, there may be restrictions against release or there may be special permitting required, but this is highly variable by state in the United States.

When health assessments occur during field immobilization projects, additional considerations include having portable equipment that can connect and operate on generators or batteries, or plug into the vessel's electrical system as well as having adequate, safe storage and preservation capacity for biological specimens. Weather and water conditions may change rapidly and in turn may complicate sample collection, processing, and safe handling. Having seaworthy staff experienced in biological sample processing is beneficial.



Figure 7.12 Collection of blood from a free-ranging sand tiger shark (*Carcharias taurus*) during a population health assessment project in Delaware Bay. Photo credit: Georgia Aquarium.

With any field immobilization technique, speed and precision are essential to reduce the stress on the animal and improve viability on release. Ultimately, limited handling or limited time in a live well is best. Some researchers have developed techniques for collecting samples and attaching tracking or identification devices without physically restraining the animals. These methods usually involve less stress or physical exertion for the animal, but may present a different set of safety hazards for the people involved.

Some studies have assessed the impacts of catching elasmobranchs for science, sport or accidentally as by-catch. Blood acid-base status can be utilized to gauge the magnitude of the stress response, which is dependent on the nature of the capture and the metabolic capacity of the animal in question (Mandelman & Skomal 2008). Changes in blood glucose, electrolytes, osmolality, and hematocrit have also been documented in various species of elasmobranchs after capture (Wells et al. 1986; Wendelaar Bonga 1997; Hoffmayer & Parsons 2001; Manire & Hueter 2001; Moyes et al. 2006). Regardless of collection technique, captured fish experience distress caused by the cumulative impacts of physical trauma and physiological stress (Skomal 2007). The importance of swift and meticulous capture, handling, and release cannot be underestimated and can greatly improve survivability in field immobilization activities.

Euthanasia

The goal of euthanasia should be the rapid loss of consciousness. This can be accomplished by an overdosage of immobilization drugs. Inhalant (immersion) drugs at five to 10 times the anesthetic concentration for a particular species can be chosen (Ross & Ross 2009). Elasmobranchs, however, may require sedation first with parenteral drugs then euthanasia with a drug such as pentobarbital, following all the previously stated techniques. Use of Doppler flow probes, ultrasonography, or electrocardiography is recommended to confirm asystole. Severing the spinal cord at the brain stem (decapitation) or exsanguination are alternatives to chemotherapeutic euthanasia and can be performed once the fish is anesthetized. The reader is directed to review euthanasia principles for fish as outlined by the American Veterinary Medical Association

(Underwood & Anthony 2020). Unacceptable methods of euthanasia include asphyxiation and hypothermia.

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8

Bony Fish (Lungfish, Sturgeon, and Teleosts)

Natalie D. Mylniczenko, Charlene Burns, Whitney Greene, and Tonya Clauss

Introduction

Do fish require anesthesia? This becomes a debate in aquaria and loops in the conversations about mitigation of fish welfare and analgesia via the use of anesthetics. The subjects of welfare and pain have been taken into account in multiple other publications, including the previous version of this chapter (Braithwaite & Boulcott 2007; Chatigny et al. 2018; Posner 2009; Sneddon 2009, 2012; Mylniczenko et al. 2014). Similarly, stress is another topic of debate for the use of anesthesia. Acute and chronic stress negatively affects fish health, but does anesthesia dampen the response or create it? Fish display robust neuroendocrine and physiologic stress responses to noxious stimuli. Consequently, there is a need to identify and reduce these stressors in individuals and groups. Although examination and sample collection can be performed using manual restraint for many minor procedures, chemical immobilization may be safer for both fish and handlers in some situations. In addition, many procedures are performed out of water, which may result in fish struggling (Harms & Bakal 1995). This chapter will highlight methods for handling fish with and without anesthesia that have minimal impact on the animal and ultimately reduce stress when performed properly.

Chemical immobilization is routinely used to reduce excitement and trauma related to hyperactivity that can occur during routine handling for medical procedures, vaccinations, hormonal implants or injections, roe or milt collection, sorting, tagging, and transportation of fish (Cooke et al. 2004; Harms 1999; Kumlu & Yanar 1999; Myszkowski et al. 2003; Ross 2001). In addition to acute trauma causing mortality and morbidity, integument damage results in acute to chronic osmoregulatory disturbances and increased susceptibility to pathogens (Kumlu & Yanar 1999; Ross 2001). Chemical immobilization during transport reduces metabolism, leading to decreased oxygen demand and waste (i.e., CO_2 and ammonia) production (Cooke et al. 2004; Crosby et al. 2006; Guo et al. 1995; Hoskonen & Pirhonen 2004; Ross & Ross 1999).

Invasive or surgical procedures require anesthesia to prevent movement and remove any doubt in the debate over pain (Harms & Bakal 1995; Myszkowski et al. 2003; Ross 2001). At the very least, movement and physiologic changes in response to nociception are minimized.

There are approximately 33,000 species of fish that comprise more than 40% of all extant chordates. Of these, teleosts (Teleostei: class Actinopterygii) comprise about 96% of living fish species. Other groups include other members of class Actinopterygii or ray-finned fishes (sturgeon, gar, bichir, paddlefish, and bowfin), class Sarcopterygii or lobe-finned fishes (lungfishes and coelacanths), class Agnatha or jawless fish (hagfishes and lampreys), and class Chondrichthyes (elasmobranchs and chimeras) (Bond 1996; Harms 2003).

The majority of immobilization studies involve only a handful of teleosts. Extrapolation to all species is potentially harmful without consideration of the wide range of anatomic, physiologic, and behavioral differences. For example, benzocaine kills Atlantic cod (*Gadus morhua*) at the same dosage that is safe and effective in Atlantic salmon (*Salmo salar*) (Hansen et al. 2003; Mattson & Riple 1989). Even within families there can be marked variation in preferred environmental parameters. Consequently, knowledge of taxonomy and natural history is essential for developing anesthetic regimens in fish. Despite that, we are often limited geographically or under law to a handful of available anesthetics, therefore careful but diligent use of drugs in new species is necessary.

An ideal anesthetic for teleosts should have the following qualities: (1) induce anesthesia rapidly with minimal hyperactivity or stress; (2) be easy to administer and should maintain the animal in appropriate anesthetic state; (3) allow for rapid recovery; (4) be effective at low

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doses with a wide margin of safety; (5) not produce any long-lasting physiological effects with rapid clearance from the body; (6) have high solubility in fresh and saltwater; (7) be readily available, cost-effective, and nontoxic to humans (Priborsky & Velisek 2018; Ross & Ross 1999, 2009). A final notion worth considering is the aversion fish may have to an anesthetic, which reflects the welfare perspective. Traditionally, 'excitation' is considered as a phase of anesthesia, but it may be a profound reaction to the actual nature of the drug, such as the popular MS-222, which can produce a profound negative reaction (Readman et al. 2013).

Stress and Anesthesia

Fish restraint activates the hypothalamic–pituitary–interrenal (HPI) axis, resulting in cortisol release causing various secondary stress responses (Bressler & Ron 2004; Myszkowski 2003; Ross & Ross 1984; Small 2003; Small & Chatakondi 2005). Details can be found in previous versions of this chapter (Mylniczenko et al. 2014). Mitigation of these responses is key and although anesthesia can minimize handling stress, it is inherently stressful (Bressler & Ron 2004) and a strong potentiator of catecholamine release, especially in salmonids (Rothwell et al. 2005; Zahl et al. 2010). Anesthesia-associated catecholamine release is due to hypoxemia rather than acidemia or direct drug effects (Ross & Ross 1984; Rothwell et al. 2005). If unbuffered, some immersives ("inhalants" or baths, e.g., tricaine methanesulfonate or MS-222) induce a stress response, possibly due to the pH change; additionally, some anesthetics are simply irritating to the gills and skin even when buffered. Hypoxemia is usually due to drug-induced hypoventilation (decreased buccal movement) or lack of appropriate oxygen infusion into the water. In air-breathing fish, hypoxemia can be exacerbated by preventing anesthetized fish access to the water's surface (Rantin et al. 1993, 1998). Hypoventilation with decreased water flow in the buccal cavity often leads to reflex bradycardia and dorsal aortic hypotension, which produces progressive hypoxemia (Ross 2001), thus emphasizing the importance of ventilation.

Despite the above-mentioned effects, well-managed chemical sedation or anesthesia produce a lower stress response when compared to drug-free handling and transport. This conclusion is based on a comparison of circulating cortisol levels, as well as secondary indicators such as blood glucose, hematocrit (HCT), hemoglobin (Hgb), lactate, and osmolarity (Bressler & Ron 2004; Crosby et al. 2006; Hseu et al. 1996; Small & Chatakondi 2005).

Of the commonly used drugs, only metomidate consistently and significantly blocks HPI activation (Davis & Griffin 2004; Iversen et al. 2003; Zahl et al. 2010) in a broad range of species (Mylniczenko et al. 2014). The effect of clove oil (eugenol and isoeugenol) on cortisol secretion in fish is variable and dependent on circumstance (water quality, dose, environment). MS-222 has highly variable effects on stress which are dependent on dosage, handling circumstance, and species. Limited information on the effects of injectable drugs on the HPI response exists. In bonito (*Sarda chiliensis*) ketamine/medetomidine did not significantly alter HCT, Hgb, or glucose although baseline values were not provided (Williams et al. 2004).

In addition to affecting the stress response, some anesthetics are immunosuppressive. This effect may be caused by direct interaction with immune components or indirectly through the nervous system. For example, in gilthead seabream (*Sparus aurata*) both humoral and cellular immune responses were significantly depressed by benzocaine (Bressler & Ron 2004). However, clove oil does not cause significant immunosuppression in the same species, demonstrating the variability between species and drug effects (Bressler & Ron 2004). Metomidate-associated blockade of the HPI axis is thought to prevent immunosuppression (Davis & Griffin 2004).

Taxonomy, Anatomy, Physiology, and Behavior

Respiration

All fish have gills although the degree of reliance on these structures for respiration varies across class, order, and family. Most fish force water over the gills through rhythmic movements of their lower jaw and opercula (buccopharyngeal respiration). However, some species utilize ram ventilation (forcing water over the fish gill by swimming through the water column) with minimal opercular movement. Some teleosts (e.g., tuna, family Scombridae) are obligate ram ventilators, with gilling alone not providing sufficient ventilation to meet metabolic demands. These species swim forward continuously with their mouth slightly agape to develop the pressure necessary for sufficient water flow over the gills. Failure to perfuse the gills during anesthesia results in suffocation (Brill & Bushnell 2001; Bushnell & Jones 1994). Tuna also rely on constant forward speed to produce lift from their pectoral fins for hydrostatic equilibrium (Brill & Bushnell 2001). Consequently, during recovery of ram-ventilating species, it is necessary to hold the fish with sufficient water flow over the gills via a pump mechanism until adequate voluntary forward motion of the sedated animal returns. Walking the animal or pulling the animal manually

through the water to ventilate is a favored option amongst fish enthusiasts; however, this does not always provide adequate oxygenation and mechanical ventilation is strongly encouraged to move water over the gills, particularly with pelagic fish species.

In response to hypoxic environments or other selective pressures, many species have evolved anatomical, physiologic, and behavioral adaptations to meet their ventilatory needs (Graham 1997). In addition to elaboration of the basic gill design for improved oxygen extraction, a diverse array of accessory respiratory organs has evolved, with a number of species capable of utilizing atmospheric air (Mylniczenko 2021). For many species, increased aerial gas exchange surface area exists in portions of the alimentary canal (i.e., buccal and pharyngeal cavities) either as a direct proliferation of the respiratory surface or as a single or a pair of pouches extending from it (Ishimatsu & Itazawa 1993). Alternatively, branchial diverticulae may develop as in anabantoids (gouramis, bettas, climbing gouramis) (Graham 1997).

Many species take in atmospheric air with a behavior termed aquatic surface respiration (ASR). The fish position their mouths to skim the air:water interface, which is richer in oxygen. Some species (e.g., pacu, *Piaractus mesopotamicus*) respond to hypoxic conditions by developing temporary dermal swellings of the lower jaw to facilitate ASR (Rantin et al. 1993, 1998). Others (e.g., channids [snakeheads], anabantoids) employ alternate filling of an air-breathing chamber (labyrinth organ in anabantoids) with air and water during aerial ventilation (Ishimatsu & Itazawa 1993). Air-breathing fishes pose unique risks for anesthesia as they may be difficult to induce via immersion (shifting oxygen exchange away from gills to accessory air organs). :is also a theory that they may "drown" by not allowing access to air but this may also happen with deoxygenation of the water; either should be monitored (Graham 1997). Not all are obligate air breathers, some are facultative and less susceptible to environmental oxygen pressure.

Lungfish (the sister group to tetrapods) and polypterids (bichirs and reedfish) possess true lungs with ventrally situated pneumatic duct openings in the alimentary canal instead of a traditional gas or "swim" bladder (Graham 1997). Of these, the African (*Propterus* sp.) and South American lungfish (*Lepidosiren* sp.) are obligatory air-breathers (Bassi et al. 2005; Graham 1997). The Australian lungfish (*Neoceratodus fosteri*) possesses gills as well as a lung (Lenfant et al. 1966). Although anatomically challenging, it is theoretically possible to cannulate the pneumatic duct of lungfish for administration of inhalant anesthesia. Conceivably, chamber induction with gas (while somewhat submerged) may be possible but has not been reported. The Australian lungfish is the only facultative breather in the group but when placed in immersive anesthetics will attempt to breathe air and not respirate through its gills; drowning is a risk (both from lack of oxygen in the air and from water infiltrating the air space) (Farrell & Randall 1978). Immersion anesthesia with MS-222, benzocaine, and eugenol has been used in lungfishes. Oxygenation should be ensured once sedated via oxygen gas (or oxygenated water in animals with gills) (Christensen et al. 2015; Delaney et al. 1976; Lederoun et al. 2019; Lenfant et al. 1966; Monteiro et al. 2018; Mylniczenko, pers. exp.).

Understanding the anatomical and physiologic range of fish respiration is important for anesthesia for two reasons. First, immersion uptake and induction rate are linked to oxygen demand. For fish that depend primarily or entirely on dissolved oxygen in water, induction rates are shorter compared to those of air-breathing species. Responding to confinement or hypoxic anesthetic baths, the latter pull air from the water surface and reduce opercular movement. Some may temporarily stop opercular activity (Hseu et al. 1997). Injectable anesthetics can be used for induction of species capable of aerial respiration (e.g., anabantoids) (Bruecker & Graham 1993). Second, although many fish that utilize an accessory respiratory organ retain gills for aquatic gas exchange, effective gill tissue is so reduced in some species (e.g., channids, lepidosirenid lungfish, and clariids or walking catfish) they will succumb or "drown" if denied access to atmospheric air (Ishimatsu & Itazawa 1993; Peters et al. 2001). Perianesthetically, these species are maintained in very shallow water, or on a moist substrate, until capable of reaching the air:water interface regardless of the anesthetic route used.

Arapaima (*Arapaima gigas*) and other osteoglossids are also obligate air-breathing fishes that use a modified swim bladder for respiration (Brauner et al. 2004). Focused spraying of immersion drugs, like benzocaine and eugenol, on the gills is an effective method of induction (Honczaryk & Inoue 2010). Full immersion with benzocaine has been used in this species for anesthesia/euthanasia (Buzete Gardinal et al. 2019). One of the authors (Mylniczenko) has experience using high-dose MS-222 (1 g/L) over the gills to sedate larger species as well as low-dose immersion MS-222 (25 ppm) in combination with valium (10 mg/kg PO) for transport. Ketamine has been successful orally in this species for transport (Raines & Clancy 2009). There is also concern that these fish are at high risk for not recovering their air-breathing reflexes once anesthetized (Chu-Koo et al. 2009) or drowning during recovery (Pelster et al. 2020), though the authors have not experienced this.

Although notable exceptions exist (e.g., tarpon, *Megalops atlanticus*), few marine species have evolved adaptations

for hypoxic environments other than surface piping or migrating from the area. Consequently, marine species may be less tolerant of hypoxic conditions during anesthesia in comparison to the freshwater species discussed above (Rothwell et al. 2005).

Metabolism

Most fish are ectothermic and dependent on ambient temperature. Though exceptions exist for some cold-adapted species, lower temperatures are usually associated with prolonged induction and recovery times during either immersion or parenteral anesthesia (Gelwicks et al. 1998). This effect is reversed at higher temperatures (Detar & Mattingly 2004; Gomes et al. 2001; Peters et al. 2001; Stehly & Gingerich 1999). During immersion anesthesia, this relationship is primarily related to altered respiratory rate. Blood acid-base status is temperature dependent, with increased temperatures leading to acidemia and hypercapnia that stimulate hyperventilation. This decreases induction and recovery times for drugs taken up or eliminated from the gills (Aguiar et al. 2002; Stehly & Gingerich 1999).

Some fish (e.g., family Scombridae, tuna) have evolved various degrees of endothermy. They have the capacity to conserve metabolic heat in slow-twitch muscle, viscera, brain, and eyes, and to elevate body tissue temperature above ambient (Bushnell & Jones 1994). Tuna gills have large surface areas and thin epithelia compared to other fish (Brill & Bushnell 2001; Bushnell & Jones 1994) with a net result of enhanced oxygen uptake. Red cells with elevated hemoglobin levels are circulated by proportionally large hearts with high cardiac outputs (Blank et al. 2004; Bushnell & Jones 1994) to well-vascularized tissues. High myoglobin levels and aerobic enzymes enhance tissue oxygen extraction. Enzyme activity is particularly high in muscle; aerobic oxidation rates are three to five times greater than other teleosts (Bushnell & Jones 1994). Elevated enzymatic activity and counter-current heat exchangers raise muscle temperatures (Cooper et al. 1994). Endothermy leads to increased rate of anesthetic uptake and metabolism compared to similarly sized ectothermic species. More primitive Scombrids (e.g., bonitos, seerfishes, and mackerels) are not endothermic and lack physiologic characteristics of tuna such as the vascular countercurrent heat exchange mechanism. However, aerobic enzyme activity is similar and these scombrids represent a transition between ectothermy and tuna endothermy (Brill & Bushnell 2001; Williams et al. 2004).

Teleost fish have an anatomic separation between aerobic, slow-oxidative muscles (red muscle) and anaerobic, fast-twitch, glycolytic muscles (white muscle). In many species, a distinct pattern of highly oxygenated slow-oxidative muscle runs along the midline of the body. Given the increased capillaries, injection of anesthetic agents into this region may result in more rapid induction times compared to injections administered elsewhere (Williams et al. 2004), but in reality this layer is very thin and has large variation in thickness and location, making consistent injections difficult.

Integument

Although most fish possess scales, marked variation in distribution and structure exists. This has implications for administration of parenteral drugs by hand and remote injection. Species that have large, hard scales (e.g., tarpon, arapaima) are difficult to dart or pole syringe, while large cobia (*Rachycentron canadum*), with smaller scales, are relatively easy to inject.

For many fish, the skin is a respiratory organ and may be responsible for up to 30% of oxygen uptake in some species (Bruecker & Graham 1993). Most marine species have well-vascularized skin capable of significant cutaneous gas exchange (Ishimatsu & Itazawa 1993). Though scaleless species (e.g., catfish, Siluriformes) are better designed for cutaneous respiration, capacity often varies with age. Younger fish, regardless of size, tend to have thinner skin and less-developed scales, which results in greater oxygen uptake (Myszkowski et al. 2003). Fish species that produce larvae lacking gills require skin respiration until full differentiation of secondary gill lamellae occurs (Oikawa et al. 1994). Like other respiratory organs, skin is a route for immersion drug uptake and presumably excretion (Ferreira et al. 1984). Some scaleless types of common carp with high skin lipid content are much more efficient at cutaneous anesthetic uptake than rainbow trout (*Oncorhynchus mykiss*) with their small, densely packed scales and comparatively lower lipid content (Ferreira et al. 1984). In some instances, skin may be more efficient than other respiratory organs. In the electric eel (*Electrophorus electricus*), quinaldine uptake across the skin was higher than for the gills (Walsh & Pease 2002).

Size

Minimum effective anesthetic concentration is directly correlated with increasing body mass (Oikawa et al. 1994). This relationship is also true for toxic concentrations. For example, MS-222 LC_{50} increases with growth in rainbow trout, brown trout (*Salmo trutta*), lake trout (*Salvelinus namaycush*), largemouth bass (*Micropterus salmoides*), and channel catfish (*Ictalurus punctatus*) (Oikawa et al. 1994).

Environmental and Other Factors

Temperature

In addition to metabolism, dissolved oxygen (DO) concentrations are influenced by temperature. At higher temperatures, DO decreases and this exacerbates any anesthetic induced hypoxia. Warmer temperatures also promote solubilization of immersion anesthetics while cooler temperatures promote precipitation.

pH

The pH of immersion solutions will influence efficacy, possibly by affecting the ratio of charged to uncharged molecules. In general, decreased efficacy is seen as the pH drops due to increased ionization, which interferes with absorption. Unfortunately, most immersion anesthetics (e.g., MS-222 and quinaldine) in solutions are acidic, requiring buffering agents (e.g., sodium bicarbonate) to neutralize the pH. In addition to promoting immersion anesthetic efficacy (Ferreira et al. 1984), buffers can help prevent metabolic acidemia, a condition precipitated by anesthetic-induced hypoxemia and anaerobic metabolism. Saltwater, with its higher pH and greater natural buffering capacity compared to freshwater, has been shown not to require addition of buffering agents in some studies (Harms & Bakal 1995; Harms 1999; Oikawa et al. 1994; Ross & Ross 1984; Ross 2001), but in the authors' experience at least MS-222 requires buffering and produces much more favorable results when that occurs. At some institutions, it is common practice to buffer marine water with sodium bicarbonate at a 2:1 ratio (2 parts bicarbonate, 1 part MS-222 based on weight). An alternative to automatic addition of a buffer is to test the pH of the anesthetic water and adjust the pH accordingly. It has recently been found that sodium carbonate is a better buffer than bicarbonate (Burns, pers. exp.; Waxman et al. 2021). Regardless of the method used, one should keep in mind that pH shifts may have metabolic effects on the fish not solely related to anesthetic efficacy, especially if exposure is prolonged. That said, in an unpublished study by one of the authors (Clauss) with crevalle jacks (*Caranx hippos*), there was no significant short-term difference in blood gas values from fish anesthetized in buffered or unbuffered MS-222. Regardless, species differences exist and without a controlled study, it is advised to buffer or measure water pH. Bicarbonate itself is considered an anesthetic (due to the secondary effects of carbon dioxide narcosis) at 50–100 g/L and has been used in freshwater fishes (Avillanosa & Marlowe 2019; Caipang et al. 2021) (see also under the CO_2 section).

Nitrogenous Compounds

Buildup of nitrogenous compounds, particularly ammonia and nitrite, can damage or induce changes in gill morphology that affect uptake and clearance of immersion anesthetics. In addition, compromised oxygen uptake affects metabolism, including that of parenteral and immersion anesthetic agents, and can lead to acidemia. When anesthetic immersion water is used for an extended period of time for one animal or is reused for consecutive procedures, there is risk of nitrogenous compound elevations. Water changes during an extended procedure or between procedures will ameliorate these effects. Additionally, measuring the water's ammonia content during the procedure will alleviate concerns and guide actions.

Drug Concentration or Dosage

At a given temperature, higher concentration immersions or drug dosages generally decrease induction and increase recovery times. However, recovery time from some immersions is independent of concentration (Hseu et al. 1997, 1998).

Drug Exposure Time

Increased immersion anesthetic exposure time usually results in increased recovery time. This effect is often associated with progressive hypoxemia and metabolic acidemia due to prolonged hypoventilation. Some immersion drugs (e.g., MS-222) continue to increase in brain and muscle despite blood equilibration. Therefore, an initially satisfactory drug dosage can produce progressively deeper anesthesia and respiratory arrest, even during recovery when the fish is in anesthetic-free water (Ross 2001). Thus, using graded anesthesia, higher dose rapid induction, and lower dose maintenance levels is sound practice. This practice has shown to reduce overall levels of physiologic stress in some species (Matsche 2011). Additionally, dilution of the anesthetic water in a longer procedure while maintaining the anesthetic plane is a good method to reduce recovery time.

Vascular Access

Most fish fall under a similar body plan and accessing their blood vessels is fairly straightforward. The caudal tail vein is accessible via the ventral midline or with a lateral approach (Fig. 8.1). Cardiac puncture is sometimes the only viable option in species where the tail is either covered by large, thick scales (e.g., parrot fish, arowana, and



Figure 8.1 (a) Midline caudal tail venipuncture at a slight oblique angle in a green moray eel (*Gymnothorax funebris*) restrained in a plastic bag with mild sedation. (b) Lateral approach to caudal vein in a sedated green moray eel (*Gymnothorax funebris*).

arapaima) that prevent access without removal of scales, or where removal would result in significant skin exposure (Fig. 8.2a,b). In large fish, spinal needles may be required due to the depth of the vessels. Cardiac puncture can be achieved by moving the operculum and inserting the needle through the skin that is cranial to the bulbus arteriosus/ventricle or ventrally through the body wall. Access to the dorsal aorta is also available through the oral cavity, midline, and immediately posterior to the hard palate (Fig. 8.2c). There is a periorbital sinus that can be reached through the oral cavity (e.g., Australian lungfish). A vessel can be found in some species along the gill arch and can be another area to draw blood (Fig. 8.2d).

Intravenous catheterization of fishes is possible but not common (Ostrander 2000; Vergneau-Grosset & Benedetti 2022). In certain settings, typically research, dorsal aorta cannulation can be performed, but it requires anchoring specialized tubing through the roof of the mouth and through the rostrum, and fixing to the dorsal fin or muscle of the fish (Smith & Bell 1964; Sovio et al. 1972). The ventral aorta is cannulated in a similar fashion but using the lower jaw. The caudal vein can be catheterized as well and uses similar tubing as described above or with standard catheters (Ostrander 2000; Smith & Bell 1964; Sovio et al. 1972; Vergneau-Grosset & Benedetti 2022). The apparatus must be affixed to the animal to prevent slippage of the catheter. In fast-moving fishes, maintaining such catheters is nearly impossible, therefore confinement may be necessary, which carries its own obvious stressors (Sumpter et al. 1986). Additionally, the shape of the oral cavity and location of the vessel make some of these approaches impossible.

Immobilization Methods and Techniques

Manual Restraint

Manual restraint, when managed appropriately, can be used for doing simple, short procedures or when preparing the animal for induction of anesthesia. For procedures lasting longer than several minutes, it is best to use chemical immobilization. Animals that are habituated or domesticated tend to tolerate handling and restraint better than nonacclimated fish. See also the operant conditioning section in this chapter.

Considerations for human safety with manual restraint should include bites, stings, abrasions, and physical trauma due to thrashing. Even with chemical immobilization, the following should be considered so that appropriate safety precautions are utilized. Venom can occur in the dorsal or pectoral spines of scorpionfish, toadfish, rabbitfish, and a number of other fishes (Williamson et al. 1996). Sharp spines or other protuberances, such as with the acanthuridae (tangs, surgeonfish) or some tetraodontidae (porcupine pufferfishes), can cause significant damage without protective clothing. Teeth have vast anatomic variety and can crush, puncture, and/or macerate. In some species, pharyngeal teeth located deep in the oral cavity can cause trauma, particularly if the handler is unaware of their presence. Finally, there is the unique group of electric animals (electric eels, Mormyridiformes, Gymnotiformes) that pose varying risks. An electric eel can produce 550 V (~1 amp), which can be fatal to a human (Harms 2003), while some mormyrids produce <1000 Hz, used for communication and electrolocation (von der Emde 1999). Wearing gloves

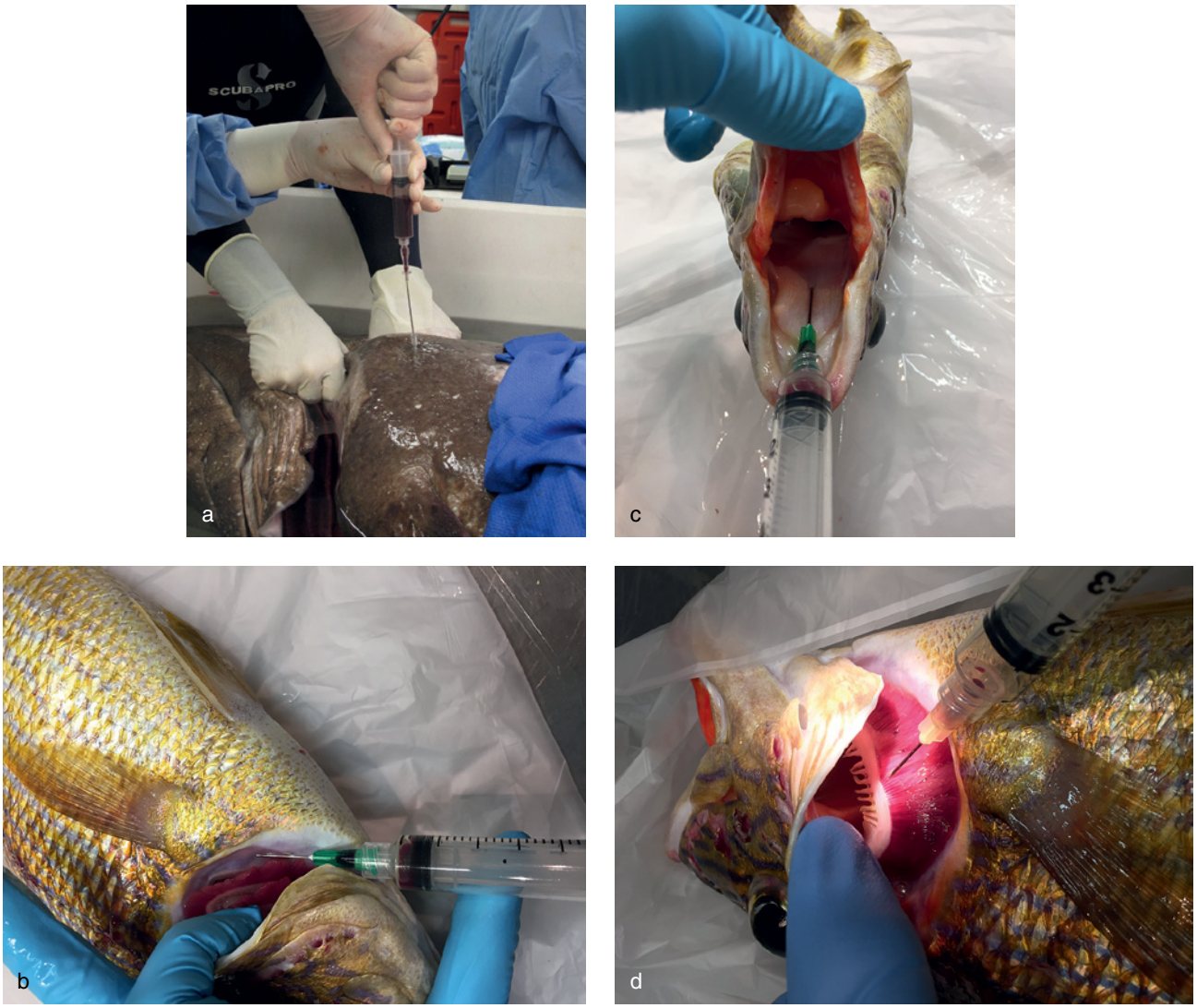


Figure 8.2 (a) Cardiac venipuncture in a giant grouper (*Epinephelus lanceolatus*) using a 16-gauge spinal needle. (b) Cardiac venipuncture in a French grunt (*Haemulon flavolineatum*). (c) Venipuncture of the dorsal aorta in the oral cavity of a French grunt (*Haemulon flavolineatum*). (d) Venipuncture along the gill arch in a French grunt (*Haemulon flavolineatum*) necropsy specimen.

that do not transmit electric current is beneficial. Several case reports have been published highlighting some best practices with these species (Poll et al. 2014; Wenger et al. 2016, 2018).

Regarding animal safety, the tubular, soft-bodied fishes are particularly challenging to hold without crushing them. Furthermore, the mucus on the skin of fishes is very slippery and, in some species, copious. This can make it challenging to securely restrain the animal and can lead to long-term consequences should the mucus be removed. Wearing disposable gloves that have been rinsed free of powder (an irritant to fish) helps with minimizing damage to fish skin and mucus, but can make secure handling more challenging. Wet materials such as cloth diapers, flannel, bubble wrap, and chamois used for automobiles are both soft and smooth, and can be useful in restraining some fish without damaging or altering the skin and mucous layer. Some fishes are scaleless and require more delicate handling to avoid abrading the skin. Additionally, keeping some basic facts in mind (such as fish lack eyelids) will help in avoiding simple mistakes. Handling can result in microabrasions and ports of entry for foreign bacteria (Foster et al. 2020). The empirical treatment of adding a topical like sodium hyaluronate is helpful to prevent progression of these minor traumas.

Nets of varying sizes and configurations (dip, seine, and box) are the first-choice tool for catching and restraining many fishes. For delicate-skinned fish, nets made of plastic or very soft fine mesh should be used (Fig. 8.3a,b), but alternately, clear plastic bags can be used. In some



Figure 8.3 (a) Soft rubber net with clear plastic. (b) Large soft rubber net.

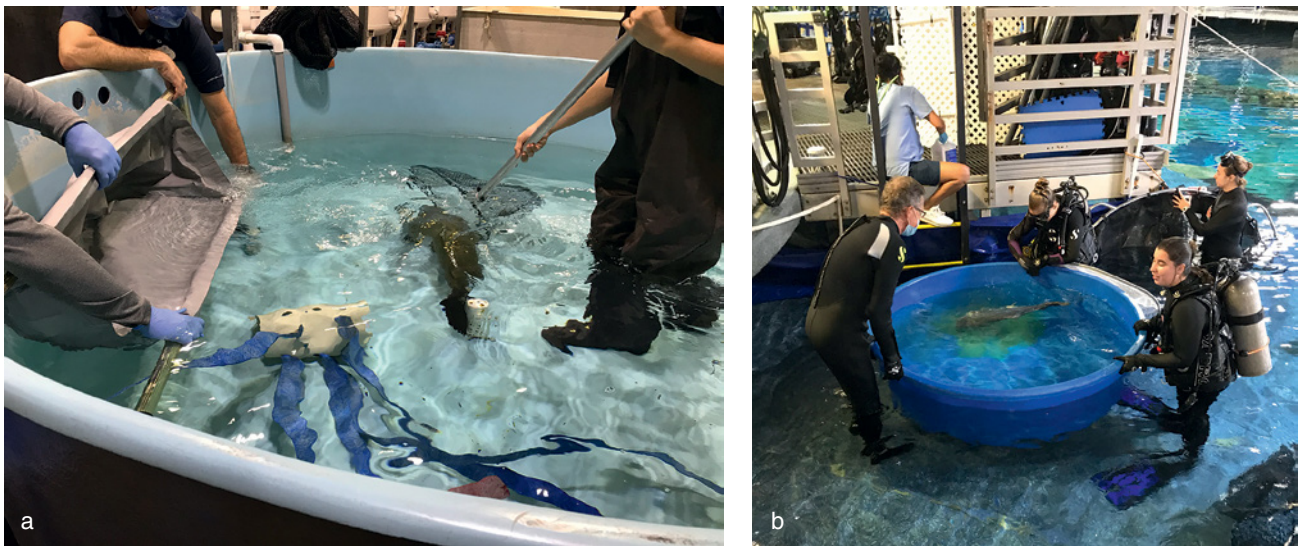


Figure 8.4 (a) Corralling a black pacu, tambaqui (*Colossoma macropomum*), fish into a sling for transfer. (b) A pool within a pool to facilitate sedation of large fish in smaller immersion volumes. The yellow tinge to the water is eugenol.

circumstances, as in large exhibits, even the hook and line approach has been successfully used. It is important to note, however, that as with wild fishes, hook traumas can pose risks to the fish and the process can be fatal as a result of exhaustive exercise.

Animals that struggle should be sedated. The concept of "learned helplessness", as with mammals, is not an appropriate parallel to draw. The fish that "gives up" is stressed and depleted of energy. Anticipation of how a fish will manage manual restraint is crucial.

Larger fish can be netted and placed in a sling (Figs 8.4 and 8.5a) but care needs to be taken when lifting; the integrity of the net must be solid and it should have drainage holes. These animals should only be moved for purposes of sedation and no further manipulation should occur due to human and animal safety concerns. One method more recently introduced for elasmobranchs handling and anesthesia (see Chapter 7) is also an effective method for larger teleosts such as grouper. This technique entails the use of a large vinyl bag with a narrow end that is open to allow water flow and a larger opening to catch the animal; this technique is best used in trained, partially sedated or sedated animals. At the Seas, Walt Disney World, Orlando, FL, a goliath grouper (*Epinephelus itajara*) was pre-sedated with oral valium, moved into the bag, and then further sedated with high doses of tricaine methanesulfonate in a 6-million-gallon aquarium and safely brought to the surface.

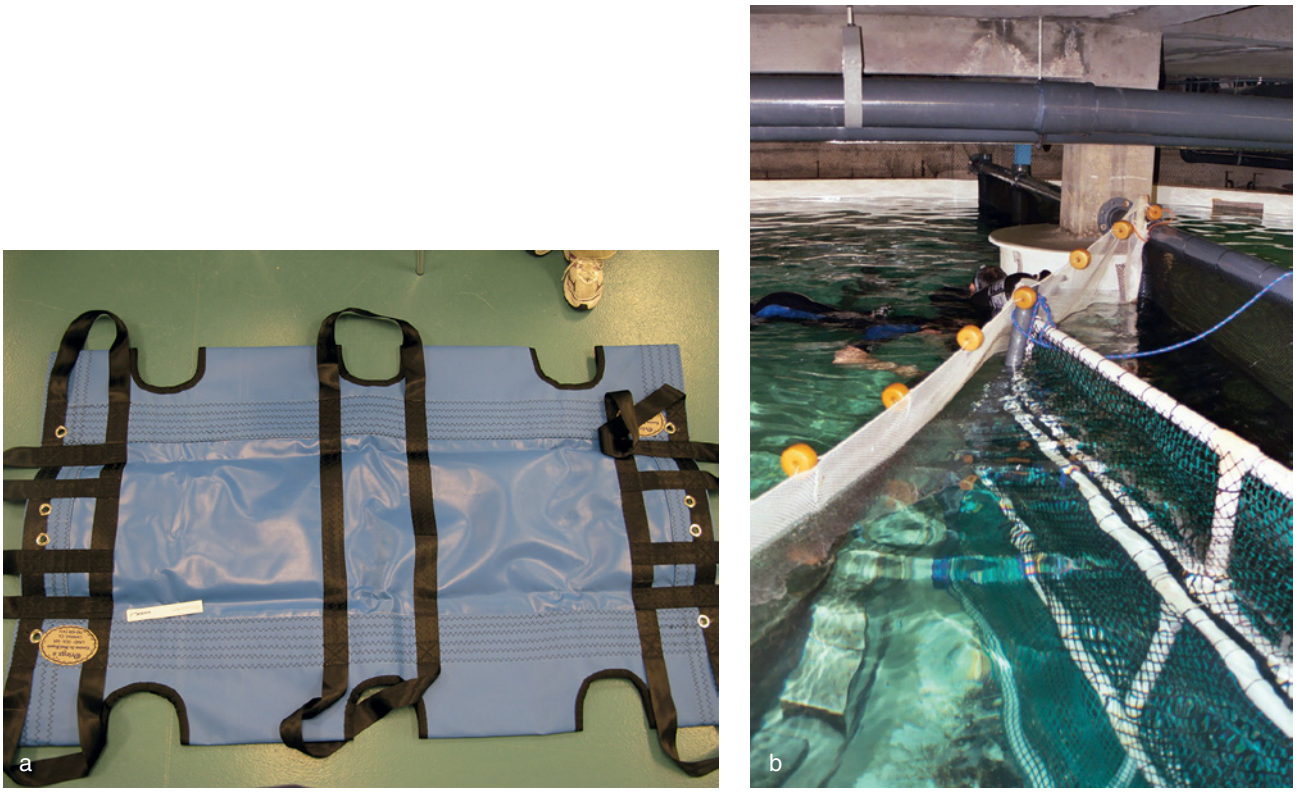


Figure 8.5 (a) Sling designed to lift large aquatic animals. (b) Squeeze device designed from polyvinyl pipe and plastic mesh. To the left of the squeeze is a net that reduces the space of the tank. The animal was corralled into the right side of the polyvinyl/mesh (animal is the far-right bottom corner).

An additional important consideration for manual restraint is time out of the water. In several studies, exposure to air increased mortality rates of angler-caught fishes (Ferguson & Tufts 1992; Gingerich et al. 2007; Veldhuizen et al. 2018). In another study, while there were no mortalities, there was significant morbidity (Schreer et al. 2005). Severity is species variable, as fishes that require oxygen-rich environments (e.g., trout) are more profoundly affected by air exposure and become acidotic with even short exposure times to air.

Operant Conditioning

Operant conditioning in fish is not a new concept and is critical to accomplish several husbandry behaviors and reduce stress (Alderman & Clayton 2021; Benhaïm et al. 2017; Bloch et al. 2019; Clayton & Mcdermott 2021; Couvillon 1984; Salena et al. 2021; Sison & Garlai 2010; Wright & Eastcott 1982). Many fish can be trained to move into certain areas of their enclosure, to swim into nets, crates, or pools. The size of the animal is not a restriction and schools of fish can be trained as well. In larger animals, operant conditioning can be an invaluable tool to isolate animals for brief examinations, treatments, or for facilitating chemical administration for inducing anesthesia (Fig. 8.6).

For induction of anesthesia, it is best to reduce the area where an animal can swim so that immersion anesthetics can be used in smaller volumes, injections are more achievable, or so that high-dose immersion agents (discussed later) can be administered with ease. Corralling animals into smaller areas with baffles, bringing them over slings (Fig. 8.4) and allowing the sling to come up around the animal's body, moving them into small inflatable pools, and finally, "squeeze" areas (Fig. 8.5) are all methods that facilitate examination, minor procedures (e.g., praziquantel immersion treatments) as well as anesthetic induction. Training animals to shift into containers like a PVC box or a plastic bin or over/into stretchers are also good options to achieve closer contact.

Fish cognitive abilities allow individuals or groups to respond to visual, auditory, or olfactory cues, and as such they can be trained or conditioned much like you would train any higher vertebrate (Alderman & Clayton 2021; Benhaïm et al. 2017; Bloch et al. 2019; Clayton & McDermott 2021; Couvillon 1984; Sison & Garlai 2010; Wright & Eastcott 1982; Salena et al. 2021).

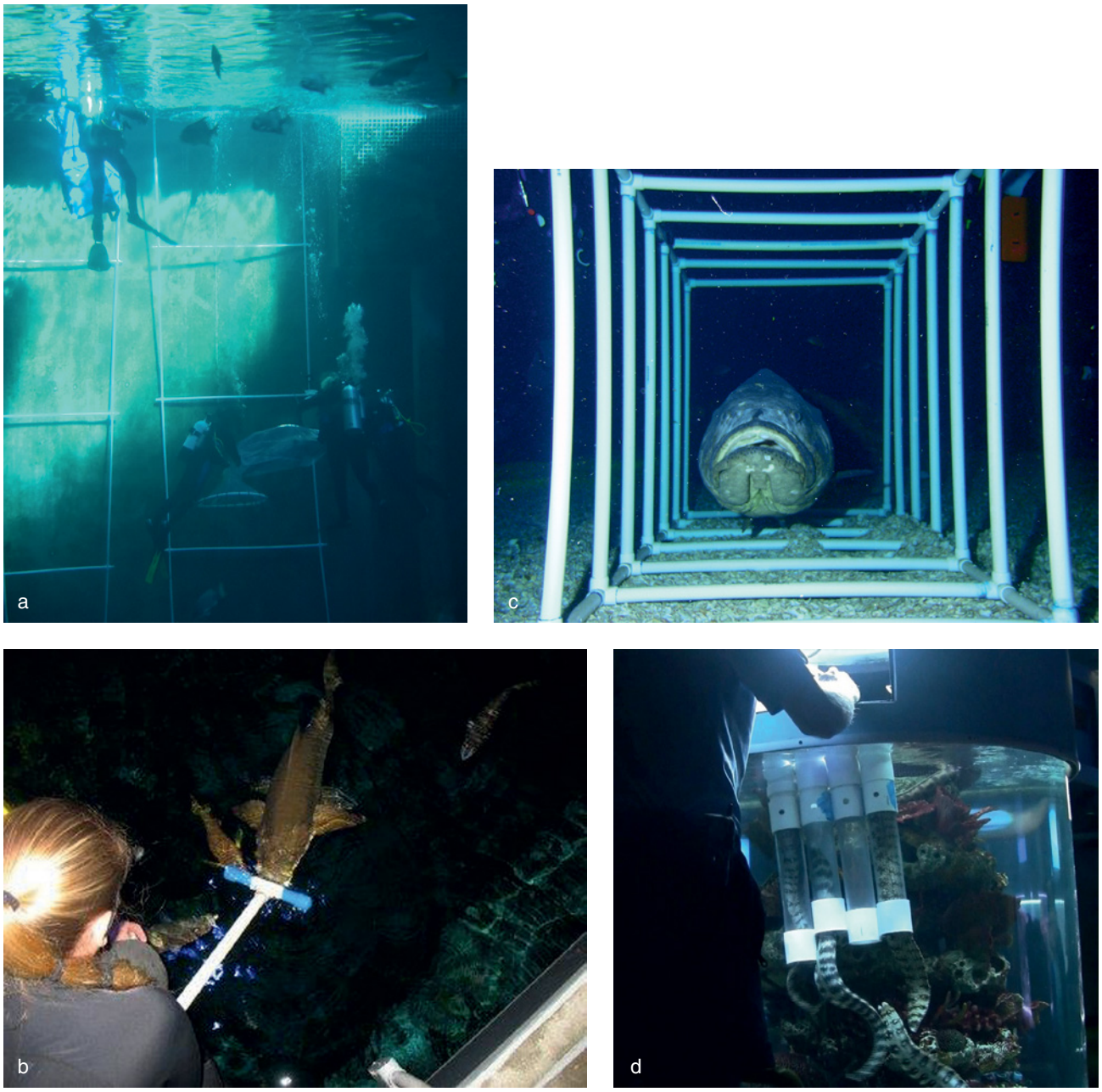


Figure 8.6 (a) Underwater image of a grouper (*Epinephelus itajara*) being transported in a vinyl sock to the surface after initial induction of high dose MS-222 delivered by a power sprayer. (b) Operant conditioning of a cobia (*Rachycentron canadum*). Note the animal is targeting a T-shaped piece of polyvinyl pipe. (c) Operant conditioning of a goliath grouper (*Epinephelus itajara*). The animal swims into a polyvinyl pipe box which can then be closed/secured to reduce the functional swimming space of the animal. (d) Operant conditioning of eels to enter a clear plastic tube for target feeding.

General Suggestions for Anesthesia

Before anesthetizing an unfamiliar species the anesthesiologist should perform a review of the available literature. Despite limited fish anesthesia publications, a literature search using the scientific name along with words or phrases such as "physiology", "anatomy", "site fidelity", "fecundity", "population assessment", etc., will identify studies that required sedation or anesthesia. Table 8.1, while listing anesthetic regimens for representatives of many families, is far from exhaustive and was accomplished, in part, as suggested above. Careful review of age class and body size in the literature should be considered when using these dosages and regimens because many studies utilize young or small fish. For example, drug

Table 8.1 A review of selected anesthetic agents used in fish anesthesia.

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Order Petromyzontiformes											
Family Petromyzontiformidae											
Entosphenus tridentatus	Lamprey, Pacific	Benzocaine, 20%	40, 60, 80 mg/L	Immersion		0.0.30			60 mg/L allowed handling at 4 minutes and recovery <6 minutes. Slight to moderately agitated on exposure, fish tended to remain attached to the recovery container wall.	Christiansen et al. (2013)	Most effective dose: 60 mg/L.
Entosphenus tridentatus	Lamprey, Pacific	Isoeugenol	50, 100, 200 mg/L	Immersion		0.0.30			100 mg/L allowed handling at <7 minutes and recovery <8 minutes. Animals extremely agitated.	Christiansen et al. (2013)	Most effective dose: 100 mg/L. Juveniles extremely agitated on exposure.
Entosphenus tridentatus	Lamprey, Pacific	Metomidate hydrochloride HCL (Aquacalm)	50, 75, 100 mg/L	Immersion		0.0.30			Fastest handling time 10 minutes, recovery same time. Better options.	Christiansen et al. (2013)	No effective concentration was identified. Juveniles showed slight agitation on exposure.
Entosphenus tridentatus	Lamprey, Pacific	MS-222 (tricaine methanesulfonate) (Finquel)	50, 100, 200 mg/L	Immersion		0.0.30	Juvenile	12	100 mg/L of MS-222 allowed handling at 4 minutes, recovery <3 minutes.	Christiansen et al. (2013)	Most effective dose: 100 mg/L. Moderate agitation on exposure.
Order Myxiniformes											
Family Myxinidae											
Eptatretus cirrhatus	Hagfish, broadgilled	MS-222 (tricaine methanesulfonate) + benzocaine	0.4 g/L + 0.4 g/L	Immersion	~1100 g			12–14	Animals required 60 minutes for surgical anesthesia, but effects lasted for 30 minutes after removal from immersion.	Foster & Forster (2007)	Prolonged induction to reach surgical plane; effects for 30 minutes after removal.
Eptatretus stoutii	Hagfish, Pacific	Clove oil	50, 100, 150, 200, 250, 300, 350, 400 mg/L	Immersion		0.0.104		5	Recommend 175 mg/L of clove oil for routine laboratory use.	McCord et al. (2020)	Recommended dose: 175 mg/L of clove oil.
Eptatretus stoutii	Hagfish, Pacific	2-phenoxyethanol		Immersion						McCord et al. (2020)	
Eptatretus stoutii	Hagfish, Pacific	MS-222 (tricaine methanesulfonate)		Immersion						McCord et al. (2020)	
Order Dipnoi											
Family Neoceratodontidae											
Neoceratodus forsteri	Lungfish, Australian	MS-222 (tricaine methanesulfonate)	100 mg/L; 125 mg/L induction to 75 mg/L maintenance	Immersion			Adult			N.D. Mylniczenko (pers. exp.)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Order Ceratodontiformes											
Family Lepidosirenidae											
Lepidosiren paradoxa	Lungfish, South American	Benzocaine	0.50%	Immersion	864 ± 169 g		Adult	25		Fernandes et al. (2004)	
Lepidosiren paradoxa	Lungfish, South American	Benzocaine	0.5 g/L –> 0.25g/L	Immersion	0.26 ± 0.2			24 ± 2	Animal placed in surgical tray with access to air, lowering to maintenance dose 0.25g/L. Recovery 20–30 minutes.	Monteiro et al. (2018)	
Family Protopteridae											
Protopterus aethiopicus	Lungfish, marbled	MS-222 (tricaine methanesulfonate)	0.50%	Immersion	2–14 kg				Used for catheter placement into the branchial arch.	Delaney et al. (1976)	
Protopterus annectens	Lungfish, West African	Medetomidine + ketamine	0.053 mg/kg + 5.26 mg/kg	Immersion	1.3 kg				Recommend higher dose.	D.L. Neiffer (pers. exp.)	Mild sedation, insuffiicient for diagnsotic workup.
Protopterus annectens	Lungfish, West African	Clove oil (100% pure)	0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1 ml/L	Immersion	50.3 ± 5.5 g			26.3 ± 1.2	The optimum concentration of benzocaine is between 1.8 and 2.6 ml/L.	Lederoun et al. (2019)	Clove oil > benzocaine and is effective at lower concentrations.
Protopterus annectens	Lungfish, West African	Benzocaine	0.85, 0.9, 0.95, 1.2, 1.5, 1.8, 2.1, 2.4, 2.5, 2.6, 2.7 ml/L	Immersion	50.3 ± 5.5 g			26.3 ± 1.2	The optimum concentration of benzocaine is between 1.8 and 2.6 ml/L.	Lederoun et al. (2019)	
Class Actinopterygii											
Order Acanthuriformes											
Family Acanthuridae											
Acanthurus bahianus	Surgeonfish, ocean	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion	~60 g				Sedation rated fair to good. Examinations performed.	D.L. Neiffer (pers. exp.)	Fair to good sedation level.
Acanthurus chirurgus	Doctorfish	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion	0.8–1.2			25	Provided surgical anesthesia for enucleation.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for enucleation.
Acanthurus chirurgus	Doctorfish	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion				25	Diagnostic examination, radiographs, surgery.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination, radiographs, surgery.
Acanthurus coeruleus	Surgeonfish, blue tang	MS-222 (tricaine methanesulfonate)	85 mg/L	Immersion				25	Sedation rated excellent. Examination and topical treatment performed.	D.L. Neiffer (pers. exp.)	Sedation rated excellent.
Acanthurus coeruleus	Surgeonfish, blue tang	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion			Adult	25	Diagnostic examination, laceration repairs.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination, laceration repairs.
Acanthurus japonicus	Tang, powder-brown	MS-222 (tricaine methanesulfonate)	50–70 mg/L	Immersion				25	Diagnostic examination.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination.

Acanthurus leucosternon	Surgeonfish, powder-blue	MS-222 (tricaine methanesulfonate)	50–70 mg/L	Immersion		25	Sedation rated excellent. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated excellent.
Acanthurus lineatus	Surgeonfish, lined	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion		25	Diagnostic examination, radiographs.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination, radiographs.
Acanthurus sohal	Surgeonfish, sohal	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion		25	Sedation rated good. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)	Good sedation.
Naso brevirostris	Unicornfish, spotted	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	~400 g	25	Go high and dilute down to prevent damage to horn.	C.M. Burns (pers. exp.)	Recommend high to low dose to prevent damage to horn.
Naso lituratus	Unicornfish, orangespine	MS-222 (tricaine methanesulfonate)	70–120 mg/L	Immersion	~300 g	25	Diagnostic examination, radiographs.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination, radiographs.
Naso unicornis	Unicornfish, bluespine	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion		25	Go high and dilute down to prevent damage to horn.	C.M. Burns (pers. exp.)	Recommend high to low dose to prevent damage to horn.
Paracanthurus hepatus	Tang, regal blue	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion		25	Diagnostic examination, laceration repairs, surgery.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination, laceration repairs, surgery.
Zebrasoma flavescens	Tang, yellow	MS-222 (tricaine methanesulfonate)	50–70 mg/L	Immersion	16–40 g	25	Diagnostic examination.	C.M. Burns (pers. exp.)	Sufficient sedation for diagnostic examination.
Family Ephippidae									
Chaetodipterus faber	Spadefish, Atlantic	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion	0.22–2.32		Effect varied from mild sedation at lower doses to surgical anesthesia at 100 mg/L, $N = 11$.	D.L. Neiffer (pers. exp.)	Variable effects ranging from mild sedation to surgical anesthesia.
Platax orbicularis	Batfish, orbicular	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion	2			C.M. Burns (pers. exp.)	
Platax teira	Batfish, longfin	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion	2			C.M. Burns (pers. exp.)	
Platax pinnatus	Batfish, pinnate	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion	2			C.M. Burns (pers. exp.)	
Family Lobotidae		MS-222 (tricaine methanesulfonate)							
Lobotes surinamensis	Tripletail	MS-222 (tricaine methanesulfonate)	70–90 mg/L	Immersion	21	25	Light to good plane of anesthesia for diagnostic examination/debridng wounds.	C.M. Burns (pers. exp.)	
Family Sciaenidae		MS-222 (tricaine methanesulfonate)							
Sciaenops ocellatus	Drum, red	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion		26–27	Anesthesia induced in 2.5–6 minutes. Sufficient for handling and phlebotomy. pH = 7.7–7.8.	Thomas & Robertston (1991)	Sufficient sedation for handling and phlebotomy.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Sciaenops ocellatus	Drum, red	Metomidate hydrochloride	7 mg/L	Immersion				26–27	Anesthesia induced in 3–7 minutes. Sufficient for handling and phlebotomy. pH = 7.7–7.8.	Thomas & Robertston (1991)	Sufficient sedation for handling and phlebotomy.
Sciaenops ocellatus	Drum, red	Quinaldine sulfate	20 mg/L	Immersion				26–27	Anesthesia induced in 2–4 minutes. Sufficient for handling and phlebotomy. pH = 7.7–7.8.	Thomas & Robertston (1991)	Sufficient sedation for handling and phlebotomy.
Atractoscion nobilis	Weakfish, white	Isoeugenol	15, 25, 35, 55, 75, 100 mg/L	Immersion		0.0.75	Juvenile	22 ± 0.64	We found that a dose range of 25–55 mg/L provided an effective plane of anesthesia (stage II, plane II) for a 10-minute procedure in our cultured WSB with no associated postanesthetic mortality.	Silbernagel & Yochem (2016)	
Family Zanclidae											
Zanclus cornutus	Idol, moorish	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Sedation rated as excellent. Examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated as excellent.
Order Acipenseriformes											
Family Acipenseridae											
Acipenser baerii	Sturgeon, Siberian	Clove oil	50, 100, 200, 400 mg/L	Immersion			Prolarvae	19–20	Reached anesthesia between 50 and 280 seconds.	Kim & Nam (2018)	Prolarvae treated with clove oil reached anesthesia <5 seconds.
Acipenser baerii	Sturgeon, Siberian	Lidocaine	50, 100, 200, 400 mg/L	Immersion					Reached anesthesia between 35 and 100 seconds.	Kim & Nam (2018)	
Acipenser baerii	Sturgeon, Siberian	MS-222 (tricaine methanesulfonate)	50, 100, 200, 400 mg/L	Immersion					MS-222 also showed dose-dependent decrease of anesthetic times, 15–125 seconds.	Kim & Nam (2018)	MS-222 showed dose-dependent decrease of anesthetic times.
Acipenser baerii	Sturgeon, Siberian	MS-222 (tricaine methanesulfonate)	80, 100, 120, 140, 160 mg/L	Immersion	30–50 g		Juvenile	~16	Concentration of MS-222 for juveniles is between 80 and 120 mg/L.	Feng et al. (2011)	
Acipenser baerii	Sturgeon, Siberian	Clove oil (85% eugenol)	60, 90, 120, 150, 180 mg/L	Immersion	30–50 g		Juvenile	~16	Concentration of clove oil for juveniles is between 60 and 90 mg/L.	Feng et al. (2011)	
Acipenser gueldenstaedtii	Sturgeon, Russian	Clove oil	0.20–0.75 g/L	Immersion		0.0.44	Larvae	18	Sedated 3 minutes, recovery in 5 minutes at 0.20 g /L.	Akbulut et al. (2011)	Effective anaesthetic in larvae; higher doses had prolonged the recoveries.
Acipenser gueldenstaedtii	Sturgeon, Russian	Isoeugenol	50 mg/L	Immersion	22.25 ± 7.64	0.0.23	Adult	24.3–25.1	Time to reach handling 1 minute and 30 seconds, sedation 2 minutes and 30 seconds with ~6 minutes sedation and recovery of 9 minutes.	Cassle et al. (2021)	

Acipenser oxyrinchus oxyrinchus	Sturgeon, Atlantic	MS-222 (tricaine methanesulfonate)	100, 150, 200, 250 mg/L (induction), 70, 85, 100 mg/L (maintenance)	Immersion	~4		Juvenile	14 ± 24	Minimum 85 mg/L. Surgical dosing was 250 mg/L induction then to 70–100 mg/L. 45-minute procedure.	Matsche (2011)	Reccomended dose: 85 mg/L. Surgical dosing: 250mg/L.
Acipenser persicus	Sturgeon, Persian	Clove oil (80% eugenol)	25, 50, 75, 100 mg/L	Immersion	6.88 ± 0.9 g	0.0.15	Juvenile	21.5 ± 1.3	Useful concentrations of anesthetics tested were between 25 and 50 mg/L.	Adel et al. (2016)	Recommended dose: 25 and 50 mg/L for clove oil, less than 1 mg/L for propofol, 330 mg/L for 2-PE, and none for ketamine HCl.
Acipenser persicus	Sturgeon, Persian	Propofol (Rapinovet®)	1, 1.25, 2.5, 5 mg/L	Immersion	6.88 ± 0.9 g	0.0.15	Juvenile	21.5 ± 1.3	Useful concentrations of anesthetics tested were less than 1 mg/L for propofol.	Adel et al. (2016)	Recommended dose: between 25 and 50 mg/L for clove oil, less than 1 mg/L for propofol, 330 mg/L for 2-PE, and none for ketamine HCl.
Acipenser persicus	Sturgeon, Persian	2-phenoxyethanol	110, 330, 550, 770 mg/L	Immersion	6.88 ± 0.9 g	0.0.15	Juvenile	21.5 ± 1.3	Useful concentrations of anesthetics tested were 330 mg/L for 2-PE.	Adel et al. (2016)	Reommended dose: between 25 and 50 mg/L for clove oil, less than 1 mg/L for propofol, 330 mg/L for 2-PE, and none for ketamine HCl.
Acipenser persicus	Sturgeon, Persian	Ketamine hydrochloride	1250, 2500, 3750, 5000 mg/L	Immersion	6.88 ± 0.9 g	0.0.15	Juvenile	21.5 ± 1.3	None of the tested concentrations for ketamine HCl were clinically useful.	Adel et al. (2016)	Recommended dose: between 25 and 50 mg/L for clove oil, less than 1 mg/L for propofol, 330 mg/L for 2-PE, and none for ketamine HCl.
Acinpenser pxyrinchus desotoi	Sturgeon, Gulf	MS-222 (tricaine methanesulfonate)	250 mg/L (induction), 87.5mg/L (maintenance)	Immersion	13–17	0.0.17	5–8 years	18–21	Time to induction was 7–11 minutes. Recovery <13 minutes on endoscopic procedure.	Hernandez-Divers et al. (2004)	
Acinpenser pxyrinchus desotoi	Sturgeon, Gulf	Medetomidine + ketamine, atipamezole	.06 mg/kg + 6 mg/kg, reverse 0. mg/kg	IM	~4		4 years	21.6 ± 3.1	Light plane of anesthesia for minor diagnostic procedures within 10 minutes. Mild bradycardia and respiratory depression noted. Atipamezole administered 30 minutes after immobilizing agents. Full recovery by 30 minutes. No mortality.	Fleming et al. (2003)	Mild bradycardia and respiratory depression. No mortality.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Acinpenser pxyrinchus desotoi	Sturgeon, Gulf	Propofol	6.5 mg/kg	IV	~4		4 years	21.6 ± 3.1	Light plane of anesthesia for minor diagnostic procedures within 5 minutes. Mild bradycardia and respiratory depression noted, with latter persisting for 60 minutes. Fish remained quiet and unresponsive for 40 minutes. At 60 minutes 70% were struggling at pre-injection levels. All fish fully recovered within 120 minutes. No mortality.	Fleming et al. (2003)	Mild bradycardia and respiratory depression. Longer recoveries with no mortality.
Acipenser transmontanus	Sturgeon, white	Clove oil	50–100 mg/L	Immersion	206–363 g				Induction 3–6 minutes. Exposed for 10 minutes. Recovery 4.5–8.5 minutes. No mortality. A dosage of 25 mg/L was effective in anesthetizing all species for 120 minutes without mortality.	Taylor & Roberts (1999)	Recommended dose: 25 mg/L.
Acipenser transmontanus		Ketamine	77–88 mg/kg	IM	5–7.7				Induction 4–7 minutes. Effect lasted 6 hours.	Williams et al. (1988)	Long-lasting effect.
Acipenser ruthenus × *Huso huso*	Sturgeon, hybrid	MS-222 (tricaine methanesulfonate)	100–125 mg/L	Immersion	1.36–2.34	0.0.10			Variable effect from mild sedation to light anesthesia.	Clauss (pers. exp.)	Variable effect from mild sedation to light anesthesia.
Acipenser naccarii × *Acipenser baerii*	Sturgeon, hybrid	Clove oil	100 mg/L	Immersion					MS-222 (3.2 minutes) compared with CLO (4.7 minutes) and MK (5.4 minutes). Recovery time was significantly longer inMK anesthetized fish (16 minutes) in comparison with CLO. (5.8 min) and MS-222 (3.8 min).	Di Marco et al. (2011)	
Acipenser naccarii × *Acipenser baerii*	Sturgeon, hybrid	MS-222 (tricaine methanesulfonate)	150 mg/L	Immersion					MS-222 (3.2 minutes) compared with CLO (4.7 minutes)and MK (5.4 minutes). Recovery time was significantly longer inMK anesthetized fish (16 minutes) in comparison with CLO. (5.8 min) and MS-222 (3.8 min).	Di Marco et al. (2011)	
Acipenser naccarii × *Acipenser baerii*	Sturgeon, hybrid	Medtomidine + ketamine	0.04 mg/kg + 4 mg/kg	IV					Induced within 5 minutes, recovery within 15 minutes. Can use atipamezole.	Di Marco et al. (2011)	Safe and effective anaesthetic protocol; atipamezole can be used.

Huso huso	Sturgeon, beluga	Clove powder	175, 225, 275, 350 mg/L	Immersion	~30 g	0.0.180	Juvenile		Exposure was 10 minutes at each dose, no concentration tested had long-lasting effects on blood parameters.	Mohammadizarejabad et al. (2010)	No concentration tested had long-lasting effects on blood parameters.
Acipenser gueldenstaedtii	Sturgeon, Russian	MS-222 (tricaine methanesulfonate)	100–150 mg/L	Immersion	~20		Adult		Varies for procedure type, longer procedures induce 150 mg/ml dilute to lower dose.	C.M. Burns (pers. exp.)	Consider dilutions for longer procedures.
Acipenser spp.	Sturgeon	Isoeugenol	20–80 mg/L	Immersion					Concentrations of 40–60 mg/L rapidly anesthetize coldwater species to the handleable stage in <3–5 minutes whereas 60–80 mg/L is necessary to anesthetize cool and warm-water species in a comparable amount of time.	Javahery et al. (2012)	Recommended dose: 40–60 mg/L (cold-water species), 60–80 mg/L (cool- and warm-water species).
Order Anabantiformes											
Family Osphronemidae											
Colisa labiosus	Gourami, thick lipped	MS-222 (tricaine methanesulfonate)	200 mg/L –> 80 mg/L	Immersion	8 g				Induction 90 seconds. Total anesthesia time 47 minutes. Flow rate of maintenance fluid 12.1 ml/min. Gill motion throughout procedure. Full recovery by 23 minutes. Surgical mass removal.	Harms et al. (1995)	
Trichogaster trichopterus	Gourami, three spot	MS-222 (tricaine methanesulfonate)	400 mg/L	Immersion	19 ± 3 g			23–25	Induction within 2 minutes. Level sufficient for deep IM injection and phlebotomy. Recovery within 2 minutes. pH 7.4–7.6.	Yanong et al. (2005)	
Trichogaster trichopterus	Gourami, three spot	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion				28–29	Level sufficient to induce light sedation within 4 minutes.	Crosby et al. (2006)	
Trichogaster trichopterus	Gourami, three spot	Metomidate hydrochloride	0.8 mg/L	Immersion				28–29	Level sufficient to induce light sedation within 4 minutes.	Crosby et al. (2006)	
Trichogaster trichopterus	Gourami, three spot	Quinaldine	5 mg/L	Immersion				28–29	Level sufficient to induce light sedation within 4 minutes.	Crosby et al. (2006)	
Trichogaster trichopterus	Gourami, three spot	Metomidate hydrochloride	0.1, 0.2, 0.3, 0.4 mg/L	Immersion		0.0.330		22.9–24.7	Use of metomidate hydrochloride as a transport sedative for three-spot gourami should be considered with caution and may be problematic at the concentrations tested. Study parameters included marketability.	Crosby et al. (2012)	Use with caution as a transport sedative due to behavioral changes and high glucose.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Order Anguilliformes											
Family Anguillidae											
Anguilla anguilla	Eel, European	Eugenol	50 mg/L	Immersion	~150 g	0.0.20		~12	Recovery noted but no other anesthetic information provided.	Renault et al. (2011)	Eugenol as an aesthetic in ecotoxicological studies measuring gene expression or plasma cortisol concentration is not appropriate. Electro-narcosis did not seem to have any impact on the parameters taken into consideration in this study.
Anguilla japonica	Eel, Japanese	2-phenoxyethanol	1–16 ml/L	Immersion		0.0.8		25	Exposure to 2-PE at any dose induced a loss of equilibrium within 3 minutes.	Chiba et al. (2006)	Exposure to 2-PE at any dose induced a loss of equilibrium within 3 minutes, while the dose of MS-222 needed to induce a similar effect was more than 200 mg/L.
Anguilla japonica	Eel, Japanese	MS-222 (tricaine methanesulfonate)	50–800 mg/L	Immersion					Dose needed to induce a similar effect of 2-PE was more than 200 mg/L.	Chiba et al. (2006)	
Anguilla japonica	Eel, Japanese	Electroanesthesia	100 V, 2A -AC power or 240 V, 6A -AC, 30 s	Immersion						Chiba et al. (2006)	Electrofisher Model 12-A (Smith-Root, Vancouver, WA, USA) was also used to shock the fish with 500 V or 1000 V at 5 A pulsating DC for 30 seconds.
Anguilla reinhardtii	Eel, speckled longfin	Benzocaine	60–80 mg/L	Immersion			Adult	17–25	Dissolved in ethanol (1:10). Induction within 6 minutes.	Walsh & Pease (2002)	
Anguilla reinhardtii	Eel, speckled longfin	Clove oil	100 mg/L	Immersion			Adult	17–25	Induction within 6 minutes. Recovery within 4 minutes.	Walsh & Pease (2002)	
Anguilla rostrata	Eel, American	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Sedation rated excellent. Examination performed.	D.L. Neiffer (pers. exp.)	Excellent sedation.
Family Muraenidae											
Echidna nebulosa	Eel, snowflake	MS-222 (tricaine methanesulfonate)	80–200 mg/L	Immersion			Juvenile-adult	25	Air gulpers, make sure animal is completely submerged. Prolonged inductions can be attributed to this. Induce high, especially in healthier specimens.	C.M. Burns (pers. exp.)	Air gulpers, make sure animal is completely submerged. Higher doses recommend for faster induction.
Echidna nebulosa	Eel, snowflake	Isoeugenol	40–70 mg/L	Immersion			Juvenile-adult	25	Sedate enough for morphometrics, blood draw. Apply to give treatments at 70, with anesthesia time <20 minutes.	C.M. Burns (pers. exp.)	Sedate enough for morphometrics, blood draw.

Gymnomuraena zebra	Moray, zebra	MS-222 (tricaine methanesulfonate)	80–200 mg/L	Immersion		0.0.2	Adult	25	Sick animal sedated at 80, up to 200 mg/L for healthy animals (induction).	C.M. Burns (pers. exp.)	Wide dose range; 80 mg/L used in debilitated animals up to 200 mg/L.
Gymnomuraena zebra	Moray, zebra	Isoeugenol	50 mg/L	Immersion		0.0.1	Adult	25	Sedate enough for morphometrics, blood draw.	C.M. Burns (pers. exp.)	
Gymnothorax funebris	Moray, green	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion	22–30		Adult		Suitable for examination. Animals that gulp air at surface may take longer to induce. Make sure animal is enclosed in a confined area since prone to leaping.	E.J. Chittick (pers. exp.)	Air gulper, may take longer to induce. Prone to jumping.
Gymnothorax funebris	Moray, green	MS-222 (tricaine methanesulfonate)	125–150 mg/L –> 75–100 mg/L	Immersion	22–30		Adult		Long procedures lower induction dose to below 100 mg/L. For short procedures 125 ppm is suitable for entire time.	C.M. Burns (pers. exp.)	Long procedures lower dose (<100 mg/L) recommended; use higher dose (125 ppm) for shorter procedures.
Gymnothorax funebris	Moray, green	Isoeugenol	25–30 mg/L	Immersion			Adult		Fast induction, dilute for longer procedures.	C.M. Burns (pers. exp.)	Fast induction. Recommend dilution for longer procedures.
Gymnothorax vicinus	Moray, purplemouth	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion			Adult		Suitable for examination. Animals that gulp air at surface may take longer to induce. Make sure animal is enclosed in a confined area since prone to leaping.	E.J. Chittick (pers. exp.)	Air gulper, may take longer to induce. Prone to jumping.
Family Ophichthidae											
Myrichthys maculosus	Eel, tiger snake	MS-222 (tricaine methanesulfonate)	175–200 mg/L	Immersion			Adult		Very active species, more profound air gulping, make sure animal is submerged. Decrease dose for longer procedures.	C.M. Burns (pers. exp.)	Very active species, ensure full submersion.
Order Atheriniformes											
Family Melanotaeniidae											
Melanotaeniidae spp.	Ornamentals	Metomidate hydrochloride	40, 60, 100, 250, 100 mg/L	Immersion				22–24	Some species were euthanized at a concentration of 40 mg/L metomidate hydrochloride for a total exposuretime of 38 minutes. Most species tested were successfully euthanized with metomidate hydrochloride at a concentration of 100 mg/L, with total exposure times ranging from 35 to 96 minutes. A few catfish species were refractory and recovered after 100 mg/L. However, *Otocinclus* sp. were successfully euthanized at 250 mg/L and bronze corydoras were euthanized at 1000 mg/L.	Yanong (2021)	Wide range of doses and time until effect.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Melanotaenia australis	Rainbowfish, western	Isoeugenol	40, 60, 80, 100, 120 mg/L	Immersion				27	For stage four anesthesia of the western rainbowfish *Melanotaenia australis* the most efficacious concentration of Aqui-S® was found to be 80 mg/L.	Young (2009)	
Order Batrachoidiformes											
Family Batrachoididae											
Opsanus beta	Toadfish, gulf	MS-222 (tricaine methanesulfonate)	670 mg/L buffered with NaOH	Immersion			Adult	24–26	Once fish were induced they were wrapped in anesthetic solution-soaked paper towels for 30-minute surgical placement of venous cannula. Species is considered tolerant of air exposure and it was not necessary to irrigate gills.	Gilmour et al. (1998)	
Opsanus tau	Toadfish, oyster	MS-222 (tricaine methanesulfonate)	50–250 mg/L	Immersion	675 ± 46 g		Adult	20	Slight sedation at 50 mg/l. Decreasing respiratory rate and ability to maintain equilibrium from 100 to 250 mg/l. Cessation of voluntary respiratory activity at 300 mg/l. These later fish resumed gilling 14 minutes after anesthetic withdrawal and all fish regained equilibrium within 23 minutes of anesthetic withdrawal.	Palmer & Mensinger (2004)	
Opsanus tau	Toadfish, oyster	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion	1.38		Adult	25	Sedated for up to 1 hour during CT starting with high dose and diluting down when necessary.	C.M. Burns (pers. exp.)	
Opsanus tau	Toadfish, oyster	Isoeugenol (Aqui-S® 20e)	0.0005–0.0060%	Immersion	281.5± 72.8 g	10.16.0	Adult	19–21	Effective in inducing the surgical plane of anesthesia. It is not recommended for acute neural preparations due to its depression of neural activity. The depression of lateral line sensitivity at low concentrations could play a role in reducing the stress response during fish transport.	Putland et al. (2020)	Increasing the concentration significantly decreased spontaneous and evoked firing rates of the anterior lateral line.

Order Beryciformes											
Family Holocentridae											
Holocentrus ascensionis	Squirrelfish	MS-222 (tricaine methanesulfonate)	70–85 mg/L	Immersion	160–500 g				Variable sedation (mild to heavy) for examination.	D.L. Neiffer (pers. exp.)	
Myripristis jacobus	Soldierfish	MS-222 (tricaine methanesulfonate)	55–75 mg/L	Immersion	140–390 g					C.M. Burns (pers. exp.)	
Neoniphon sammara	Squirrelfish, sammara	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion						T.M. Clauss (pers. exp.)	
Sargocentron spp.	Squirrelfish	MS-222 (tricaine methanesulfonate)	70–75 mg/L	Immersion	27–335 g					C.M. Burns (pers. exp.)	
Order Beloniformes											
Family Adrianichthyidae											
Oryzias dancena	Medaka, Merine	Clove oil	50 , 75, 100, 125, 150 mg/L	Immersion	334.9 ± 60.0 mg	0.0.50		26	Both drugs tested in salinities of 0 to 40 ppt. Anesthetic time increased as salinity increased.	Park et al. (2017)	10 ppt had fastest time to effect.
Oryzias dancena	Medaka, Merine	Clove oil (85%)	50, 75, 100, 125, 150, 175 mg/L	Immersion	11.0 ± 1.31, 324.3 ± 58.6 mg	0.0.40	20–40 phd, 100–160 phd	23, 26, 29	Exposure to 125 mg/L at 23°C, 100 mg/L at 26°C, and 75 mg/L at 29°C were considered the optimal concentrations.	Park et al. (2011)	Recommended dose: 125 mg/L at 23°C, 100 mg/L at 26°C, and 75 mg/L at 29°C.
Oryzias dancena	Medaka, Merine	Lidocaine-HCl	50 , 75, 100, 125, 150 mg/L	Immersion	334.9 ± 60.0 mg	0.0.50		26	Both drugs tested in salinities of 0 to 40 ppt. Anesthetic time increased as salinity increased.	Park et al. (2017)	
Oryzias dancena	Medaka, Merine	Lidocaine HCL	300, 400, 500, 600, 700, 800 mg/L	Immersion	11.0 ± 1.31, 324.3 ± 58.6 mg	0.0.40	20–40 phd, 100–160 phd	23, 26, 29	Exposure to 800 mg/L at 23°C and 700 mg/L at 26 and 29°C were considered the optimal concentrations for anesthesia within 1 minute.	Park et al. (2011)	Recommended dose: 800 mg/L at 23°C and to 700 mg/L at 26 and 29°C.
Oryzias latipes	Medaka, Japanese	Menthol	3.0 mM	Immersion	1.6 ± 0.2 cm			25 ± 1	Applied by injection to one side of a gill (50 μL), oral cavity (50 μL), and one side of the body surface (100 μL) of medaka fish and goldfish (100, 100, and 300 μL, respectively) by injection with a 1-ml syringe, and the peritoneal cavity (10 μL for medaka fish and 30 μL for goldfish) was injected with a 100-μL Hamilton microsyringe.	Kasai et al. (2014)	Menthol (d-, l-, dl-types) at 0.4 mM produced surgical anesthesia in medaka, goldfish, and zebrafish.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Order Blenniiformes											
Family Tripterygiidae											
Enneapterygius rufopileus	Triplefin, redcap	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion				18	Induction within 3 minutes. Recovery within 10 minutes. Sufficient for handling and measurement.	Griffiths (2000)	Induction within 3 minutes. Recovery within 10 minutes. Sufficient for handling and measurement.
Order Carangiformes											
Family Carangidae											
Caranx bartholomaei	Jack, yellow	MS-222 (tricaine methanesulfonate)	55–80 mg/L	Immersion				25	Examination, quarantine checkouts.	C.M. Burns (pers. exp.)	
Caranx crysos	Blue runner	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion				25	Diagnostic examinations performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good for diagnostic examination.
Caranx crysos	Blue runner	Alphaxalone + alphadolone	0.3 ml/kg	IM	1.5				Anesthesia with marked depression of ventilation.	Harvey et al. (1988)	Produced stage 3 anesthesia.
Caranx hippos	Jack, crevalle	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion				25	Transport, unable to obtain blood.	C.M. Burns (pers. exp.)	
Caranx latus	Jack, horse-eye	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion			Adult	25	Fast sedation prior to injectable euthasol for euthanasia.	C.M. Burns (pers. exp.)	
Caranx latus	Jack, horse-eye	Isoeugenol + MS-222 (tricaine methanesulfonate)	25–40 mg/L induction –> 70 mg/L maintenance	Immersion			Adult	25	40 mg/L was a deep anesthesia prior to moving to MS-222.	C.M. Burns (pers. exp.)	
Caranx latus	Jack, horse-eye	MS-222 (tricaine methanesulfonate)	50–80 mg/L	Immersion				25	Sedation rated as good to excellent. Examinations performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good-excellent for diagnostic examination.
Carangoides ruber	Jack, bar	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion	70 g			25	Sedation rated as good. Adequate for examination and enucleation.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Adequate for examination and enucleation.
Carangoides ruber	Jack, bar	MS-222 (tricaine methanesulfonate)	45–80 mg/L	Immersion			Juvenile-adult	25	Examination, quarantine checkouts.	C.M. Burns (pers. exp.)	
Caranx stellatus	Bluefin trevally	Alphaxalone + alphadolone	0.4 ml/kg	IM	18				Sedation with partial loss of equilibrium within 2–5 minutes. More than one dart used to deliver total dose. Able to be netted, but responsive. Recovered within 30 minutes.	Harvey et al. (1988)	Produced stage 1 anesthesia.
Caranx stellatus	Bluefin trevally	Metomidate hydrochloride	10–100 mg/kg	IM	16–35				Light sedation with partial loss of equilibrium. Directed net avoidance.	Harvey et al. (1988)	Produced stage 1–2 anesthesia.

Selene vomer	Lookdown	MS-222 (tricaine methanesulfonate)	75–125 mg/L	Immersion				25	Varied effect from mild sedation to light anesthesia (125 mg/L) for examinations.	D.L. Neiffer (pers. exp.)	Varied effect from mild sedation to light anesthesia (125 mg/L) for examination.
Selene vomer	Lookdown	MS-222 (tricaine methanesulfonate)	50–70 mg/L	Immersion			Juvenile-adults	25	Species places head in corner/against wall during sedation. Careful of eyes.	C.M. Burns (pers. exp.)	
Seriola dumerili	Amberjack, greater	Alphaxalone + alphadolone	0.3 ml/kg	IM	8				Sedation with partial loss of equilibrium within 2–5 minutes. Able to be netted, but responsive. Recovered within 30 minutes.	Harvey et al. (1988)	Produced stage 2 anesthesia.
Seriola dumerili	Amberjack, greater	Metomidate hydrochloride	10–100 mg/kg	IM	9				Sedation with partial loss of equilibrium. Able to be netted, but responsive.	Harvey et al. (1988)	Produced stage 2 anesthesia.
Seriola lalandi	Amberjack, yellowtail	Isoeugenol	25, 35, 55, 75 mg/L	Immersion		0.0.50	Juvenile	20.7 ± 0.37	In cultured YT species, the safe and effective dose range was narrower, 25–35 mg/L, with significant mortality noted at 55 mg/L and above.	Silbernagel & Yochem (2016)	Safe and effective dose range was narrow: 25–35 mg/L. Significant mortality noted at 55 mg/L and above.
Seriola lalandi	Amberjack, yellowtail	Tiletamine-zolazepam	8–9 mg/kg (avg. 70 mg per jack)	Oral	6–9	0.0.15	Adult, juvenile		Used dry form of drug for oral sedation. Within 6–8 hours of ingestion, fish receiving an intended 70-mg dose began to show signs of sedation consisting of dark coloration, altered swim patterns, and loss of righting ability. Maximum sedative effect of oral tiletamine-zolazepam was 8–12 hours. Recovery from sedation, defined as return of normal swimming patterns and equilibrium, ranged from 12 to 48 hours.	Steers & Sherrill (2001)	10 out of 14 (71.4%) animals were transported, with the remaining as mortalities.
Trachinotus carolinus	Pompano, Florida	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion				25	Provided sedation to light anesthesia for examinations, tagging, and ocular surgery.	D.L. Neiffer (pers. exp.)	
Trachinotus falcatus	Permit	MS-222 (tricaine methanesulfonate)	100–125 mg/L => 70–90 mg/L	Immersion	3.8–18		Adult	25	If adult start at high dose and dilute to lower dose as needed. Juveniles can start at a lower dose if desired.	C.M. Burns (pers. exp.)	
Trachinotus goodei	Pompano, great	MS-222 (tricaine methanesulfonate)	70–100 mg/L					25	Light to heavy sedation for surgery.	C.M. Burns (pers. exp.)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Family Rachycentridae										
Rachycentron canadum	Cobia	Medetomidine + ketamine	0.122–0.240 mg/kg + 6–13.5 mg/kg	IM	24–40 kg	Adult	5	Injected using spring-loaded pole syringe. Dose resulted in mild sedation. Supplemental dose of 0.100 mg/kg medetomidine and 2.8 mg/kg ketamine necessary for final capture.	D.L. Neiffer (pers. exp.)	Supplemental dose of 0.100 mg/kg medetomidine and 2.8 mg/kg ketamine.
Rachycentron canadum	Cobia	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion	9–40 kg	Adult	25	Transport, diagnostic examination, treatments.	C.M. Burns (pers. exp.)	
Order Characiformes										
Family Characidae										
Brycon cephalus	Matrinxã/ brycon, red-tailed	MS-222 (tricaine methanesulfonate)	150 mg/L	Immersion	31.56 ± 8.08 g	Juvenile	25	Buffered with $CaCO_3$ time to anesthesia: ~6 minutes, duration 10 minutes, recovery <10 minutes. Zero mortality at 150 mg/L.	Roubach et al. (2001)	Mortality: 0% at 150 mg/L, 16.7% at 200 mg/L, and 33.3% at 300 mg/L. Pronounced stress response at 200 and 300 mg/L.
Colossoma macropomum	Tambaqui/ cachama	Benzocaine	100–150 mg/L	Immersion	9.32 ± 3.7 g	Juvenile	24	Dissolved in acetone (10 g/100 ml). Induction: 0.11–1.01 minutes. Recovery following exposure for 10 minutes: 2.32–9.04 minutes. Recovery following exposure for 30 minutes: 30 ± 20 minutes.	Gomes et al. (2001)	Fish exposed to ≥ 220 mg/L exhibited stress response. Mortality 30% at 350 mg/L.
Colossoma macropomum	Tambaqui/ cachama	Eugenol	65 mg/L	Immersion	56.6 ± 7.7 g, 1100 ± 90.7 g	Juveniles to subadults	26–27	Dissolved in alcohol to make 1:2 stock solution. Handling at 1.45 minutes, surgical stage in 2.54 minutes, recovery <10 minutes. Exposure for 30 minutes was not associated with mortality. Dose up to 100 mg/L considered safe.	Roubach et al. (2005)	Exposure for 30 minutes was not associated with mortality. Dose up to 100 mg/L was considered safe.
Colossoma macropomum	Tambaqui/ cachama	MS-222 (tricaine methanesulfonate)	30 mg/L	Immersion		Adult		In-tank sedation, then transport.	Mylniczenko (pers. exp.)	
Colossoma macropomum	Tambaqui/ cachama	Medetomidine, butorphanol, midazolam	100 μg/mkg + 1 mg/kg + 1 mg/kg	IM		Adult		Used in combination prior to euthanasia with MS-222. Very light sedation.	Mylniczenko (pers. exp.)	Used in combination prior to euthanasia with MS-222. Very light sedation.

Colossoma macropomum	Tambaqui/ cachama	Tea tree oil + clove oil	10.4 mg/L	Immersion	65.2 ± 1.20g	0.0.300	Juvenile	27 ± 1.7	Favorable results for 15- and 36-hour transportations using combined tea tree and clove essential oils at 10.4 mg/L for sedation.	Santos et al. (2020)	Good for 15- and 36-hour transports.
Colossoma macropomum	Tambaqui/ cachama	Alphaxalone + alphadolone	0.3–0.8 ml/kg	IM	6–10				Deepest stage within 1 hour 0–3.	Harvey et al. (1988)	
Colossoma macropomum	Tambaqui/ cachama	Metomidate hydrochloride	20–165 mg/kg	IM	4–9				Deepest stage within 1 hour 0–3.	Harvey et al. (1988)	
Colossoma macropomum	Tambaqui/ cachama	Gallamine triethiodide (Flaxedil)	1.3–1.4 mg/kg	IM	7–13				Deepest stage within 1 hour 2–3.	Harvey et al. (1988)	
Hyphessobrycon spp.	Tetra	Clove oil	0.05 ml (50 mg), 0.10 ml (100 mg), and 0.20 ml (200 mg) per 500 ml of water	Immersion		0.0.40			Most effective dose is 0.05 ml for recovery. 0.20 ml is recommended for studies that require fish euthanization.	Fernandes et al. (2016)	Recommended dose: 0.05 ml for recovery procedures.
Piaractus brachypomus	Pirapitinga	MS-222 (tricaine methanesulfonate)	100–125 mg/L	Immersion	18		Adult	25	Diagnostic examination, radiographs, recovered quickly.	C.M. Burns (pers. exp.)	Quick recovery.
Piaractus brachypomus	Pirapitinga	MS-222 (tricaine methanesulfonate)	100, 200 mg/L	Immersion	500–727 g		4-year-old adults	20–23	Induction: 100 mg/L, average 550 seconds; 200 mg/L, average 350 seconds. Recovery 300–500 seconds. pH 5.5–7.0.	Sladky et al. (2001)	
Piaractus brachypomus	Pirapitinga	Eugenol	0, 25, 50, 75, 100, 125 mg/L	Immersion	0.87 ± 0.20, 17.14 ± 3.27 g	0.0.120	Juveniles I, II		Able to induce deep anesthesia at 50–100 mg/L for both size classes.	Ferreira et al. (2021)	
Piaractus brachypomus	Pirapitinga	Menthol	0, 25, 50, 75, 100, 125 mg/L	Immersion	0.83 ± 21, 16.83 ± 2.78 g	0.0.120	Juveniles I, II		Able to induce deep anesthesia at 25–100 mg/L for juvenile I and between 50 and 25 mg/L for juvenile II.	Ferreira et al. (2021)	
Piaractus mesopotamicus	Pacu	Benzocaine	99 mg/L	Immersion	315.2–745.2 g		Adult	15–35	Used for surgical implantation of ECG electrodes, and buccal and opercular catheters.		Used for surgical implantation of ECG electrodes, buccal and opercular catheters.
Pygocentrus cariba	Piranha, black spot	MS-222 (tricaine methanesulfonate)	70–90 mg/L	Immersion			Adult		Good anesthesia for mass removal, ocular aspirations, and assisted feeding.	T.M. Clauss (pers. exp.)	Good anesthesia for mass removal, ocular aspirations, and assist feeding.
Pygocentrus nattereri	Piranha, red	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion			Adult		Good anesthesia for minor and surgical procedures.	N.D. Mylniczenko, T.M. Clauss (pers. exp.)	Good anesthesia for minor and surgical procedures.
Astyanax altiparanae	Lampari	Eugenol	50, 75, 100, 125, 150 mg/L	Immersion	~0.6 g		Fry		50 mg/L is an efficient and safe concentration.	Pereira da Silva et al. (2009)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Family Erythrinidae											
Hoplerythrinus unitaeniatus	Aimara	Urethane	1% solution	Immersion						Farrell & Randall (1978)	
Hoplerythrinus unitaeniatus	Aimara	MS-222 (tricaine methanesulfonate)	0.01% solution	Immersion						Farrell & Randall (1978)	
Hoplias lacerdae	Characin	Benzocaine	50 mg/L	Immersion	375 ± 47 g		Adult	25 ± 1	Provided light anesthesia for brief procedures.	Rantin et al. (1993)	
Hoplias malabaricus	Trahira	Benzocaine	50 mg/L	Immersion	312 ± 47 g		Adult	25 ± 1	Provided light anesthesia for brief procedures.	Rantin et al. (1993)	
Family Prochilodontidae											
Prochilodus nigricans	Prochilodus, black	Eugenol	25, 50, 100, 200 mg/L	Immersion	221.34 ± 9.0 g	0.0.50		29.47 ± 0.30	The concentration of 50 mg/L surgical anesthesia induction ~3 minutes.	Viegas et al. (2020)	
Order Cichliformes											
Family Cichlidae											
Aulonocara spp.	Cichlid, peacock	Alfaxalone	5 mg/L	Immersion		0.0.11				Zellar et al. (2018)	
Aulonocara spp.	Cichlid, peacock	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion		0.0.11				Zellar et al. (2018)	Buffered with 200 mg/L bicarbonate.
Astronotus ocellatus	Oscar	Alfaxalone	5 mg/L	Immersion		0.0.6	Subadult	25.1	Induction time <15 minutes, recovery up to 55 minutes. OpR and RR decreased over time in anesthetic but HR remained the same.	Bugman et al. (2016)	Respirations decreased over time but heart rate remained steady.
Amphilophus citrinellus	Cichlid, midas	MS-222 (tricaine methanesulfonate)	150 mg/L for induction;	Immersion	800 g				Induction in 8 minutes. Flow rate of maintenance solution 3 L/min. Procedure 71 minutes.	Lewbart et al. (1994)	
Amphilophus citrinellus	Cichlid, midas	Ketamine	30 mg/kg	IV	206 ± 36 g			22 ± 2	Fish sedated first in buffered MS-222 (100–125 mg/L) for 8–10 minutes, at which point fish became unresponsive. Fish removed from bath and ketamine injected. Induction <10 seconds. In some fish complete cessation of ventilation occurred, while in others intermittent coughing or rapid ventilation was noted. Anesthesia lasted 1–41 minutes with balance regained at 57–263 minutes.	Bruecker & Graham (1993)	Sedated first in buffered MS-222 then injected with ketamine. Wide range in effect.

Cichlidae spp.	Misc. species	Metomidate hydrochloride	40, 60, 100, 250, 100 mg/L	Immersion		22–24	Some species were euthanized at a concentration of 40 mg/L metomidate hydrochloride for a total exposuretime of 38 minutes. Most species tested were successfully euthanized with metomidate hydrochloride at a concentration of 100 mg/L, with total exposure times ranging from 35 to 96 minutes. A few catfish species were refractory and recovered after 100 mg/L. However, *Otocinclus* sp. were successfully euthanized at 250 mg/L and bronze corydoras were euthanized at 1000 mg/L.	Yanong (2021)	Wide range in anesthetic doses and duration until effect.
Cichlasoma nigrofasciatum	Cichlid, convict	Quinaldine sulphate	3.25, 6.5, 9.75, 13, 27, 40, 54 mg/L	Immersion	~54 g	26	Introduction of diazepam in combination with QS helped eliminate the undesired effects of QS during sedation. The combination of QS + D is a potent anesthetic for convict cichlids. For light anesthesia: 9.75 ppm QS + 0.5 ppm D. For deep anesthesia: 9.75 ppm QS + 1.0 ppm D.	Bircan-Yildirim et al. (2010)	Addition of diazepam with QS helped eliminate undesired effects.
Cichlasoma nigrofasciatum	Cichlid, convict	Quinaldine sulphate + diazepam	Above with added 0.5 and 1.0 mg/L	Immersion				Bircan-Yildirim et al. (2010)	
Haplochromis obliquidens	Cichlid, Lake Victoria	Clove oil	5–30 µL/L	Immersion			18–20 µL/L suggested a narrow margin of safety as this concentration range induced mortality.	Kaiser et al. (2006)	Narrow margin of safety and this concentration range induced mortality.
Sarotherodon linellii	Cichlid, blackfin	MS-222 (tricaine methanesulfonate)	1000 mg/L	Immersion			Euthanasia: After a 60-minute immersion in the euthanasia solution, the presence of an audible heartbeat was identified in 90% or more of the cichlids, indicating that they were not reliably euthanized. A two-step protocol is therefore recommended in cichlids for euthanasia: heavy anesthesia via immersion followed by an IV or intracardiac injection of euthanasia solution or other secondary method of euthanasia.	Bradley et al. (2021)	Euthanasia methods utilized in this study were not reliable.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Sarotherodon linellii	Cichlid, blackfin	2-phenoxyethanol	2 ml/L	Immersion						Bradley et al. (2021)	
Sarotherodon linellii	Cichlid, blackfin	Clove oil	500 mg/L	Immersion						Bradley et al. (2021)	
Oreochromis spp.	Tilapia	Isoeugenol	20–80 mg/L	Immersion					Concentrations of 40–60 mg/L rapidly anesthetize cold-water species to the handleable stage in <3–5 minutes whereas 60–80 mg/L is necessary to anesthetize cool- and warm-water species in a comparable amount of time.	Javahery et al. (2012)	Recommended dose: 40–60 mg/L (cold-water species); 60–80 mg/L (cool- and warm-water species).
Oreochromis spp.	Tilapia, red hybrid	Sodium bicarbonate	50, 100 g/L	Immersion	1–4.5 g		Juvenile	26–29	Fish that were reared in brackishwater (20 ppt) took a longer time to be fully anesthetized than those reared in freshwater for either concentration. The concentration of the anesthetic has an effect on the time to induce anesthesia of the fish. In addition, the time to full recovery of the fish was not significantly different in both rearing environments and was not affected by the dose of anesthetic.	Avillanosa et al. (2019)	Fish that were reared in brackishwater (20 ppt) took a longer time to be fully anesthetized than those reared in fresh water at either concentration.
Oreochromis macrochir	Tilapia, longfin	Sodium bicarbonate	5.0, 10.0, 15.0, 20.0 and 30.0 g/L	Immersion	160 ± 10 g	0.0.90	Adult	25 ± 0.5	5.0 g/L produced no anesthetic effects. The induction for this study varied up to 11 minutes and recovery times varied up to 22 minutes.	Hasimuna et al. (2020)	5.0 g/L produced no anesthetic effects.
Oreochromis mossambicus	Tilapia, Mozambique	2-phenoxyethanol	600 mg/L	Immersion	3.83 ± 0.55 g		Juvenile	30	Induction: 7.43 + 13.25 minutes. Recovery (fish placed in fresh water immediately after induction): 1.38 + 1.77 minutes.	Hseu et al. (1997)	
Oreochromis mossambicus	Tilapia, Mozambique	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion			Juvenile, adult			N.D. Mylniczenko (pers. exp.)	
Oreochromis mossambicus	Tilapia, Mozambique	MS-222 (tricaine methanesulfonate)	110–150 mg/L	Immersion					Light sedation at low range.	T.M. Clauss (pers. exp.)	Light sedation at low range.

Oreochromis mossambicus	Tilapia, Mozambique	Lidocaine	100–750 mg/L	Immersion					Although both induced anesthesia, the mixture was more effective for induction and recovery (titrated at 50-mg doses).	Carrasco et al. (1984)	
Oreochromis niloticus	Tilapia, Nile	Propofol	0.15, 0.30, or 0.60 ml/L	Immersion	30–50 g			25	We found that low concentrations of propofol at 0.15, 0.30, and 0.60 ml/L induce anesthesia in ~17. 9, 7.2, and 5.6 minutes, respectively.	Valenca-Silva et al. (2014)	
Oreochromis niloticus	Tilapia, Nile	Saturated nitric oxide (NO)	Solubility of NO was 136 ml/1000 ml	Immersion		0.0.72		20	No treatment resulted in shorter euthanasia time (~20 minutes), less stress than CO_2.	Wang et al. (2017)	No treatment resulted in shorter euthanasia time; less stress than CO_2.
Oreochromis niloticus	Tilapia, Nile	Eugenol (99%)	30 mg/L	Immersion	35 ± 2.3 g	0.0.18		24 ± 2	Induction 5.75 ± 3.32 minutes, anesthesia 56.25 ± 21.6 minutes, recovery 33.6 ± 13.9 minutes.	Zahran et al. (2021)	
Oreochromis niloticus	Tilapia, Nile	Propofol	2.5 mg/L	Immersion	35 ± 2.3 g	0.0.18		24 ± 2	Induction 2.5 ± 1.3 minutes, anesthesia 19.87 ± 3.4 minutes, recovery 45.6 ± 12.02 minutes.	Zahran et al. (2021)	
Oreochromios niloticus	Tilapia, Nile	2-phenoxyethanol	0.5, 1, 2 ml/L	Immersion	61 ± 3 g			26	4 minutes in 2-phenoxyethanol (0.5 ml/L). Fish from an aquarium were anesthetized in less than 1 minute in 2-phenoxyethanol (1 or 2 ml/L). The use of higher concentrations of 2-phenoxyethanol (1 or 2 ml/L) provided anesthetized fish in less than 1 minute.	Auperin et al. (1997)	
Oreochromisb niloticus	Tilapia, Nile	Benzocaine	1.5, 3.25, 6.5, 13, 26 ml/L	Immersion	22.85 ± 2.57 g	0.0.40	Juvenile	24.5 ± 0.16	Propofol is a more powerful anesthetic than benzocaine in Nile tilapia, with longer duration and deeper effect. Immersion propofol is efficient as an anesthetic in fish and could be adopted as a protocol in experimentation as well aquaculture management. Best results seen were 6.5 ml/L of benozocaine and 0.3ml/L of propofol.	Gonçalves and Giaquinto (2020)	Propofol is a more powerful anesthetic than benzocaine, with longer duration and deeper effect.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Oreochromisb niloticus	Tilapia, Nile	Propofol (Diprivan 1%)	0.075, 0.15, 0.3, 0.6, 1.2 ml/L	Immersion	22.85 ± 2.57 g	0.0.40	Juvenile	24.5 ± 0.16		Gonçalves and Giaquinto (2020)	
Oreochromisb niloticus	Tilapia, Nile	Ethanol	500 µL/L	Immersion	224.05 ± 67.56 g	0.0.40		28.05	Ethanol did not elicit any anesthetic effect or sedation in the fish. Induction of deep anesthesia was faster in the OA group (126 seconds), than PE (152 seconds) and LA (170 seconds). OA or LA essential oils at 500 µL/L were effective in inducing deep anesthesia with unconsciousness duration of 126–180 seconds, allowing time for bleeding.	Rucinque (2021)	Ethanol did not elicit any anaesthetic effect or sedation in the fish.
Oreochromisb niloticus	Tilapia, Nile	2-phenoxyethanol	500 µL/L	Immersion	224.05 ± 67.56 g	0.0.40		28.05		Rucinque (2021)	
Oreochromisb niloticus	Tilapia, Nile	*Ocimum americanum* (Basil)	500 µL/L	Immersion	224.05 ± 67.56 g	0.0.40		28.05		Rucinque (2021)	
Oreochromisb niloticus	Tilapia, Nile	*Lippia alba* (Verbena)	500 µL/L	Immersion	224.05 ± 67.56 g	0.0.40		28.05		Rucinque (2021)	
Oreochromis niloticus	Tilapia, Nile	Cooling treatment –> carbon dioxide (CO_2)	Reduction in temperature from 30°C to 15°C (at a rate of 3.5°C/h, by adding slurry ice) moved to 15°C hyperoxic (1.0–0.2 L/min)	Immersion	500–550 g			30 ± 2 to 15	Cooling followed by hyperoxic CO_2 anesthesia would be suitable for handling tilapia in a short-time air exposure procedure. Fish were deeply sedated within 69 seconds, completely anesthetized within 276 seconds and recovered within 308 seconds without any mortality.	Guan et al. (2017)	
Oreochromis niloticus	Tilapia, Nile	Eugenol plant	30, 60, 120, 180, 240, 300 mg/L	Immersion	~600 g	0.0.12			60 mg/L concentration required more time to reach the desired stage of profound anesthesia (206.3 seconds), while the 300 g/L concentration reached this stage more rapidly (77.8 seconds).Results suggest that the optimal concentration of eugenol for biometry procedures is 120 mg/L and that increased anesthetic dosage results in reduced opercular beat rate.	Moreira et al. (2010)	Recommended dose: 120 mg/L. Increased anesthetic dosage results in reduced opercular beat rate.
Oreochromis niloticus	Tilapia, Nile	Propofol (1%)	2.5, 5, 7.5, 10, 12.5 mg/L	Immersion	5–200 g	300.0.0		29.7 ± 0.9	Except for the 2.5 mg/L dosage, all concentrations induced full and smooth anesthesia in <5 minutes in all the Nile tilapia size classes. A <10-minute recovery time only occurred in a few sizes, most >10-minute however recovery was complete for all fish.	Obirikorang et al. (2020)	Except for the 2.5 mg/L dosage, all concentrations induced full and smooth anaesthesia.

Oreochromis niloticus	Tilapia, Nile	Menthol	50–300, 500 mg/L	Immersion	13.70 g			~27	Surgical anesthesia 250 mg/L, brief handling 150–200 mg/L, doses at 500 mg/L showed no mortalities.	Simoes & Gomes (2009)	Doses at 500 mg/L showed no mortalities.
Oreochromis niloticus	Tilapia, Nile	Clove oil	100, 150, 200, 250, 350 mg/L	Immersion	670.00 ± 75.28 g	0.0.70		26.98 ± 1.41	The concentration of 250 mg/L of clove oil was adequate to induce lower opercular movement in adult tilapia. For anesthesia for biometrics and brief management, the recommended concentration is 100 mg/L clove oil is an effective anesthetic for the management of adult tilapia as a routine procedure in fish farming.	Simoes et al. (2010)	Recommended dose: 100 mg/L for the management of adult tilapia as a routine procedure in fish farming.
Pterophyllum scalare	Angelfish, freshwater	Eugenol	0 (control), 10.6, 15.9, 21.2, 31.8,42.4, 53.0 or 63.6 mg/L (each concentration diluted 1:10 with ethanol)	Immersion	0.80 ± 0.08 g	0.0.56	Juvenile		The minimum effective concentration for sedation and anesthesia occurred with 15.9 and 53.0 mg/L eugenol. It is concluded that 15.9 and 53.0 mg/L eugenol are effective concentrations for sedation andanesthesia in juveniles.	de Oliveira et al. (2019)	Recommended dose: 15.9 and 53.0 mg/L eugenol were effective concentrations for sedation andanesthesia in juveniles.
Pterophyllum scalare	Angelfish, freshwater	Eugenol	15.9 mg/L	Immersion	1.75 ± 0.17 g	0.0.40	Juvenile		Simulated transport with evaluations at 4- and 7-hour marks. 15.9 mg/L eugenol has the potential to be used for the transportation of freshwater angelfish for up to 7 hours.	de Oliveira et al. (2019)	Eugenol has the potential to be used for the transportation of freshwater angelfish for up to 7 hours.
Order Clupeiformes											
Family Clupeidae											
Alosa pseudoharengus	Alewife	MS-222 (tricaine methanesulfonate)	87.5–112.5 mg/L (adult), 62.5,75, 87.5, 100 mg/L (juvenile), 37.5, 50.0, 62.5, 75.0, 87.5 mg/L (larval)	Immersion	27.5 ± 8.9, 200 g		Adult, juvenile, larval	15–17	Optimal doses: 75–100 mg/L MS-222 for all sizes.		Metomidate hydrochloride may be better for longer sedation.
Alosa pseudoharengus	Alewife	Clove oil	25–40 mg/L (adult), 2.5, 5, 20, 25, 30, 35, 40 mg/L (juvenile), 20, 25, 30, 35, 40 mg/L (larval)	Immersion					Optimal doses: 40 mg/L clove oil for all sizes.		

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Alosa pseudoharengus	Alewife	Metomidate hydrochloride	0.5–5.0 mg/L (adult), 0.25, 0.50, 3.0, 4.0, 5.0, 6.0, 7.0 mg/L (juvenile/larval)	Immersion					Optimal doses: 5–7 mg/L metomidate hydrochloride. Noting metomidate hydrochloride may be better for longer sedation.		
Alosa pseudoharengus	Alewife	2-phenoxyethanol	500 mg/L (adult), 300, 350, 400, 450, 500 mg/L (juvenile/larval)	Immersion					Optimal doses: 500 mg/L 2-PE.		
Alosa pseudoharengus	Alewife	MS-222 (tricaine methanesulfonate)	87.5–112.5 mg/L	Immersion			Adult, juvenile, larval		Optimal doses for anesthesia: 75–100 mg/L MS-222.	Berlinsky et al. (2016)	
Alosa pseudoharengus	Alewife	Clove oil	25–40 mg/L	Immersion					Optimal doses for anesthesia: 40 mg/L clove oil.	Berlinsky et al. (2016)	
Alosa pseudoharengus	Alewife	Metomidate hydrochloride	0.5–5.0 mg/L	Immersion					Optimal doses for anesthesia: 5–7 mg/L metomidate hydrochloride.	Berlinsky et al. (2016)	
Alosa pseudoharengus	Alewife	2-phenoxyethanol	125–550 mg/L	Immersion					Optimal doses for anesthesia: 500 mg/L 2-PE.	Berlinsky et al. (2016)	
Alosa pseudoharengus	Shad, hickory	MS-222 (tricaine methanesulfonate)	50, 75, 100 mg/L	Immersion		64.64.27		11.5–13.0	75–100 mg/L MS-222 is effective in anesthetizing in <2 minutes to a level of anesthesia sufficient for handling.	Matsche (2017)	Muscle spasms, coughing, decreased respiration were evident at 400 mg/L.
Alosa pseudoharengus	Shad, hickory	2-phenoxyethanol	25, 100, 400 mg/L	Immersion					400 mg/L PhE anesthetizes in <2 minutes to a level of anesthesia sufficient for handling. External signs of stress were evident in fish during anesthesia with the highest concentration of PhE.	Matsche (2017)	
Alosa pseudoharengus	Shad, hickory	Isoeugenol	25, 50, 100 mg/L	Immersion					50–100 mg/L eugenol is effective in anesthetizing in <2 minutes to a level of anesthesia sufficient for handling (stage III, plane 1).	Matsche (2017)	
Order Cypriniformes											
Family Cyprinidae											
Carassius auratus	Goldfish	2-phenoxyethanol	0.25–0.35 ml/L	Immersion	3.93 ± 1.99 g			24	Provided light sedation.	Kaiser & Vine (1998)	Provided light sedation.
Carassius auratus	Goldfish	2-phenoxyethanol	0.45 ml/L	Immersion					Provided anesthesia with loss of equilibrium.	Kaiser & Vine (1998)	Provided anesthesia with loss of equilibrium.

Carassius auratus	Goldfish	2-phenoxyethanol	0.3, 0.4, 0.5 ml/L	Immersion	2.15 ± 0.05, 9.19 ± 0.17 g		20, 25, 30	At temperatures at and below 25°C, 0.4 ml/L was needed to induce anesthesia. Above 25°C, 0.5 ml/L was required.	Weyl et al. (1996)	At temperatures at and below 25°C, 0.4 ml/L was needed to reach effect within 15 minutes; above 25°C, 0.5 ml/L was required to induce anesthesia.
Carassius auratus	Goldfish	Alfaxalone	0.15, 0.5, 2.0, 5.0 and 7.5 mg/L	Immersion		0.0.30	23–25	Lowest concentrations to induce sedation were 0.5 and 5 mg/L.	Bauquier et al. (2013)	
Carassius auratus	Goldfish	Alfaxalone	6, 7, 9 mg/L	Immersion		0.0.30	2.24–25	Immersion of 6 mg/L provided best induction of anesthesia.	Leonardi et al. (2019)	Recommended dose: 6 mg/L.
Carassius auratus	Goldfish	Alfaxalone	10 mg/L (induction), 5 mg/L (maintenance)	Immersion	460 g			Administered for analgesia 0.4 mg/kg IM. 60 minutes surgical event with 35 minutes of recovery.	Fernández-Parra et al. (2017)	Used for analgesia at 0.4 mg/kg IM.
Carassius auratus	Goldfish	Butorphanol mg/kg	0.1, 0.2, 0.4 mg/kg	IM				Fish were anesthetized with MS-222 for injectioms in concentrations >120 ppm. Morphine and ketoprofen decrease anesthetic needs in goldfish and may provide analgesia.	Ward et al. (2012)	Morphine and ketoprofen decreased anesthetic needs in goldfish and may provide analgesia.
Cyprinus carpio	Goldfish	Eugenol (99%)	6.25, 12.5, 25, 50, 75, 100, 125, 150, 200 mg/L; 43 mg/L (5 min); 10 mg/L (3 h)	Immersion	110 ± 5.65 g	0.0.98	25.3 ± 1.25	Eugenol anesthetized the fish within 600–900 seconds (with recovery time of 190–380 seconds) at concentrations of 25–150 mg/L.	Yousefi et al. (2018)	Anesthesia in 600–90 seconds with recovery times of 190–380 seconds.
Carassius auratus	Goldfish	Fentanyl + (MS-222 + gallamine)	10 µg/g + 100 mg/L + 100, 500, 2500 µg/g	IM	30–70 g	0.0.16		Animals were only anesthetized to stop moving for fentanyl injection, returned to nonanesthetic water. Gallamine was given to stop animals from moving for experiment. Recovery not noted due to euthanization after experiment.	Cordova & Braurn (2007)	Gallamine was given to stop animal from moving for experiment; no recovery data.
Carassius auratus	Goldfish	Ketamine	50, 67, 100, 200 mg/kg	PO	3–20 g	0.0.22	70–73F	Ketamine can be safely administered orally and in food up to at least 500 mg/kg in less primitive teleost fish and 50 mg/kg in elasmobranchs to induce a hypnotic sedation plane.	Raines & Clancy (2009)	Ketamine can be administered orally up to 500 mg/kg in fish and 50 mg/kg in elasmobranchs.
Carassius auratus	Goldfish	Medetomidine	0.01, 0.015, 0.025 mg/kg	IM				Fish were anesthetized with MS-222 for injectioms in concentrations >120 ppm. Morphine and ketoprofen decrease anesthetic needs in goldfish and may provide analgesia.	Ward et al. (2012)	Morphine and ketoprofen decrease anesthetic needs in goldfish and may provide analgesia.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Carassius auratus	Goldfish	Morphine sulfate 15 mg/ml, Baxter Healthcare Corporation, Deerfield, Illinois, 60015, USA	10, 20, 40 mg/kg	IM					Fish were anesthetized with MS-222 for injectioms in concentrations >120 ppm. Morphine and ketoprofen decrease anesthetic needs in goldfish and may provide analgesia.	Ward et al. (2012)	Morphine and ketoprofen decrease anesthetic needs in goldfish and may provide analgesia.
Carassius auratus	Goldfish	Propofol	1, 5, 10 mg/L	Immersion	0.02–0.03	0.0.38	Adult	23.1–23.3	Propofol at 1 mg/L did not produce anesthesia. Propofol at 5 and 10 mg/L produced anesthesia, and anesthetic needs were similar following repeated procedures.	Balko et al. (2017)	Propofol at 1 mg/L did not produce anesthesia while 5 and 10 mg/L did.
Carassius auratus	Goldfish	Propofol	25 mg/L	Immersion	0.02–0.04	0.0.6	Adult	23.1–23.3	Euthanasia: 30 minutes in 25 mg/L.	Balko et al. (2018)	Very light sedation after 30 minutes in 25 mg/L.
Cyprinus carpio	Goldfish	Thymol (98.5%)	6.25, 12.5, 25, 50, 75, 100, 125, 150, 200 mg/L; 52 mg/L (5 min); 20 mg/L (3 h)	Immersion	110 ± 5.65 g	0.0.98		25.3 ± 1.25	Thymol induced anesthesia within 850–60 seconds at concentrations of 25–200 mg/L.	Yousefi et al. (2018)	
Carassius auratus	Goldfish	Tricaine methansulfonate	150, 200, 300, 400, 500 mg/L	Immersion	230 ± 25 mg	0.0.5		25.6	Recommended ideal concentration was 200 mg/L at 12 ppt.	Küçük & Çoban (2016)	Recommended dose: 200 mg/L at 12 ppt.
Carassius auratus	Goldfish	Tricaine methanesulfonate	500 mg/L	Immersion	0.02–0.04	0.0.6	Adult	23.1–23.3	Euthanasia: at 15 and 30 minutes in 500 mg/L.	Balko et al. (2018)	Very light sedation at 15 and 30 minutes in 500 mg/L.
Carassius auratus	Goldfish	Tricaine methanesulfonate	1,000 mg/L	Immersion	0.02–0.04	0.0.6	Adult	23.1–23.3	Euthanasia: at 15 minutes in 1000 mg/L.	Balko et al. (2018)	Very light sedation at 15 minutes in 1000 mg/L.
Carassius carassius	Carp, Crucian	Benzocaine	25, 50, 100 mg/L	Immersion	~370 g	0.0.36		~22	100 mg/L benzocaine produced a fast induction anesthesia time.	Heo & Shin (2010)	Quick induction with low circulating cortisol and glucose concentrations.
Ctenopharyngodon idella	Carp, grass	MS-222 (tricaine methanesulfonate)	100 mg/L –> 75mg/L	Immersion	1.0–2.5 kg			22	Induction within 5 minutes. Allowed for surgical implantation of radio transmitters. Recovery took 5–25 minutes. Mortality occurred with 100 mg/L at temperatures >31°C.	Schramm & Black (1984)	Mortality occurred with 100 mg/L at temperatures >31°C.
Ctenopharyngodon idella	Carp, grass	2-phenoxyethanol	0.2 ml/L	Immersion	3–12 kg		Brood stock	25	Mixed with 500 ml of tank water and added to chamber. Induction to light sedation in 2–3 minutes. Females stripped of ova with this dose.	McCarter (1992)	Mixed with 500 ml of tank water and added to chamber.

Ctenopharyngodon idella	Carp, grass	2-phenoxyethanol	0.4 ml/L	Immersion					Induction to anesthesia in 5–10 minutes. Males stripped of milt with this dose.	McCarter (1992)	
Ctenopharyngodon idella	Carp, grass	Etomidate	1.0–3.0 ml/L	Immersion			Spawners	23	Propiscin applied in a water bath can provide up to 1 hour of general anesthesia.	Kazuñ & Siwicki (2012)	
Ctenopharyngodon idella	Carp, grass	MS-222 (tricaine methanesulfonate)	100 mg/L (control group)	Immersion	107.78 ± 22.11 g	0.0.165	Juvenile	18–21	Induction time in MS-222 139 seconds.	Khara et al. (2020)	MS-222 had fastest induction followed by ketamine then tobacco.
Ctenopharyngodon idella	Carp, grass	Ketamine	5.5, 8, 11, 18.5, 22 mg/L	Immersion	107.78 ± 22.11 g	0.0.165	Juvenile	18–21	Induction time in 18.5 mg/L of ketamine 140.	Khara et al. (2020)	
Ctenopharyngodon idella	Carp, grass	Tobacco extract	10, 13.33, 20, 26.27, 40 mg/L	Immersion	107.78 ± 22.11 g	0.0.165	Juvenile	18–21	Induction time in 40 mg/L tobacco 174 seconds.	Khara et al. (2020)	
Ctenopharyngodon idella	Carp, grass	Benzocaine	30, 40, 50, 60, 70 mg/L	Immersion	12 g	0.0.350	Juvenile	15	Optimal concentration was 0.3 mg/L for xylazine, more effective in deep anesthesia and recovery times.	Shakeri et al. (2016)	Recommended dose: 0.3 mg/L for xylazine and 50 mg/L for benzocaine. Xylazine was more effective in deep anesthesia and recovery times.
Ctenopharyngodon idella	Carp, grass	Xylazine	0.1, 0.2, 0.3, 0.4, 0.5 mg/L	Immersion	12 g	0.0.350	Juvenile	15	Optimal concentration was 50 mg/L for benzocaine.	Shakeri et al. (2016)	Recommended dose: 0.3 mg/L for xylazine and 50 mg/L for benzocaine. Xylazine was more effective in deep anesthesia and recovery times.
Cyprinus carpio	Carp, common	Alphaxalone-alphadolone	0.3 ml/kg	IM	2 kg				Sedation with partial loss of equilibrium. Able to be netted, but responsive.	Harvey et al. (1998)	Sedation with partial loss of equilibrium. Able to be netted, but responsive.
Cyprinus carpio	Carp, common	Alphaxalone	10 mg/L then 1–2.5 mg/L	Immersion	0.292–0.405			17–19	10 mg/L to immobile, maintained 1 or 2.5 mg/L.	Bailey et al. (2014)	
Cyprinus carpio	Carp, common	Alphaxalone	10 mg/L –> 1 mg/L or 2.5 mg/L	Immersion	292.0–405.0 g	0.0.6	Adult	17.4–18.5	Maintenance dose of 2.5 mg/L was sufficient to prevent response to noxious stimuli.	Minter et al. (2014)	The maintenance dose of 2.5 mg/L was sufficient for nociception but showed clinically relevant respiratory depression. No mortalities.
Cyrpinus carpio	Carp, common	Alphaxalone + alphadolone	0.3 ml/kg	IM	2				Achieved level 2 sedation.	Hansen et al. (2003)	Achieved level 2 sedation
Cyprinus carpio	Carp, common	Isoeugenol	20, 40, 60, 80, 100, 150, 200, 500 mg/L	Immersion		0.0.216	Juvenile		40–80 mg/L induced anesthesia within 4–11 minutes. 500 mg/L caused death in 50% of the study.	Gladden et al. (2010)	Recommended dose: 40 to 80 mg/L induced anesthesia. 500 mg/L = 50% mortality.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Cyprinus carpio L.	Carp, common	Etomidate	1.0 ml/L	Immersion			Fingerlings, 2yro	17–19	Propiscin applied in a water bath can provide up to 1 hour of general anesthesia.	Kazuñ & Siwicki (2012)	
Cyprinus carpio	Carp, common	Lidocaine	100–750 mg/L	Immersion					Although both induced anesthesia, the mixture was more effective for induction and recovery, and was able to achieve the required time for the fish to be out of water (titrated at 50-mg doses).	Carrasco et al. (1984)	A combination of lidocaine and sodium carbonate was better than the drugs in isolation.
Cyprinus carpio	Carp, common	MS-222 (tricaine methanesulfonate)	75–150 mg/L	Immersion	340–5000		Juvenile-adult		125 mg/L used frequently, surgeries start 150 mg/L titrate down.	C.M. Burns (pers. exp.)	125 mg/L used frequently, surgeries start 150 mg/L titrate down.
Cyprinus carpio	Carp, common	MS-222 (tricaine methanesulfonate)	100, 150 mg/L	Immersion	62–402 g	0.0.50	1–2 years	18–19	100 and 150 mg/L represent safe anesthetic concentrations.	Parker-Graham et al. (2020)	150 mg/L had changes in blood gases, acid-base balance, and electrolyte concentrations.
Cyprinus carpio	Carp, common	MS-222 (tricaine methanesulfonate)	100–200 mg/L	Immersion	123 ± 53 g			22–27	Utilized for exploratory celiotomy.	Harms et al. (2005)	Utilized for exploratory celiotomy.
Cyprinus carpio	Carp, common	MS-222 (tricaine methanesulfonate)	200 mg/L	Immersion	144 ± 44 g			23–25	Induction within 2 minutes. Level sufficient for deep IM injection and phlebotomy. Recovery within 2 minutes.	Yanong et al. (2005)	Quick induction and recovery. Level sufficient for deep IM injection and phlebotomy.
Cyprinus carpio	Carp, common	MS-222 (tricaine methanesulfonate)	150 mg/L (high dose), 100–125 mg/L (low dose)	Immersion		0.0.8				Hanley et al. (2010)	
Cyrpinus carpio	Carp, common	MS-222 (tricaine methanesulfonate)	500 mg/L + 10 mEq/kg	Immersion + IC, ICe, topical over gills, or none		0.0.28			For euthanasia: koi were left in 500 mg/L for 10–12 minutes before removing and performing IC, ICe, or topical treatment of KCl. In cardiac arrest in anesthetized koi.	Louis et al. (2020)	Used for euthanasia.
Cyprinus carpio	Carp, common	Propofol	1, 2.5, 5, 10 mg/L	Immersion	325 ± 81 g	0.0.10	Adult	23.1–23.3	5 mg/L provided anesthetic induction.	Oda et al. (2014)	Recommended dose: 5 mg/L for anesthetic induction.
Cyprinus carpio	Carp, common	Xylazine	11.4 ml of xylazine (2% solution) in 10 L of water	Immersion	40–91 g			25	Xylazine alone induced a state of sedation and anesthesia in the fish in 5–12 minutes.	Al-Hamdani et al. (2010)	Xylazine and ketamine combined took longer for induction, but duration was longer.
Cyprinus carpio	Carp, common	Ketamine hydrochloride	14.4 ml of ketamine (5% solution) in 10 L of water	Immersion					Ketamine alone induced similar effects in 7.2–9.7 minutes.	Al-Hamdani et al. (2010)	Xylazine and ketamine combined took longer for induction, but duration was longer.

Cyprinus carpio	Carp, common	Xylazine + ketamine	11.4 ml xylazine + 14.4 ml ketamine in 10 L	Immersion					Xylazine and ketamine combined took longer (14–22.8 minutes) to induce sedation and anesthesia, but duration was longer.	Al-Hamdani et al. (2010)	Xylazine and ketamine combined took longer for induction, but duration was longer.
Cyprinus carpio	Carp, common	Calamus oil (*Acorus calamus*)	1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 mg/L	Immersion	37.6 ± 4.27 g			28 ± 2	A concentration of 2.5 mg/L calamus oil showed rapid anesthetic and recovery times.		Reocmmended dose: 2.5 mg/L calamus oil.
Cyprinus carpio	Carp, common	Clove powder	200, 300, 400 mg/L	Immersion	60 ± 10		Juvenile	28 ± 1		Abdulrahman et al. (2018)	
Cyprinus carpio	Carp, common	Clove powder	200, 300, 400 mg/L	Immersion	60 ± 10 g	0.0.117		9 ± 1, 27 ± 1, 33 ± 1	Multiple parameters tested including water temperature/DO. Complete anesthesia at 137 seconds in 400 mg/L clove powder.	Hassan et al. (2016)	
Cyprinus carpio	Carp, common	Mustard powder	200, 300, 400 mg/L	Immersion					No anesthetic events noted in any of the mustard oil or powder concentrations.	Hassan et al. (2016)	
Cyprinus carpio	Carp, common	Clove oil	1, 1.5, 2 ml/L	Immersion					Complete anesthesia at 93 seconds in 2 ml/L clove oil.	Hassan et al. (2016)	No anesthetic events noted in any of the mustard oil or powder concentrations.
Cyprinus carpio	Carp, common	Mustard oil	1, 1.5, 2 ml/L	Immersion					No anesthetic events noted in any of the mustard oil or powder concentrations.	Hassan et al. (2016)	
Cyrpinus carpio	Carp, common	Cineole oil	200, 400, 600, 800, 1000, 1200 µL/L	Immersion	56.7 ± 1.88 g	0.0.60	Juvenile	20.3 ± 1.52	Anesthesia with 1000 µL/L cineole proved suitable for rapid sampling.	Hoseini et al. (2020)	1000 µL/L cineole proved suitable for rapid sampling.
Cyprinus carpio	Carp, common	Clove buds (*Eugenia caryophyllata*)	3 ml extract/L	Immersion					Obtained S4 within 5.5 minutes and recovered in 15 minutes.	Ramanayaka et al. (2006)	Obtained S4 within 5.5 minutes, recovery 15 minutes.
Cyprinus carpio	Carp, common	Clotalaria (possible misspell in paper, suspect Crotalaria)	2.5 ml/L	Immersion					Obtained S4 within 4.3 minutes and recovered in 40minutes.	Ramanayaka et al. (2006)	Obtained S4 within 4.3 minutes, recovery >40 minutes.
Cyprinus carpio	Carp, common	Kalawel (*Derris scandens*)	2 ml/L	Immersion					Obtained S4 within 8.7 minutes and recovered in >40 minutes.	Ramanayaka et al. (2006)	Obtained S4 within 8.7 minutes, recovery >40 minutes.
Cyprinus carpio	Carp, common	Kukuru (nuts/ fruits)	3.75 ml/L	Immersion					Obtained S4 within 20 minutes and recovered in 60 minutes.	Ramanayaka et al. (2006)	Obtained S4 within 20 minutes, recovery 60 minutes.
Cyprinus carpio	Carp, common	Welan, Medella (*Barringtonia raecemosa*)		Immersion					Each showed some anesthetic properties less effective (long induction/ recovery).	Ramanayaka et al. (2006)	Each showed some anesthetic properties less effective (long induction/ recovery).
Cyprinus carpio	Carp, common	Thiththawel (*Anamirla coculus*), Thala (*Corypha ambraculifera*), Daluk (*Euphorabhia antiqurum*)		Immersion					Showed no anesthetic properites and were toxic.	Ramanayaka et al. (2006)	Showed no anesthetic properites and was toxic.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Cyprinidae spp.	Carp	Isoeugenol	20–80 mg/L	Immersion					Concentrations of 40–60 mg/L rapidly anesthetize cold-water species to the handleable stage in <3–5 minutes whereas 60–80 mg/L is necessary to anesthetize cool- and warm-water species in a comparable amount of time.	Javahery et al. (2012)	Recommended dose: 40–60 mg/L (cold-water species); 60–80 mg/L (cool- and warm-water species).
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	250 mg/L	Immersion		0.0.10	Larvae		Euthanasia: the heartbeat was not lost in any larvae held in any euthanasia solution.	Collymore et al. (2016)	The heartbeat was not lost in any larvae held in any euthanasia solution, indicating a lack of efficacy for all chemical methods tested.
Danio rerio	Zebrafish	Lidocaine hydrochloride	400, 500, 600, 700, 800, 900, or 1000 mg/L	Immersion		0.0.70	Larvae		Euthanasia: no fish in the lidocaine hydrochloride groups recovered.	Collymore et al. (2016)	
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	250 mg/L	Immersion		0.0.10	Adult		Euthanasia: one fish recovered.	Collymore et al. (2016)	One fish in the MS-222 group recovered from euthanasia. Overall, the time to death was significantly reduced with lidocaine hydrochloride at all doses compared with MS-222 in adult fish.
Danio rerio	Zebrafish	Lidocaine hydrochloride	400, 500, 600 mg/L	Immersion		0.0.30	Adult		Euthanasia: no fish in the lidocaine hydrochloride groups recovered.	Collymore et al. (2016)	
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	1.7, 5.1, 17 mM	Immersion				27 ± 2	Euthanasia:	Davis et al. (2015)	
Danio rerio	Zebrafish	Clove oil	0.01%, 0.03%, 0.1%	Immersion					Euthanasia:	Davis et al. (2015)	
Danio rerio	Zebrafish	Lidocaine gel	4%	Topical		0.0.175	Adult	27 ± 0.3	Each fish was touched gently with a cotton ball (soaked in lidocaine gel) at each lateral line for <30 seconds. Demonstrated that local bilateral lidocaine application evokes overt behavioral effects in zebrafish, suppressing locomotor activity and top exploration.	de Abreu et al. (2019)	

Danio rerio	Zebrafish	Lidocaine hydrochloride	1, 5, 10 mg/L	Immersion				Immersible lidocaine had similar effects to topical application at the 10 mg/L dose.	de Abreu et al. (2019)	Immersible lidocaine had similar effects to topical application at the 10 mg/L dose.
Danio rerio	Zebrafish	Diazepam	1–10 mg/L	Immersion				Diazepam causes a disinhibition of motor activity at doses of 1 and 5 mg/L. Diazepam 20 mg/L has a depriving effect. Diazepam acts in a higher dose range (1–10 mg/L) than phenazepam (0.1–1 mg/L) in *Danio rerio*.	Devyashin et al. (2020)	Diazepam causes a disinhibition of motor activity at doses of 1 and 5 mg/L.
Danio rerio	Zebrafish	Alfaxalone, unpreserved	10 mg/L	Immersion	0.0.10			Immersion anesthesia using 10 mg/L of either formulation of alfaxalone resulted in anesthesia of similar quality and duration in laboratory zebrafish.	Farry et al. (2019)	10 mg/L of either formulation had a similar quality and duration in laboratory zebra fish.
Danio rerio	Zebrafish	Alfaxalone, preserved	10 mg/L	Immersion	0.0.10				Farry et al. (2019)	
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	205 mg/L	Immersion	0.0.12			Rapid cooling induced a faster loss of equilibrium, response to a painful stimuli, and ceassation of opercular movements than other treatments.	Ferreira et al. (2018)	Rapid cooling induced a faster loss of equilibrium, response to a painful stimuli, and ceassation of opercular movements than other treatments.
Danio rerio	Zebrafish	Propofol + lidocaine	20 mg/L + 100 mg/L	Immersion	0.0.12				Ferreira et al. (2018)	
Danio rerio	Zebrafish	Etomidate	6 mg/L	Immersion	0.0.12				Ferreira et al. (2018)	
Danio rerio	Zebrafish	Clove oil	50 mg/L	Immersion	0.0.12				Ferreira et al. (2018)	
Danio rerio	Zebrafish	Rapid cooling	Ice	Immersion	0.0.12		2–4o	Rapid cooling induced a faster loss of equilibrium, response to a painful stimuli, and ceassation of opercular movements than other treatments.	Ferreira et al. (2018)	
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	100, 120, 140, 160, 180, 200 mg/L	Immersion		Adult	28.5		Huang et al. (2010)	The combined use of MS-222 with isoflurane effectively extended the time of anesthesia, and fish recovered faster.
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	50–80 mg/L + 50–80 mg/L	Immersion		Adult	28.5	The combined use of MS-222 with isoflurane effectively extended the time of anesthesia, and the zebrafish recovered faster than when anesthetized with the traditional MS-222.	Huang et al. (2010)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Danio rerio	Zebrafish	Ketamine choridrate solution 10%	2, 20, 40 mg/L	Immersion		0.0.36	4–6 months	27 ± 1	Ketamine (2 mg/L) increased aggression-related phenotypes, while 20 and 40 mg/L reduced aggression and elicited stereotypic behaviors by causing hyperlocomotion, altering motor patterns, and increasing circling behavior at the higher concentration tested. 100 mg/L induced anesthesia in zebrafish, opted for lower doses to see neuro effects.		Ketamine (2 mg/L) increased aggression while 20 and 40 mg/L reduced aggression and elicited stereotypic behaviors.
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	300, 600, 900 mg/L	Immersion			14 days	27.8 ± 1.2	Euthanasia: MS-222 and eugenol were ineffective methods for euthanasia at this stage of development.	Strykowski & Schech (2015)	MS-222 and eugenol were ineffective methods for euthanasia at this stage of development.
Danio rerio	Zebrafish	Isoeugenol	500 ,1000, 1500 μL/L	Immersion					Euthanasia: MS-222 and eugenol were ineffective methods for euthanasia at this stage of development.	Strykowski & Schech (2015)	
Danio rerio	Zebrafish	Isoeugenol	540 mg/L	Immersion		0.0.1409	7–27 months	28	Euthanasia:	Von Krogh et al. (2021)	
Danio rerio	Zebrafish	Clove oil	0.10%	Immersion					Euthanasia:	Von Krogh et al. (2021)	
Danio rerio	Zebrafish	2-Phenoxyethanol	3.0 ml/L	Immersion					Euthanasia:	Von Krogh et al. (2021)	
Danio rerio	Zebrafish	MS-222 (tricaine methanesulfonate)	0.5 g/L, 1.0 g/L	Immersion					Euthanasia:	Von Krogh et al. (2021)	
Danio rerio	Zebrafish	Benzocaine	1.0 g/L	Immersion					Euthanasia: having high efficacy, 1 g/L benzocaine was too aversive to be recommended for zebrafish euthanasia.	Von Krogh et al. (2021)	1 g/L benzocaine was too aversive to be recommended for zebrafish euthanasia.
Danio rerio	Zebrafish	Lidocaine HCl	1.0 g/L	Immersion					Euthanasia: 1 g/L lidocaine HCl buffered with 2 g/L $NaHCO_3$ and 50 ml/L 96% ethanol as a humane, reliable, and effective method for induction of euthanasia by overdose in adult zebrafish.	Von Krogh et al. (2021)	Recommended dose: 1 g/L lidocaine HCl buffered with 2 g/L $NaHCO_3$ and 50 ml/L 96% ethanol for humane, reliable, and effective method for induction of euthanasia.

Danio rerio	Zebrafish	Etomidate	50 mg/L	Immersion					Effect as an anesthetic but maintained reflexes >10 minutes.	Von Krogh et al. (2021)	Effect as an anaesthetic but maintained reflexes >10 minutes.
Danio rerio	Zebrafish	Rapid cooling	From 28 to 0–4	Immersion			3–90 dpf	0–4	Euthanasia: <14 dpf requires >12 hours, those 16 to 28 dpf of age require 5 minutes, and >28 dpf require 30 seconds of minimal exposure to rapid cooling for reliable euthanasia.	Wallace et al. (2018)	Variable times needed for exposure to rapid cooling for reliable euthanasia; influenced by age.
Pethia nigrofasciata	Barb, black ruby	Lidocaine	40, 60, 80, 100, 120, 140 mg/L	Immersion		66.66.130	immature, mature		Immature barbs have optimal dose of lidocaine at 80mg/L, adults 100 mg/L.	Priyangika et al. (2007)	Lower concentration of both lidocaine and clove oil required for the induction of anaesthesia compared to other species. May have a limited safety margin.
Pethia nigrofasciata	Barb, black ruby	Clove oil	2, 4, 6, 8, 10, 12, 14 mg/L	Immersion		66.66.130	immature, mature		Immature 8 mg/L and adults 10 mg/L of clove oil.	Priyangika et al. (2007)	
Dawkinsia filamentosa	Barb, blackspot	Alfaxalone	5 mg/L	Immersion		0.0.11		25.5–26.6		Zellar et al. (2018)	
Dawkinsia filamentosa	Barb, blackspot	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion		0.0.11			Buffered with 200 mg/L bicarbonate.	Zellar et al. (2018)	Buffered with 200 mg/L bicarbonate.
Epalzeorhynchos bicolor	Sharkminnow, redtail	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	1.4 ± 0.4 g		Juveniles	25.5	Anesthesia sufficient for handling.	Russo et al. (2006)	Anesthesia sufficient for handling and vaccination.
Hypselobarbus kurali		2-phenoxyethanol	300, 400, 500, 600 µL/L	Immersion		0.0.80			The lowest induction time (<180 seconds) was observed at 500 µL/L and therefore this was considered the lowest effective concentration for anesthesia. At 500 µL/L, recovery time was 133 ± 16 seconds.	Nair & Williams (2015)	The lowest induction time (<180 seconds) was observed at 500 µL/L.
Hypophthalmichthys molitrix	Carp, silver	2-phenoxyethanol	0.2 ml/L	Immersion	3–12 kg		Brood stock	25	Induction to light sedation in 2–3 minutes.	McCarter (1992)	Induction to light sedation in 2–3 minutes.
Hypophthalmichthys molitrix	Carp, silver	2-phenoxyethanol	0.4 ml/L	Immersion					Induction to anesthesia in 5–10 minutes.	McCarter (1992)	Induction to anesthesia in 5–10 minutes.
Hypophthalmichthys molitrix	Carp, silver	Carbon dioxide (dry ice state)	25 kg dry ice/100,000 L (low) to 50 kg/100,000 L (high)	Immersion				9.5–9.7	Solid state CO_2 was used in ice-covered ponds with the three species (two invasive, one noninvasive) together. Fathead minnows were less susceptible to CO_2 exposure than the carps, with 26–96% survival in low-treatment ponds and 4–68% survival in high-treatment ponds.	Cupp et al. (2018)	Minnows were less susceptible to CO_2 than carp.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Hypophthalmichthys nobilis	Carp, bighead	Carbon dioxide (dry ice state)	25 kg dry ice/100,000 L (low) to 50 kg/100,000 L (high)	Immersion				9.5–9.7	Solid state CO_2 was used in ice-covered ponds with the three species (two invasive, one noninvasive) together. Fathead minnows were less susceptible to CO_2 exposure than the carps, with 26–96% survival in low-treatment ponds and 4–68% survival in high-treatment ponds.	Cupp et al. (2018)	Minnows were less susceptible to CO_2 than carp.
Phoxinus erythrogaster	Dace, southern redbelly	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion	0.35–4.46 g		Adult, juvenile		Induction to total loss of equilibrium in 5–13 minutes. Recovery <2 minutes with faster recovery at higher temperatures. Mortality 0%.	Detar & Mattingly (2004)	Induction in 5–13 minutes. Recovery <2 minutes, faster at higher temperatures. Mortality 0%.
Phoxinus erythrogaster	Dace, southern redbelly	Clove oil	40–60 mg/L	Immersion	0.35–4.46 g		Adult, juvenile		Induction to total loss of equilibrium within 3 minutes. Recovery: <5 minutes with faster recovery at higher temperatures. No mortality.	Detar & Mattingly (2004)	Faster recovery at higher temperatures. No mortality.
Phoxinus cumberlandensis	Dace, blackside	Clove oil	40 mg/L	Immersion			Adult, juvenile		Used for anesthesia in the field during elastomer tag placement and fin clipping.	Detar & Mattingly (2004)	Used for anesthesia in the field during elastomer tag placement and fin clipping.
Rhinichthys atratulus	Dace, blackside	MS-222 (tricaine methanesulfonate)	300–500 mg/L	Immersion			Adult		Light anesthesia within 3 minutes. Allowed for handling. Recovery following 9 minutes exposure 4–7 minutes. Exposure to this dose range beyond 15 minutes associated with mortality.	MacAvoy & Zaepfel (1997)	Exposure to this dose range beyond 15 minutes associated with mortality.
Rutilus rutilus	Roach	Clove oil	4 mg/L	Immersion	71 g			15	Provided sedation for 6 hours without loss of equilibrium, at which time fish removed from anesthetic. Considered useful for transport. No mortality.	Hoskonen & Pirhonen (2004)	Considered useful for transport. No mortality.
Tinca tinca	Tench	2-phenoxyethanol	0.5 g/L	Immersion	0.08–1.82 g		Juvenile	25	Induction time 2.2–12.6 minutes. Recovery after 15 minutes of exposure 1.1–3.3 minutes. Recommended for short-term anesthesia.	Myszkowski et al. (2003)	Recommended for short-term anesthesia.

Pimephales promelas	Fathead minnow	Carbon dioxide (dry ice state)	25 kg dry ice/100,000 L (low) to 50 kg/100,000 L (high)	Immersion				9.5–9.7	Solid state CO_2 was used in ice-covered ponds with the three species (two invasive, one noninvasive) together. Fathead minnows were less susceptible to CO_2 exposure than the carps, with 26–96% survival in low-treatment ponds and 4–68% survival in high-treatment ponds.	Cupp et al. (2018)	Minnows were less susceptible to CO_2 than carp.
Pimephales promelas	Fathead minnow	Carbon dioxide (gas state)	12 h continuous flow-through CO_2 exposure at 5, 15, and 25°C water temperatures	Immersion	2.6 ± 1.0 g	0.0.18	Adult		CO_2 toxicity can differ by species and water temperature. Bluegill were more sensitive than fathead minnow at all water temperatures.	Cupp et al. (2020)	CO_2 toxicity can differ by species and water temperature; bluegill were more sensitive than fathead minnow at all water temperatures.
Rutilus frisii kutum	Kutum, Caspian	Clove essence	50, 200, 400 ppm	Immersion		30.0.0		18	No mortalities occurred at any doses.	Farahi et al. (2011)	No mortalities occurred at any doses.
Carassius auratus, *Danio rerio*	Goldfish, zebrafish	Menthol (dl-menthol Nacalai Tesque Inc., Japan)	0.1–3.0 mM	Immersion				25 ± 1	Applied by injection to one side of a gill (50 μL), oral cavity (50 μL), and one side of the body surface (100 μL) of medaka fish and goldfish (100, 100, and 300 μL, respectively) by injection with a 1-ml syringe, and the peritoneal cavity (10 μL for medaka fish and 30 μL for goldfish) was injected with a 100-μL Hamilton microsyringe.	Kasai et al. (2014)	Menthol (d-, l-, dl-types) at 0.4 mM produced surgical anesthesia in medaka, goldfish, and zebrafish. GABAA mediated.
Family Leuciscidae											
Gila elegans	Bonytail	Metomidate hydrochloride	0.2, 0.5, 1.0, 2.5, 3.0, 3.5, 4.0 mg/L	Immersion	193.9 g	0.0.20		16.4–29.98	Aqui-S® 20e had better survivability during 4-, 8-, and 12-hour transport.	Tennant et al. (2019)	
Gila elegans	Bonytail	MS-222 (tricaine methanesulfonate)	55.0, 60.0, 65.0, 70.0 mg/L	Immersion						Tennant et al. (2019)	
Gila elegans	Bonytail	Isoeugenol	10.0, 15.0, 17.0, 20.0 mg/L	Immersion						Tennant et al. (2019)	
Order Cyprinodontiformes											
Family Poeciliidae											
Poecilia velifera	Molly, sailfin	2-phenoxyethanol	600 mg/L	Immersion	1.56 ± 0.27 g		Adult	23	Induction: 7.50 ± 11.97 minutes. Recovery (fish placed in fresh water immediately after induction): 1.28 ± 2.53 minutes.	Hseu et al. (1997)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Xiphophorus maculatus	Platyfish, southern	MS-222 (tricaine methanesulfonate)	30 mg/L	Immersion	1.71 ± 0.36 g		Adult		Provides light sedation.	Guo et al. (1995)	
Xiphophorus maculatus	Platyfish, southern	Metomidate hydrochloride	1 mg/L	Immersion	1.71 ± 0.36 g		Adult		Provides light sedation.	Guo et al. (1995)	
Xiphophorus maculatus	Platyfish, southern	Quinaldine sulphate	10 mg/L	Immersion	1.71 ± 0.36 g		Adult		Provides light sedation.	Guo et al. (1995)	
Xiphophorus maculatus	Platyfish, southern	2-phenoxyethanol	220 mg/L	Immersion	1.71 ± 0.36 g		Adult		Provides light sedation.	Guo et al. (1995)	
Poecilia spp.	Mollies	Sodium bicarbonate	1, 100 g/L	Immersion				27–29	Sedation in 100 g/L took 83.2–104.6 seconds and recovery 47–62.5 seconds. 1 week after exposure author noted a 40–60% survival rate. Simulated transport of fish for 6 hours in water containing 1 g/L of sodium bicarbonate showed survival ranging from 70% to 100% a week after transport.	Caipang et al. (2021)	
Poeciliidae spp.	Ornamentals	Metomidate hydrochloride	40, 60, 100, 250, 100 mg/L	Immersion				22–24	Euthanasia: euthanized at a concentration of 40 mg/L metomidate hydrochloride for a total exposure time of 38 minutes. Most species tested were successfully euthanized with metomidate hydrochloride at a concentration of 100 mg/L, with total exposure times ranging from 35 to 96 minutes.	Yanong (2021)	
Order Elopiformes											
Family Megalopidae											
Megalops Atlanticus	Tarpon	Diazepam => MS-222 (tricaine methanesulfonate)	5–22.5 mg/kg => 25–40 mg/L	PO, immersion		0.0.4			Given oral diazepam, MS-222 immersion to new system, did well for transfer.	C.M. Burns, N.D. Mylniczenko (pers. exp.)	
Megalops Atlanticus	Tarpon	MS-222 (tricaine methanesulfonate)	40–60 mg/L	Immersion		0.0.6			Good sedation, prolonged procedures in 60 deep anesthesia.	C.M. Burns, N.D. Mylniczenko (pers. exp.)	
Order Gadiformes											
Family Gadidae											
Gadus morhua	Cod, Atlantic	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion	84 ± 5 g			8.4	Anesthesia within 4 minutes. Exposure time 2.8–3.4 minutes. Recovery time 3.7–7.1 minutes.	Mattson & Riple (1989)	

Gadus morhua	Cod, Atlantic	Benzocaine dissolved in ethanol	40 mg/L	Immersion	101 ± 6 g	9.5	Anesthesia reached within 3 minutes. Exposure time 2.1–3.2 minutes. Recovery time 3.9–10.8 minutes. Mortality 50% at 75–100 mg/L.	Mattson & Riple (1989)
Gadus morhua	Cod, Atlantic	Metomidate hydrochloride	5 mg/L	Immersion	101 ± 6 g	9.6	Anesthesia reached within 4 minutes. Exposure time 4.8–10.8 minutes. Recovery time 8.2–19.2 minutes. Used for sorting and handling broodstock.	Mattson & Riple (1989)
Gadus morhua	Cod, Atlantic	Benzocaine	25–35 mg/L	Immersion	10, 100, 1000 g	8, 16	Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)
Gadus morhua	Cod, Atlantic	MS-222 (tricaine methanesulfonate)	55–60 mg/L	Immersion			Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)
Gadus morhua	Cod, Atlantic	Metomidate hydrochloride	3–6 mg/L	Immersion			Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)
Gadus morhua	Cod, Atlantic	2-phenoxyethanol (Sigma-Aldrich AS, Oslo, Norway)	0.25 mg/L	Immersion			Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Gadus morhua	Cod, Atlantic	Metomidate hydrochloride + benzocaine	1.0–3.0 + 15–22 mg/L	Immersion					Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)	
Gadus morhua	Cod, Atlantic	Metomidate hydrochloride + MS-222	0.5–2.0 + 37.5–45 mg/L	Immersion					Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)	
Gadus morhua	Cod, Atlantic	2-phenoxyethanol + benzocaine	0.1–1.5 + 15–20 mg/L	Immersion					Induction and recovery times varied in relation to water temperature and were generally shorter at 16°C for all weight groups and treatments compared to 8°C. Concentrations varied by size and no suitable dose for found for benzocaine at 8°C in 1000 g of fish.	Zahl et al. (2009)	
Gadus morhua	Cod, Atlantic	Benzocaine (Benzoak Vet, A.C.D Pharmaceuticals, Leknes, Norway)	20 mg/L	Immersion	400 g	0.0.114		~9	Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	
Gadus morhua	Cod, Atlantic	MS-222 (tricaine methanesulfonate)	55 mg/L	Immersion					Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	
Gadus morhua	Cod, Atlantic	Metomidate hydrochloride	3 mg/L	Immersion					Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	
Family Lotidae											
Lota lota	Burbot	Etomidate	0.5 ml/L	Immersion	0.5–5000 g	0.0.1600	Spawners	5	When applied in immersion did not cause a change in pH or CO_2 content. Propiscin applied in a water bath can provide up to 1 hour of general anesthesia.	Kazuñ & Siwicki (2012)	

Order Gobiiformes									
Family Gobiidae									
Afurcagobius tamarensis	Goby, Tammar river	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion		18	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)	Sufficient for handling and measurement.
Bathygobius cocosensis	Goby, cocos frill	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion		18	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)	Sufficient for handling and measurement.
Favonigobius lateralis	Goby, southern longfin	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion		18	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)	Sufficient for handling and measurement.
Gobiidae spp.	Ornamentals	Metomidate hydrochloride	40, 60, 100, 250, 100 mg/L	Immersion		22–24	Some species were euthanized at a concentration of 40 mg/L metomidate hydrochloride for a total exposure time of 38 minutes. Most species tested were successfully euthanized with metomidate hydrochloride at a concentration of 100 mg/L, with total exposure times ranging from 35 to 96 minutes. A few catfish species were refractory and recovered after 100 mg/L. However, *Otocinclus* sp. were successfully euthanized at 250 mg/L and bronze corydoras were euthanized at 1000 mg/L.	Yanong (2021)	Wide range in doses and time till effect.
Nemateleotris decora	Firefish, elegant (purple cap)	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion			Deep anesthesia used for parasite removal.	C.M. Burns (pers. exp.)	
Synchiropus splendidus	Mandarinfish	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion			For skin scrape/gill clips.	C.M. Burns (pers. exp.)	Approprate for skin scrape/gill clips.
Order Gonorynchiformes									
Family Chanidae									
Chanos chanos	Milkfish	2-phenoxyethanol	400 mg/L	Immersion	24 ± 1.07 g	28	Provided total loss of equilibrium, allowing phlebotomy.	Hseu et al. (1996)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Chanos chanos	Milkfish	2-phenoxyethanol	80 mg/L	Immersion			Juvenile	15–17, 20–22, 25–27	The study showed that a temperature of 20–22°C in combination with anesthetic (2-phenoxyethanol) application was the optimum condition for long-duration confinement of milkfish juveniles in transport bags.	Failaman et al. (2021)	
Order Gymnotiformes											
Family Gymnotidae											
Electrophorus electricus	Eel, electric	MS-222 (tricaine methanesulfonate)	300 mg/L	Immersion	18				Animal sedated in two separate events at the same dose. Aerated water containing MS-222 was applied over the gills every 2–5 minutes.	Wenger et al. (2016, 2018)	Supplemented with 0.11 mg/kg medetomidine and 2.2 mg/kg ketamine IM.
Electrophorus electricus	Eel, electric	Medetomidine (Dorbene) + ketamine (Narketan)	0.11 mg/kg + 2.2 mg/kg	IM						Wenger et al. (2016, 2018)	
Electrophorus electricus	Eel, electric	MS-222 (tricaine methanesulfonate)	150 mg/L	Spray over gills						Wenger et al. (2016, 2018)	
Electrophorus electricus	Eel, electric	Atimpamezole	0.28 mg/kg	IM						Wenger et al. (2016, 2018)	
Electrophorus electricus	Eel, electric	MS-222 (tricaine methanesulfonate)	205–300 mg/L => 100–150 mg/L	Immersion					Anesthesia involved forced immersion in high concentration, buffered MS-222 (250–300 ppm) in oxygenated water and maintenance out of water at lower concentrations (100–150 ppm) with mechanical gill ventilation, oral oxygen supplementation, and temperature regulation. During induction strong electric pulses ceased before the weaker background sensory pulses (about 10 V) and both ceased when the eel was fully anesthetized, allowing for safe handling.	Poll et al. (2014)	

Order Istiophoriformes										
Family Sphyraenidae										
Sphyraena barracuda	Barracuda, great	MS-222 (tricaine methanesulfonate)	30, 50 mg/L	Immersion			Adult		Lower dose for whole-tank sedation, higher dose for transport. Once transported, blood was drawn from the animal.	N.D. Mylniczenko (pers. exp.)	Lower dose for whole-tank sedation, higher dose for transport.
Sphyraena barracuda	Barracuda, great	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion			Juvenile		Excellent sedation for physical examination and treatments.	N.D. Mylniczenko (pers. exp.)	Excellent sedation for physical examination and treatments.
Order Kurtiformes										
Family Apogonidae										
Pterapogon kauderni	Cardinalfish, banggai	MS-222 (tricaine methanesulfonate)	70–90 mg/L	Immersion				25		C.M. Burns (pers. exp.)	
Sphaeramia nematoptera	Cardinalfish, pajama	MS-222 (tricaine methanesulfonate)	65–90 mg/L	Immersion		0.0.15		25	Good to heavy sedation.	C.M. Burns (pers. exp.)	
Order Labriformes										
Family Labridae										
Bodianus anthioides	Hogfish, lyretail	MS-222 (tricaine methanesulfonate)	70 mg/L	Immersion	0.04–0.13				Good sedation, diagnostic examination, debridement.	C.M. Burns (pers. exp.)	Used for a diagnostic examination.
Bodianus rufus	Hogfish, Spanish	MS-222 (tricaine methanesulfonate)	70 mg/L	Immersion					Diagnostic examination.	C.M. Burns (pers. exp.)	Used for a diagnostic examination.
Bodianus pulchellus	Hogfish, spotfin	MS-222 (tricaine methanesulfonate)	70 mg/L	Immersion					Diagnostic examination.	C.M. Burns (pers. exp.)	Used for a diagnostic examination.
Cheilinus fasciatus	Wrasse, redbreasted	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion	0.2–0.4				Good sedation for diagnostic examination.	C.M. Burns (pers. exp.)	
Cheilinus undulatus	Wrasse, humphead	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion					Induction at 100 mg/L, maintenance at 50 mg/L. Excellent for transport and physical examination.	N.D. Mylniczenko (pers. exp.)	Induction at 100 mg/L, maintenance at 50 mg/L. Excellent for transport and physical examination.
Choerodon fasciatus	Tuskfish, harlequin	MS-222 (tricaine methanesulfonate)	60–65 mg/L	Immersion	0.16–0.36				Good sedation for diagnostic examination.	C.M. Burns (pers. exp.)	
Clepticus parrae	Wrasse, creole	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion	0.04–0.05				Good sedation, diagnostic examination, and wound care.	C.M. Burns (pers. exp.)	
Epibulus insidiator	Wrasse, sling-jaw	MS-222 (tricaine methanesulfonate)	45–75 mg/L	Immersion	0.04–0.2				Light to very deep, used for diagnostic examination and radiographs.	C.M. Burns (pers. exp.)	
Gomphosus varius	Wrasse, bird	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion					Deep anesthesia. Take care during sedation to not injury beak.	C.M. Burns (pers. exp.)	
Halichoeres radiatus	Wrasse, puddingwife	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion					Sedation rated as good. Diagnostic examinations performed.	D.L. Neiffer (pers. exp.)	Used for a diagnostic examination. Sedation rated as good.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Lachnolaimus maximus	Hogfish	MS-222 (tricaine methanesulfonate)	25, 50, 100, 125, and 150 mg/L	Immersion	0.2–1.2 kg, 5–50 g		Adult, juvenile		For adult hogfish, Tricaine-S® was effective at inducing light anesthesia at 100–150 mg/L and was preferred over the effective range of Aqui-S® 20e doses (100–200 mg/L) based on fish behavioral observations while undergoing anesthesia.	Shopnitz et al. (2022)	Tricaine-S® preferred over Aqui-S® 20e based on fish behavioral observations while undergoing anesthesia.
Lachnolaimus maximus	Hogfish	Eugenol	50, 75, 100, 200, 300, 400, 500 mg/L	Immersion					For adult hogfish, Tricaine-S® was effective at inducing light anesthesia at 100–150 mg/L and was preferred over the effective range of Aqui-S® 20e doses (100–200 mg/L) based on fish behavioral observations while undergoing anesthesia.	Shopnitz et al. (2022)	
Lachnolaimus maximus	Hogfish	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion			Juvenile		Diagnostic examination.	C.M. Burns (pers. exp.)	Used for a diagnostic exam.
Thalassoma duperreyi	Wrasse, saddle	MS-222 (tricaine methanesulfonate)	90 mg/L	Immersion					Sedation rated as good. Diagnostic examinations performed.	C.M. Burns (pers. exp.)	Used for a diagnostic exam. Sedation rated as good.
Thalassoma lunare	Wrasse, moon	MS-222 (tricaine methanesulfonate)	30 mg/L	Immersion	0.9				Animal compromised.	C.M. Burns (pers. exp.)	
Family Scaridae											
Sparisoma aurofrenatum	Parrotfish, redband	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Provided surgical anesthesia for enucleation.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for enucleation.
Scarus coelestinus	Parrotfish, midnight	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Provided light anesthesia for diagnostic examination.	D.L. Neiffer (pers. exp.)	Used for a diagnostic examination.
Scarus guacamaia	Parrotfish, rainbow	MS-222 (tricaine methanesulfonate)	50–80 mg/L	Immersion	2.03–7.45 kg				Effect varied from moderate sedation to light anesthesia. Diagnostic examinations performed. $N = 4$.	D.L. Neiffer (pers. exp.)	Used for a diagnostic examination. Effect varied from moderate sedation to light anesthesia.
Scarus vetula	Parrotfish, queen	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion					Provided mild to heavy sedation. Diagnostic examinations performed.	D.L. Neiffer (pers. exp.)	Used for a diagnostic examination. Provided mild to heavy sedation.
Sparisoma viride	Parrotfish, stoplight	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion	0.48				Diagnostic eye examination, treatments.	C.M. Burns (pers. exp.)	Used for a diagnostic examination and treatments.

Order Lepisosteiformes											
Family Lepisosteidae											
Lepisosteus platostomus	Shortnose gar	Isoeugenol	240–250 mg/L	Immersion	0.0.15			Stage V surgerical anesthesia. Fish given 240 and 250 mg/L of sedative remained anesthetized for the entire time they were held in the surgery trough.		Gar were induced via a method that did not allow air gulping at high dosages and this facilitiated induction.
Order Lophiiformes											
Family Antennariidae											
Antennarius commerson	Frogfish, Commerson's	MS-222 (tricaine methanesulfonate)	50–80 mg/L	Immersion		Adult	25	Anesthesia was up to 95 minutes for surgery in one case.	C.M. Burns (pers. exp.)	
Antennarius maculatus	Frogfish, warty	MS-222 (tricaine methanesulfonate)	50–60 mg/L	Immersion				Heavy sedation for radiographs and swim bladder aspiration.	T.M. Clauss (pers. exp.)	
Antennarius maculatus	Frogfish, warty	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion		Juvenile-adult	25	Diagnostic examination, radiographs, surgery, treatments.	C.M. Burns (pers. exp.)	
Antennarius striatus	Frogfish, striated	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion		Adult		Diagnostics performed.	Yanong et al. (2003)	
Antennarius striatus	Frogfish, striated	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion	200 g			Negatively buoyant, air aspiration.	D.L. Neiffer (pers. exp.)	
Fowlerichthys ocellatus	Frogfish, ocellated	MS-222 (tricaine methanesulfonate)	30–80 mg/L	Immersion	350–450 g			Sedation rated fair to excellent (higher doses better). Examination and topical treatments performed.	D.L. Neiffer (pers. exp.)	
Histrio histrio	Sargassumfish	MS-222 (tricaine methanesulfonate)	30 mg/L	Immersion				Sedation adequate for examination and injections.	D.L. Neiffer (pers. exp.)	
Order Mugiliformes											
Family Mugilidae											
Mugil cephalus	Mullet, flathead grey	2-phenoxyethanol	400 mg/L	Immersion	38.49 ± 3.85 g		31	Provided total loss of equilibrium, allowing phlebotomy.	Hseu et al. (1996)	Provided total loss of equilibrium, allowing phlebotomy.
Myxus elongates	Mullet, sand grey	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion			18	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)	
Order Osteoglossiformes											
Family Mormyridae											
Gnathonemus petersii	Fish, elephantnose	Alphaxalone/ alphadolone acetate	2 mg/L for induction and 1.5 mg/L for maintenance	Immersion	~15 g		23	Loss of equilibrium and cessation of opercular movement at 20 minutes. Recovery took an average of 17 minutes following 2.5 hours of exposure.	Peters et al. (2001)	Recovery took average of 17 minutes following 2.5 hours of exposure.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Family Osteoglossidae											
Arapaima gigas	Arapaima/ pirarucu	Chloroform	3 ml in a 2-L gas mask supplied with atmospheric air	Inhalation	~400 g	0.0.10	Adult	28	Anesthetic induction occured shortly after chloroform inhalation (10 ± 3 seconds). Therecovery time recorded for chloroform was 15 ± 4 minutes. This study demonstrates theusefulness of chloroform-induced anesthesia in air-breathing fish.	Carreiro et al. (2011)	
Arapaima gigas	Arapaima/ pirarucu	Urethane	1% solution	Immersion					Arapaima did not recover from anesthesia unassisted. Revived via artifically ventilting the bladder with air until the fish could surface and breath unassisted.	Farrell & Randall (1978)	Arapaima were artifically air ventilated until the fish could surface and breath unassisted.
Arapaima gigas	Arapaima/ pirarucu	MS-222 (tricaine methanesulfonate)	25, 50, 75, 100 mg/L	Immersion		0.0.6	Juvenile		Efficient anesthetic effects in juvenile paiches at a concentration of 100 mg/L.	Hinostroza & Serrano-Martinez (2013)	
Arapaima gigas	Arapaima/ pirarucu	Benzocaine	25, 50, 75, 100 mg/L	Spray on gills					Benzocaine sprinkled directly in the gills of pirarucu shown to be an efficient anesthetic both for juveniles and adult fish. Absence of movements was observed for 2 minutes, time enough for most handling procedures. No mortality occurred even 1e month after experiments.	Honczaryk & Inoue (2009)	No mortality occurred up to 1 month after experiments.
Arapaima gigas	Arapaima/ pirarucu	Eugenol	30, 60 mg/L	Spray on gills						Honczaryk & Inoue (2009)	
Arapaima gigas	Arapaima/ pirarucu	MS-222 (tricaine methanesulfonate)	500 mg/L (euthanasia)	Immersion	4.75 ± 0.07 g	0.0.41	2–3 weeks, 3–4 months	27–30	Animals were euthanized for this study.	Pelster et al. (2020)	
Arapaima gigas	Arapaima/ pirarucu	Ketamine	10 mg/kg	PO	664 ± 38 g	0.0.1	Adult	68–74F	Placed in whole trout, 27 minutes later sedated sufficiently for transportation. Permitted being placed in a sling.	Raines & Clancy (2009)	Longer induction produced sufficient level for transportation.

Order Ovalentaria										
Family Grammatidae										
Gramma loreto	Gramma, royal	MS-222 (tricaine methanesulfonate)	65–90 mg/L	Immersion				Sedation rate was good. Diagnostic examinations performed.	D.L. Neiffer (pers. exp.)	Sedation rate as good. Diagnostic examinations performed.
Family Plesiopidae										
Calloplesiops altivelis	Comet	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion	0.03			Good sedation.	C.M. Burns (pers. exp.)	
Paraplesiops meleagris	Blue devil, southern	MS-222 (tricaine methanesulfonate)	65–90 mg/L	Immersion		0.0.2	25	Light to good for diagnostic examination, treatments.	D.L. Neiffer (pers. exp.)	
Family Pomacentridae										
Abudefduf saxatilis	Sergeant major	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion			25	Provided surgical anesthesia for kidney culture.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for kidney culture.
Amphiprion melanopus	Clownfish, fire	MS-222 (tricaine methanesulfonate)	50–70 mg.L	Immersion			25	Provided light to good sedation.	C.M. Burns (pers. exp.)	Provided light to good sedation.
Amphiprion ocellaris	Anemonefish, clown	MS-222 (tricaine methanesulfonate)	60–70 mg/L	Immersion			25		C.M. Burns (pers. exp.)	
Amphiprion percula	Clownfish, orange	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion			25	Provided mild to heavy sedation for examinations.	D.L. Neiffer (pers. exp.)	Sedation level varied from mild to heavy.
Amphiprion sebae	Anenomefish, sebae	Clove oil derivative (prepared from dry clove)	10.0, 17.5, 25.0, 40.0, 50.0, 75.0, and 100.0 mg/L	Immersion		0.0.110	25	To determine the optimum concentration of clove extract to anesthetize and transport the fish under packed conditions. Optimal dosage with no mortalities 17.5 mg/L.	Balamurugan et al. (2016)	Recommended dose: 17.5 mg/L. No mortalities.
Chromis cyanea	Chromis, blue	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion			25	Sedation rated as good. Examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Diagnostic examination performed.
Chromis multilineata	Chromis, brown	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion			25	Sedation rated as good. Examination and transport.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Examination and transport.
Chromis viridis	Chromis, blue-green	MS-222 (tricaine methanesulfonate)	50–65 mg/L	Immersion			25	Good for diagnostic examination, surgeries.	C.M. Burns (pers. exp.)	
Dascyllus melanurus	Humbug, blacktail	MS-222 (tricaine methanesulfonate)	90 mg/L	Immersion			25	Sedation rated as good. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Diagnostic examination performed.
Dascyllus trimaculatus	Dascyllus, threespot	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion			25	Provided heavy sedation for examinations.	D.L. Neiffer (pers. exp.)	Provided heavy sedation for examinations.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Pomacentridae spp.	Misc species	Metomidate hydrochloride	40, 60, 100, 250, 100 mg/L	Immersion				22–24	Some species were euthanized at a concentration of 40 mg/L metomidate hydrochloride for a total exposuretime of 38 minutes. Most species tested were successfully euthanized with metomidate hydrochloride at a concentration of 100 mg/L, with total exposure times ranging from 35 to 96 minutes. A few catfish species were refractory and recovered after 100 mg/L. However, *Otocinclus* sp. were successfully euthanized at 250 mg/L and bronze corydoras were euthanized at 1000 mg/L.	Yanong (2021)	Wide dose range for euthanasia and exposure time to effect.
Premnas biaculeatus	Anenomefish, spinecheek	MS-222 (tricaine methanesulfonate)	60–90 mg/L	Immersion				25	Light to good sedation. Examination, tissue biopsy.	C.M. Burns (pers. exp.)	Light to good sedation. Dignostic examinations and biopsy performed.
Order Perciformes											
Family Caesionidae											
Caesio cuning	Fusilier, redbelly yellowtail	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion	0.06				Light to good to excessively deep.	C.M. Burns (pers. exp.)	
Family Centrarchidae											
Lepomis macrochirus	Bluegill	Carbon dioxide (gas state)	12-h continuous flow-through CO_2 exposure at 5, 15, and 25°C water temperatures	Immersion	2.7 ± 1.0 g	0.0.18	Juvenile	5, 15, 25	CO_2 toxicity can differ by species and water temperature. Bluegill were more sensitive than fathead minnow at all water temperatures.	Cupp et al. (2020)	Bluegill were more sensitive than fathead minnow at all water temperatures.
Lepomis macrochirus	Bluegill	Electric handling gloves	FHGs vs. PES vs. handling	Electroanesthesia		0.0.36			(1) Lower-voltage, non-pulsed-DC fish-handling gloves that tend to only sedate fish while the gloves are touching the animal. (2) A comparatively high-voltage, pulsed-DC portable electrosedation system.	Abrams et al. (2018)	

Lepomis macrochirus	Bluegill	Isoeugenol	20 mg/L	Immersion	213 ± 118 g	Juveniles-young adults	12 ± 2	Induction within 3 minutes. Total exposure time ≤15 minutes. Recovery within 8 minutes. Useful for basic handling procedures.	Stehly & Gingerich (2001)	Useful for basic handling procedures.
Lepomis macrochirus	Bluegill	Isoeugenol	20 mg/L	Immersion	0.54 ± 0.2 g	Fry-fingerling		Induction within 4.1 minutes. Total exposure time ≤15 minutes. Recovery within 5 minutes. Useful for basic handling procedures.	Stehly & Gingerich (2001)	Useful for basic handling procedures.
Micropterus salmoides	Bass, largemouth	Clove oil	5–9 mg/L	Immersion		Fingerling, subadult	21	Time to deep sedation 368 seconds. Sufficient for transport (reduced activity while maintaining equilibrium). Recovery 417 seconds.	Cooke et al. (2004)	
Micropterus salmoides	Bass, largemouth	Clove oil	15–20 mg/L	Immersion				Time to moderate anesthesia 651 seconds. Recovery 1699 seconds.	Cooke et al. (2004)	
Micropterus salmoides	Bass, largemouth	MS-222 (tricaine methanesulfonate)	50 mg/L => 25 mg/L	Immersion				Induction to maintenance. Provided sufficient sedation for transport.	Cooke et al. (2004)	Provided sufficient sedation for transport.
Micropterus salmoides	Bass, largemouth	Electroanesthesia	FHGs vs. PES vs. handling	Electroanesthesia	0.0.37			(1) Lower-voltage, non-pulsed-DC fish-handling gloves that tend to only sedate fish while the gloves are touching the animal. (2) A comparatively high-voltage, pulsed-DC portable electrosedation system.	Abrams et al. (2018)	
Micropterus salmoides	Bass, largemouth	Electric handling gloves	4mA at 30 and 120 s	Electroanesthesia			12–19	After a 30-minute post-treatment retention period, blood chemistry and ventilation rates were similar between fish held with fish-handling gloves and those held with bare hands. This study supports the notion that electric fish-handling gloves are a safe and effective tool for practitioners who need to temporarily immobilize fish for handling, enumeration, or performing various scientific procedures.	Ward et al. (2017)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Family Centropomidae											
Centropomus undecimalis	Snook, common	MS-222 (tricaine methanesulfonate)	50–60 mg/L	Immersion					Provided mild sedation for diagnostic examinations.	D.L. Neiffer (pers. exp.)	
Family Chaetodontidae											
Forcipiger longirostris	Butterflyfish, longnose	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion					Sedation was rated good and provided good anesthesia for examination and radiographs.	C.M. Burns (pers. exp.)	
Chaetodon spp.	Butterflyfish spp.	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion						C.M. Burns (pers. exp.)	
Chelmon rostratus	Butterflyfish, copperband	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion						C.M. Burns (pers. exp.)	
Hemitaurichthys polylepis	Butterflyfish, pyramid	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion						C.M. Burns (pers. exp.)	
Hemitaurichthys zoster	Butterflyfish, brown and white	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion						C.M. Burns (pers. exp.)	
Heniochus acuminatus	Coralfish, pennant	MS-222 (tricaine methanesulfonate)	90 mg/L	Immersion					Sedation rated as good. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Diagnostic examination performed.
Heniochus sp.	Bannerfish	MS-222 (tricaine methanesulfonate)	90 mg/L	Immersion					Provided heavy sedation for diagnostic examinations.	D.L. Neiffer (pers. exp.)	Provided heavy sedation for diagnostic examinations.
Family Gerreidae											
Eucinostomus gula	Mojarra, jenny	MS-222 (tricaine methanesulfonate)	70–90 mg/L	Immersion					Light to deep anesthesia.	C.M. Burns (pers. exp.)	
Gerres cinereus	Mojarra, yellow fin	MS-222 (tricaine methanesulfonate)	70–90 mg/L	Immersion					Light to deep anesthesia.	C.M. Burns (pers. exp.)	
Family Haemulidae											
Anisotremus virginicus	Porkfish	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion					Provided surgical anesthesia for enucleation and kidney culture.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for enucleation and kidney culture.
Anisotremus surinamensis	Margate, black	MS-222 (tricaine methanesulfonate)	90–100 mg/L	Immersion					Good sedation for diagostic examination.	C.M. Burns (pers. exp.)	
Haemulon aurolineatum	Grunt, tomtate	MS-222 (tricaine methanesulfonate)	80–100 mg/L	Immersion					Sedation rated good. Examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated good. Examination performed.
Haemulon carbonarium	Grunt, caesar	MS-222 (tricaine methanesulfonate)	60–85 mg/L	Immersion					Diasnostic examination, skin scrapes/gill clips.	C.M. Burns (pers. exp.)	Diasnostic examination, skin scrapes/gill clips.
Haemulon chrysargyreum	Grunt, smallmouth	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion					Provided surgical anesthesia for kidney culture.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for kidney culture.

Haemulon flavolineatum	Grunt, french	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion				Provided surgical anesthesia for enucleation and kidney culture.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for enucleation and kidney culture.
Haemulon melanurum	Grunt, cottonwick	MS-222 (tricaine methanesulfonate)	70–110 mg/L	Immersion				Sedation rated as good. Examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Examination performed.
Haemulon plumieri	Grunt, white	MS-222 (tricaine methanesulfonate)	85–100 mg/L	Immersion				Sedation rated good. Examinations performed.	D.L. Neiffer (pers. exp.)	Sedation rated good. Examinations performed.
Haemulon sciurus	Grunt, bluestriped	MS-222 (tricaine methanesulfonate)	70–110 mg/L	Immersion				Most sedations rated as good. Diagnostic examinations, injections, and enucleation (one case) performed.	D.L. Neiffer (pers. exp.)	Most sedations rated as good. Diagnostic examinations, injections, and enucleation.
Plectorhinchus spp.	Sweetlips	MS-222 (tricaine methanesulfonate)	60–80 mg/L	Immersion	2.7–3.7		25	Good anesthesia for diagnostic examination, blood draw.	C.M. Burns (pers. exp.)	
Family Kyphosidae										
Girella elevata	Drummer, black	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion			18	Induction within 3 mininutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)	Sufficient for handling and measurement.
Microcanthus strigatus	Tang, convict	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion				Provide heavy sedation.	D.L. Neiffer (pers. exp.)	Provided heavy sedation.
Scorpis lineolatus	Sweep, silver	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion			18	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.
Family Lateolabracidae										
Lateolabrax japonicus	Sea bass, Japanese	2-phenoxyethanol	400 mg/L	Immersion	48.98 ± 3.47 g		29	Provided total loss of equilibrium, allowing phlebotomy.	Hseu et al. (1996)	Provided total loss of equilibrium allowing phlebotomy.
Lateolabrax japonicus	Sea bass, Japanese	2-phenoxyethanol	400 mg/L	Immersion	4.4 ± 0.86 g	Juvenile	28	Induction 2.13 + 0.45 minutes. Recovery (fish placed in fresh water immediately after induction) 0.69 + 0.15 minutes.	Hseu et al. (1997)	
Lateolabrax japonicus	Sea bass, Japanese	2-phenoxyethanol	400 mg/L	Immersion	4.8 ± 1.46 g	Juvenile	24	Induction 1.75 ± 0.16 minutes. Recovery (fish placed in non-medicated water immediately after induction) 0.49 ± 0.08 minutes.	Hseu et al. (1997)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Lateolabrax maculatus	Sea bass	Eugenol (98.5%)	20, 30, 40, 50, 60 mg/L	Immersion	533.92 ± 20.88 g			20.0 ± 2.0	Based on ideal induction (<3 minutes) and recovery (<10 minutes), the lowest effective concentrations for spotted sea bass were 60 mg/L for eugenol, 120 mg/L for clove oil, and 140 mg/L for MS-222 at around 20°C.		
Lateolabrax maculatus	Sea bass	Clove oil (85%)	100, 110, 120, 130, 140 mg/L	Immersion	533.92 ± 20.88 g			20.0 ± 2.0	Based on ideal induction (<3 minutes) and recovery (<10 minutes), the lowest effective concentrations for spotted sea bass were 60 mg/L for eugenol, 120 mg/L for clove oil, and 140 mg/L for MS-222 at around 20°C.		The lowest effective concentrations were 60 mg/L for eugenol, 120 mg/L for clove oil, and 140 mg/L for MS-222.
Lateolabrax maculatus	Sea bass	MS-222 (tricaine methanesulfonate)	120, 130, 140, 150 and 160 mg/L	Immersion	533.92 ± 20.88 g			20.0 ± 2.0	Based on ideal induction (<3 minutes) and recovery (<10 minutes), the lowest effective concentrations for spotted sea bass were 60 mg/L for eugenol, 120 mg/L for clove oil, and 140 mg/L for MS-222 at around 20°C.		Based on ideal induction (<3 minutes) and recovery (<10 minutes), the lowest effective concentrations for spotted sea bass were 60 mg/L for eugenol, 120 mg/Lfor clove oil, and 140 mg/L for MS-222 at around 20°C.
Family Latidae											
Lates calcarifer	Barramundi	Clove oil	6–9 mg/L		42 ± 9.74 g			29–30	Dissolved in boiled water induction 1.8–4.5 minutes. Exposed to clove oil for 4 minutes. Recovery 0.5–5.0 minutes. No mortality though some distal gill filament necrosis noted with repeated exposure to 9 mg/l.	Afifi et al. (2001)	
Family Lutjanidae											
Lutjanus sp.	Snapper sp.	Metomidate hydrochloride	50 mg/kg	IM	14 kg				Anesthesia with marked depression of ventilation. Two or more darts used to deliver total.	Harvey et al. (1988)	Anesthesia with marked depression of ventilation. Two or more darts used to deliver total.
Lutjanus apodus	Snapper, schoolmaster	MS-222 (tricaine methanesulfonate)	70–125 mg/L	Immersion					Provided surgical anesthesia for kidney culture.	D.L. Neiffer (pers. exp.)	Provided surgical anesthesia for kidney culture.

Lutjanus argentimaculatus	Snapper, mangrove red	2-phenoxyethanol	400 mg/L	Immersion	39.21 ± 2.08 g		29	Provided total loss of equilibrium, allowing phlebotomy.	Hseu et al. (1996)	Provided total loss of equilibrium, allowing phlebotomy.
Lutjanus bohar	Snapper, two-spot red	Metomidate hydrochloride	50 mg/kg	IM	14			Level 3 sedation.	Harvey et al. (1988)	
Lutjanus coeruleolineatus	Snapper, blueline	MS-222 (tricaine methanesulfonate)	70–85 mg/L	Immersion				Diagnostic and quarantine examinations.	C.M. Burns (pers. exp.)	
Lutjanus griseus	Snapper, grey	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion				Diagnostic examination, good sedation.	C.M. Burns (pers. exp.)	
Ocyurus chrysurus	Snapper, yellowtail	MS-222 (tricaine methanesulfonate)	75–85 mg/L	Immersion	50–120 g			Effect varied from mild to heavy sedation. Examinations performed. $N = 17$.	D.L. Neiffer (pers. exp.)	Effect varied from mild to heavy sedation. Examinations performed.
Ocyurus chrysurus	Snapper, yellowtail	Medetomidine + ketamine	1.1–1.7 + 27–42 mg/kg	IM	2.35–3.65 0.0.6			All fish injected by dives using a jab stick. Initial effect seen in 4–12 minutes. For complete injections, mild to moderate sedation achieved. Fish netted and transferred to MS-222 bath for phlebotomy. Fish culled as part of disease surveillance and thus no reversal agent given.	D.L. Neiffer (pers. exp.)	All fish injected by divers using pole syringe. For complete injections, mild to moderate sedation achieved.
Ocyurus chrysurus	Snapper, yellowtail		(ratio M:K averages 24:1)							
Symphorichthys spilurus	Snapper, sailfin	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion				Diagnostic examination, good sedation.	C.M. Burns (pers. exp.)	
Family Moronidae										
Dicentrarchus labrax	Sea bass, European	Quinaldine sulphate + diazepam	7.5 mg/L + 2 mg/L	Immersion	8–9 g	Juvenile	24–25	Induction time 1–2 minutes. Recovery time 4–6 minutes. Provides deep anesthesia suitable for marking, surgery, and handling. Note: Quinaldine sulfate alone at 15 mg/L associated with 10% mortality and at 20–25 mg/L associated with 30–100% mortality. pH 7.9–8.2.	Yanar & Kumlu (2001)	Quinaldine sulfate alone at 15 mg/L associated with 10% mortality and at 20–25 mg/L associated with 30–100% mortality. pH = 7.9–8.2.
Dicentrarchus labrax	Sea bass, European	Quinaldine sulphate + diazepam	5 mg/L + 2 mg/L	Immersion	8–9 g	Juvenile	24–25	Induction time 1–2 minutes. Recovery time 3–5 minutes. Provides light anesthesia suitable for transportation. pH 7.9–8.2.	Yanar & Kumlu (2001)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Morone saxatilis	Bass, striped	Benzocaine dissolved in 100% ethanol at 1 g/30 ml	55–80 mg/L	Immersion	0.118–3.5		Juvenile, adult	22	Induction 3 minutes. Recovery 1.5–14.25 minutes.	Gilderhus et al. (1991)	
Morone saxatilis	Bass, striped	MS-222 (tricaine methanesulfonate)	20 mg/L	Immersion	48–81 cm		Adult	21	Prior to placement in bath, gills were sprayed twice with MS-222 solution (3200 mg/L). Procedure: mock intracoelomic transmitter placement. Induction 38–58 seconds. Recovery after 5 minutes of exposure to drug 156–272 seconds. No mortalities. Note from author (D.N.): species appears to be sensitive to MS-222.	Jennings & Looney (1998)	Species appears to be sensitive to MS-222.
Morone saxatilis × *M. chrysops*	Hybrid striped bass	Ketamine	125, 300, 500 mg/kg	Oral	13–31 g	0.0.6			Offering varying doses of ketamine (125, 300, and 500 mg/kg) injected into pieces of earthworm due to ways species fed. 125 mg/kgresulting in light sedation and 300 mg/kg induced a deeper stage of anesthesia.	Raines & Clancy (2009)	
Morone saxatilis x M. chrysops	Bass, hybrid striped	MS-222 (tricaine methanesulfonate)	25 mg/L	Immersion	87 ± 24.4 g			23	Light sedation.	Davis & Griffin (2004)	Light sedation.
Morone saxatilis x M. chrysops	Bass, hybrid striped	Clove oil	8 μL/L	Immersion	87 ± 24.4 g			23	Light sedation.	Davis & Griffin (2004)	Light sedation.
Morone saxatilis x M. chrysops	Bass, hybrid striped	Isoeugenol	3.6 mg/L	Immersion	87 ± 24.4 g			23	Light sedation.	Davis & Griffin (2004)	Light sedation.
Morone saxatilis x M. chrysops	Bass, hybrid striped	Quinaldine sulphate	8.3 mg/L	Immersion	87 ± 24.4 g			23	Light sedation.	Davis & Griffin (2004)	Light sedation.
Morone saxatilis x M. chrysops	Bass, hybrid striped	Metomidate hydrochloride	1.5 mg/L	Immersion	87 ± 24.4 g			23	Light sedation.	Davis & Griffin (2004)	Light sedation.
Micropterus salmoides, *Morone saxatilis* × *M. chrysops*	Bass, largemouth; hybrid striped	Isoeugenol	20–80 mg/L	Immersion					Concentrations of 40–60 mg/L rapidly anesthetize cold-water species to the handleable stage in <3–5 minutes whereas 60–80 mg/L is necessary to anesthetize cool- and warm-water species in a comparable amount of time.	Javahery et al. (2012)	Recommended dose: 40–60 mg/L (cold-water species); 60–80 mg/L (cool- and warm-water species).

Family Mullidae										
Parupeneus multifasciatus	Goatfish, manybar	MS-222 (tricaine methanesulfonate)	30–70 mg/L	Immersion				Light to heavy sedation for examination.	C.M. Burns (pers. exp.)	Light to heavy sedation for examination.
Pseudupeneus maculates	Goatfish, spotted	MS-222 (tricaine methanesulfonate)	30–50 mg/L	Immersion				Heavy sedation.	D.L. Neiffer (pers. exp.)	Heavy sedation.
Family Percidae										
Perca flavescens	Perch, American yellow	Isoeugenol	20 mg/L	Immersion	126 ± 50.1 g	Juvenile-young adult	12 ± 2	Induction within 3 minutes. Total exposure time ≤15 minutes. Recovery within 8 minutes. Useful for basic handling procedures. pH 8.1.	Stehly & Gingerich (1999)	Useful for basic handling procedures.
Perca flavescens	Perch, American yellow	Isoeugenol	20 mg/L	Immersion	1.1 ± 0.22 g	Fry-fingerling	12 ± 2	Induction within 4.1 minutes or less. Total exposure time ≤15 minutes. Recovery within 5 minutes. Useful for basic handling procedures. pH 8.1.	Stehly & Gingerich (1999)	Useful for basic handling procedures.
Perca flavescens	Perch, American yellow	MS-222 (tricaine methanesulfonate)	80, 120 mg/L	Immersion	2.7 ± 1.4		18.9 ± 0.2	Treatment periods 4.0–10.5 minutes for yellow perch.	Bowker et al. (2017)	
Perca flavescens	Perch, American yellow	MS-222 (tricaine methanesulfonate)	100, 150, 200, 250, 300 mg/L	Immersion	~7 g		22 ± 0.5	Exposed to 250 mg/L MS-222 combined with bicarbonate buffer at three ratios (w/w 1:0.5, 1:1, and 1:2) showed significantly ($P < 0.05$) reduced anesthesia induction and recovery times. The shortest times of anesthesia induction and recovery were observed in treatments using the 1:1 MS-222 to buffer ratio (dose maybe optimal for minimizing handling disturbance).	Zhai et al. (2018)	
Perca flavescens	Perch, American yellow	MS-222 (tricaine methanesulfonate)	150 mg/L (high dose), 100–125 mg/L (low dose)	Immersion	0.0.10		17		Hanley et al. (2010)	
Perca fluviatilis	Perch, European	Clove oil dissolved in 95% ethanol at 1:10 ratio.	6 mg/L	Immersion	17 g		15	Provided sedation for 6 hours without loss of equilibrium, at which time fish were removed from anesthetic. Considered useful for transport. No mortality.	Hoskonen & Pirhonen (2004)	Provided sedation for 6 hours and useful for transport. No mortality.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Perca fluviatilis L.	Perch, European	Etomidate	1, 2 ml/L	Immersion	162.98 ± 29.40 g	0.0.20		19.7 ± 0.1	Taking into consideration the anesthesia recovery rates of the fish and recovery times, the low intensity of stress reactions, and the 100% fish survival rate following the procedure, it is justified to recommend using a propiscin solution at a concentration of 2 ml/L during rearing procedures that require anesthetizing this species.	Rożyński et al. (2018)	
Sander vitreus	Walleye	MS-222 (tricaine methanesulfonate)	150 mg/L –>100–125 mg/L	Immersion		0.0.5				Hanley et al. (2010)	
Stizostedion vitreum	Walleye	Isoeugenol	50 mg/L	Immersion	58.3 ± 12.2 g		Fry-fingerling	12 ± 2	Induction averaged 4.3 minutes. Total exposure time <15 minutes. Recovery within 8 minutes. Useful for basic handling procedures. pH 8.1.	Stehly & Gingerich (1999)	
Family Pomacanthidae											
Centropyge bicolor	Angelfish, bicolor	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion				25	Sedation rated excellent. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated excellent. Diagnostic examination performed.
Holacanthus passer	Angelfish, king	MS-222 (tricaine methanesulfonate)	60–75 mg/L	Immersion	0.5			25	Good sedation, diagnostic examination.	C.M. Burns (pers. exp.)	Good sedation. Diagnostic examination performed.
Pomacanthus arcuatus	Angelfish, gray	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion	0.2–1.7 kg	0.0.16		25	Provided mild to heavy sedation. Diagnostic examinations and topical treatments performed.	D.L. Neiffer (pers. exp.)	Provided mild to heavy sedation. Diagnostic examination and topical treatments performed.
Pomacanthus asfur	Angelfish, Arabian	MS-222 (tricaine methanesulfonate)	60–90 mg/L	Immersion				25	High end sedation for swim bladder surgery.	C.M. Burns (pers. exp.)	Good sedation for surgery.
Pomacanthus annularis	Angelfish, bluering	MS-222 (tricaine methanesulfonate)	75–85 mg/L	Immersion	0.5			25	Good sedation, diagnostic examination.	C.M. Burns (pers. exp.)	Good sedation. Diagnostic examination performed.
Pomacanthus imperator	Angelfish, emperor	MS-222 (tricaine methanesulfonate)	75–85 mg/L	Immersion				25	Good sedation, diagnostic examination.	C.M. Burns (pers. exp.)	Good sedation. Diagnostic examination performed.
Pomacanthus paru	Angelfish, French	MS-222 (tricaine methanesulfonate)	60–90 mg/L	Immersion	0.40–1.95 kg	0.0.10		25	Good sedation, diagnostic examination.	D.L. Neiffer (pers. exp.)	Provided mild to heavy sedation. Diagnostic examinations performed.
Pomacanthus semicirculatus	Angelfish, semicircle	MS-222 (tricaine methanesulfonate)	60–85 mg/L	Immersion		0.0.4		25	Variable sedative effect (fair to excellent). Diagnostic examinations and treatments performed.	D.L. Neiffer (pers. exp.)	Variable sedative effect (fair to excellent). Diagnostic examination and treatments performed.

Family Priacanthidae											
Priacanthus arenatus	Bigeye, Atlantic	MS-222 (tricaine methanesulfonate)	60–90 mg/L	Immersion	0.3–0.6	0.0.9		25	Diagnostic examination, exopthalmia treatments. Care taken regarding the eyes during sedation.	C.M. Burns (pers. exp.)	
Family Serranidae											
Centropristis striata	Sea bass, black	Ketamine + dexmedetomidine + midazolam	1-2 mg/kg + 0.025–0.1 mg/kg + 0.2 mg/kg	IM	0.148–0.374			20–22	The protocol was effective in black sea bass, and the fish were consistently sedated and easily handled when anesthetised. Reversals given of atipamezole ranging from 0.25 to 1.0 mg/kg based on dexmed dose.	Christiansen et al. (2014)	
Cephalopholis cruentata	Graysby	MS-222 (tricaine methanesulfonate)	75–100mg/L	Immersion	2.00			25	Examination to surgical dosing.	C.M. Burns (pers. exp.)	
Cromileptes altivelis	Grouper, humpback	MS-222 (tricaine methanesulfonate)	65–70 mg/L	Immersion	0.60			25	Examination and blood draw.	C.M. Burns (pers. exp.)	
Epinephelus itajara	Grouper, Atlantic goliath	MS-222 (tricaine methanesulfonate)	75–95 mg/L	Immersion	7.7–106.2 kg	0.0.5		25	Provided mild to heavy sedation. Diagnostic examinations, injections, and topical treatments performed.	D.L. Neiffer (pers. exp.)	Provided mild to heavy sedation. Diagnostic examination, injections, and topical treatments performed.
Epinephelus itajara	Grouper, Atlantic goliath	MS-222 (tricaine methanesulfonate)	95–125 mg/L	Immersion	3.4–10 kg	0.0.6		25	Effect varied from heavy sedation to anesthesia (swim bladder surgeries and sampling).	D.L. Neiffer (pers. exp.)	Effect varied from heavy sedation to anesthesia.
Epinephelus lanceolatus	Grouper, giant	MS-222 (tricaine methanesulfonate)	1 g/L, 75 mg/L	Immersion			Adult		Induction with high-dose power sprayer over gills, following by maintenance in lower dose.	N.D. Mylniczenko (pers. exp.)	Induction with high dose via pump sprayer over gills, followed by maintenance in lower dose.
Epinephelus morio	Grouper, red	MS-222 (tricaine methanesulfonate)	70–95 mg/L	Immersion	0.51–8.64 kg	0.0.7		25	Effect ranged from mild sedation to light anesthesia. Examinations performed.	D.L. Neiffer (pers. exp.)	Effect ranged from mild sedation to light anesthesia.
Epinephelus ongus	Grouper, white-streaked	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion	610 g				Good for diagnostics (clips and scrapes).	T.M. Clauss (pers. exp.)	Good sedation. Diagnostic examination performed.
Epinephelus polyphekadion	Grouper, camouflage	Clove oil	10 mg/L	Immersion					Suitable for sampling and transportation.	Afifi et al. (2001)	Suitable for sampling and for transportation.
Mycteroperca bonaci	Grouper, black	MS-222 (tricaine methanesulfonate)	80–100 mg/L	Immersion	183–800 g	0.0.5		25	Provided adequate sedation for examination.	D.L. Neiffer (pers. exp.)	
Mycteroperca venenosa	Grouper, yellowfin	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion				25	Provided adequate sedation for examination.	D.L. Neiffer (pers. exp.)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Paralabrax maculatofasciatus	Bass, spotted sand	Isoeugenol	45 –> 35 mg/L	Immersion	40–160 g	0.0.6		20.1 ± 1.36	Mean anesthetic exposure time was 6 minutes and 54 seconds for wild finfish. Induction to maintenance.	Silbernagel & Yochem (2016)	
Paralabrax nebulifer	Bass, barred sand	Isoeugenol	45 –> 35 mg/L	Immersion	40–160 g	0.0.6			Mean anesthetic exposure time was 6 minutes and 54 seconds for wild finfish. Induction to maintenance.	Silbernagel & Yochem (2016)	
Pseudanthias bicolor	Anthias, bicolor	MS-222 (tricaine methanesulfonate)	60–70 mg/L	Immersion	0.02–0.04			25		C.M. Burns (pers. exp.)	
Pseudanthias pleurotaenia	Basslet, square-spot fairy	MS-222 (tricaine methanesulfonate)	60–70 mg/L	Immersion	0.02			25		C.M. Burns (pers. exp.)	
Pseudoanthias sp.	*Anthias* sp.	MS-222 (tricaine methanesulfonate)	77 mg/L	Immersion			Adult		Sedation rated excellent. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)	Sedation rated excellent. Diagnostic examination performed.
Family Siganidae											
Siganus lineatus	Spinefoot, golden-lined	Clove oil	100 mg/L	Immersion	7–39 g		Juvenile	27–29	Time to anesthesia <3 minutes. Time to recovery <5 minutes. Suitable for examination. No mortality observed.		Diagnostic examination performed. No mortality observed.
Family Sparidae											
Acanthopagrus schlegelii	Seabream, blackhead	2-phenoxyethanol	400 mg/L	Immersion	11.55 ± 3.47 g			29	Provided total loss of equilibrium, allowing phlebotomy.	Hseu et al. (1996)	Provided total loss of equilibrium, allowing phlebotomy.
Calamus calamus	Porgy, saucereye	MS-222 (tricaine methanesulfonate)	70–75 mg/L	Immersion				25	Diagnostic examination, treatments.	C.M. Burns (pers. exp.)	
Calamus penna	Porgy, sheepshead	MS-222 (tricaine methanesulfonate)	70–75 mg/L	Immersion	1.7			25	Diagnostic examination, treatments, phlebotomy.	C.M. Burns (pers. exp.)	
Calamus pennatula	Porgy, pluma	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion					Suitable for evaluation of exophthalmia though 100 mg/L excessive in one case.	D.L. Neiffer (pers. exp.)	100 mg/L suitable for examination but dose was high in one case.
Chrysophrys auratus	Seabream, silver	Isoeugenol	120 mg/L => 60 mg/L	Immersion	861.3 ± 64.6 g			11 ± 0.2	Time to surgical anesthesia was 20–25 minutes. During surgery (cannula placement) 60 mg/L oxygenated solution flushed continuously over gills. Poor survival with possible relation to prolonged surgery and/or hypoxemia.	Rothwell et al. (2005)	Poor survival with possible relation to prolonged surgery and/or hypoxemia.

Lagodon rhomboides	Pinfish	MS-222 (tricaine methanesulfonate)	60 mg/L	Immersion	0.6–0.7		25	Good sedation for treatments, tube feeding, blood draw.	C.M. Burns (pers. exp.)	
Pagrus major	Seabream, red	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	320 g	595 days old	20	Induction 3–5 minutes. 100% recovery after 30 minutes of exposure. Observations: maintained stage III anesthesia.	Oikawa et al. (1994)	Stage III anesthesia
Pagrus pagrus	Porgy, red	Ketamine + dexmedetomidine + midazolam	1 mg/kg + 0.025 mg/kg + 0.2 mg/kg	IM	0.05–0.307		20–22	The response of red porgy was extremely variable, and even at the lowest dose tested multiple fish exhibited a severe, often fatal lactic acidosis.	Christiansen et al. (2014)	Variable response with multiple fish exhibiting a severe, often fatal lactic acidosis.
Rhabdosargus sarba	Seabream, goldlined	2-phenoxyethanol	400 μL/L	Immersion	3.2 ± 0.15 g	Juvenile	27–29	Induction 1.25 ± 0.08 minutes. Recovery 0.51 ± 0.04 minutes. No mortality.	Hseu et al. (1998)	
Rhabdosargus sarba	Seabream, goldlined	Benzocaine dissolved in 95% ethanol	50 mg/L	Immersion	3.2 ± 0.15 g	Juvenile	27–29	Induction 1.94 ± 0.03 minutes. Recovery 0.52 ± 0.04 minutes. No mortality.	Hseu et al. (1998)	
Rhabdosargus sarba	Seabream, goldlined	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	3.2 ± 0.15 g	Juvenile	27–29	Induction 1.31 ± 0.06 minutes. Recovery 0.63 ± 0.03 minutes. No mortality.	Hseu et al. (1998)	
Rhabdosargus sarba	Seabream, goldlined	Quinaldine dissolved in 95% ethanol	9 μL/L	Immersion	3.2 ± 0.15 g	Juvenile	27–29	Induction 1.19 ± 0.11 minutes. Recovery 0.40 ± 0.03 minutes. No mortality.	Hseu et al. (1998)	
Rhabdosargus sarba	Seabream, goldlined	Quinaldine sulphate	20 mg/L	Immersion	3.2 ± 0.15 g	Juvenile	27–29	Induction 2.40 ± 0.11 minutes. Recovery 0.51 ± 0.02 minutes. No mortality.	Hseu et al. (1998)	
Sparus aurata	Seabream, gilthead	2-phenoxyethanol	0.15, 0.3, 0.45, 0.6, 0.75 ml/L	Immersion				Optimal doses for deep anesthesia for ongrowing gilthead seabrea was determined to be 0.45 ml/L for 2-PE.	Pires (2017)	
Sparus aurata	Seabream, gilthead	2-phenoxyethanol (99%)	35 μL/L	Immersion	48.5 ± 3.9 g	Juvenile	18		Toni et al. (2015)	EOLA did not produce anesthesia in under 30 minutes for 35 μL/L or less; 50–200 μL/L produced anesthesia and quicker recovery thus an effective anesthetic, but it was unable to prevent a stress response.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Sparus aurata	Seabream, gilthead	Benzocaine dissolved in 100% ethanol (1:20)	22.5 µL/L	Immersion	220 ± 15 g			24 ± 0.5	Used for diagnostic sampling. Loss of sensation and equilibrium within 8 minutes. Recovery within 90 seconds of transfer to anesthetic-free water. No mortality.	Bressler & Ron (2004)	Used for diagnostic sampling. Loss of sensation and equilibrium within 8 minutes. Recovery within 90 seconds of transfer to anesthetic-free water. No mortality.
Sparus aurata	Seabream, gilthead	Clove oil	0.2, 0.4, 0.6, 0.8, 1.0 ml/L	Immersion					Optimal dose for deep anesthesia for ongrowing gilthead seabream was determined to be 0.6 ml/L for clove oil.	Pires (2017)	
Sparus aurata	Seabream, gilthead	Clove oil	2.5, 5, 10, 20, 40, 60 mg/L	Immersion	42.7 ± 6.8 g	0.0.160	Juvenile	19	Optimal clove oil was 60 mg/L.	Jerez-Cepa et al. (2019)	Recommended dose: 80 mg/L (MS-222), 60 mg/L (clove oil). No mortality.
Sparus aurata	Seabream, gilthead	Clove oil dissolved in 100% ethanol (1:5)	44.5 µL/L	Immersion	220 ± 15 g			24 ± 0.5	Used for diagnostic sampling. Loss of sensation and equilibrium within 8 minutes. Recovery within 90 seconds of transfer to anesthetic-free water. No mortality.	Bressler & Ron (2004)	
Sparus aurata	Seabream, gilthead	Etomidate (dissolved in 1:3 96°-ethanol (EtOH))	0.15, 0.3, 0.5, 1.0, 1.5, 2.0 mg/L	Immersion					Etomidate was more effective to minimize stress responses in seabream juveniles transported for 6 hours (in 0.15 mg/L).	Jerez-Cepa et al. (2021)	
Sparus aurata	Seabream, gilthead	Isoeugenol	2, 5, 8, 15, 30, 60 mg/L	Immersion	65.1 ± 5.3 g	0.0.170	Juvenile	19	Aqui-S® resulted more suitable in short-term procedures where deep anesthesia (at 60 mg/L) is required.	Jerez-Cepa et al. (2021)	Aqui-S® better for short-term deep anesthesia while etomidate was more effective to minimize stress responses.
Sparus aurata	Seabream, gilthead	*Lippia alba* oil (EOLA , extracted)	25, 35, 50, 100, 200, 300 µL/L	Immersion		0.0.54				Toni et al. (2015)	
Sparus aurata	Seabream, gilthead	MS-222 (tricaine methanesulfonate)	5, 10, 25, 50, 70, 80, 100 mg/L	Immersion						Jerez-Cepa et al. (2019)	
Sparus aurata	Seabream, gilthead	MS-222 (tricaine methanesulfonate)	50, 100, 150, 200, 250 mg/L	Immersion	151 ± 4.3 g	0.0.108		22 ± 1	Optimal dose for deep anesthesia for ongrowing gilthead seabream was determined to be 150 mg/L for MS-222.	Pires (2017)	Recommended dose: 0.45 ml/L (2-PE), 150 mg/L (MS-222), and 0.6 ml/L (clove oil).

Sparus aurata	Seabream, gilthead	Quinaldine sulphate (plus diazepam)	5 mg/L	Immersion	6–7 g	Juvenile	25–26	Use for light anesthesia and transportation. Induction 1–2 minutes. Recovery 2–4 minutes. Observations: opercular rate 150/min, which is less than the opercular rate when quinaldine sulfate is used alone to reach the same level of anesthesia. Mortality 0%.	Yanar & Kumlu (2000)	
Sparus aurata	Seabream, gilthead	Quinaldine sulphate (plus diazepam)	7.5 mg/L	Immersion	6–7 g	Juvenile	25–26	Light anesthesia achieved. Induction 0–1 minute. Recovery: 3–5 minutes. Observations: opercular rate 190/min. All fish remained sensitive to external stimuli. Mortality 0% at light sedation dose, but 30–100% at deep sedation dose of 15–20 mg/L. In these cases the opecular rate increased to 190/min and then ceased.	Yanar & Kumlu (2000)	Mortality: 0% at light sedation dose, but 30–100% at higher dose.
Sparus aurata	Seabream, gilthead	Quinaldine sulphate	1 mg/L	Immersion	6–7 g	Juvenile	25–26		Yanar & Kumlu (2000)	
Sparus aurata	Seabream, gilthead	Quinaldine sulphate	10 mg/L	Immersion	6–7 g	Juvenile	25–26		Yanar & Kumlu (2000)	
Family Terapontidae										
Bidyanus bidyanus	Perch, silver	Benzocaine	20 mg/L	Immersion	682 ± 99 g			Used for sedation during transport.	Kildea et al. (2004)	
Bidyanus bidyanus	Perch, silver	Clove oil	15, 50 mg/L	Immersion	682 + 99 g			15 mg/L sufficient for light handling, tagging, and harvesting (exposure time 60 minutes). 50 mg/L produced anesthesia suitable for surgical procedures (exposure time 30 minutes).	Kildea et al. (2004)	Recommended dose: 15 mg/L (light handling, tagging, and harvesting); 50 mg/L (surgical anesthesia).
Bidyanus bidyanus	Perch, silver	Isoeugenol	15 mg/L	Immersion	682 + 99 g			Sufficient for light handling, tagging, and harvesting (exposure time 60 minutes).	Kildea et al. (2004)	Sufficient for light handling, tagging, and harvesting (exposure time 60 minutes).
Family Toxotidae										
Toxotes jaculatrix	Archerfish, banded	MS-222 (tricaine methanesulfonate)	90–100 mg/L	Immersion					N.D. Mylniczenko, T.M. Clauss (pers. exp.)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Order Pleuronectiformes											
Family Achiridae											
Trinectes maculatus	Sole, hogchoker	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion					Good anesthesia for examination, cultures.	C.M. Burns (pers. exp.)	
Family Paralichthyidae											
Paralichthys lethostigma	Southern flounder	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Provided adequate sedation for examination.	D.L. Neiffer (pers. exp.)	Provided adequate sedation for examination.
Family Pleuronectidae											
Hippoglossus hippoglossus	Halibut, Atlantic	Benzocaine	40 mg/L	Immersion	200 g	0.0.180		~9	Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Hippoglossus hippoglossus	Halibut, Atlantic	Metomidate hydrochloride	20–30 mg/L	Immersion	2915 $\pm$ 592 g			10	Induction to anesthesia 189–310 seconds. Dose allowed for handling and phlebotomy. Recovery time 220–320 seconds.	Malmstrøm et al. (1993)	
Hippoglossus hippoglossus	Halibut, Atlantic	Metomidate hydrochloride	3 mg/kg	IV				10.5	Metomidate hydrochloride rapidly immobilized the fish, with respiratory depression, reduced heart rate, and loss of balance /motor control within 1 minute (mean). Recovery was slow, with resumed balance /motor control after 26.4 minutes. Opercular respiration movements were resumed more rapidly with a recorded mean of 1.7 minutes. Oral administration was demonstrated to be a way of immobilizing fish, for example in large aquariums, without exposing them to unwanted stress.	Hansen et al. (2003)	Rapid induction, slow recovery.

Hippoglossus hippoglossus	Halibut, Atlantic	Metomidate hydrochloride	9 mg/L	Immersion		10.5	Metomidate hydrochloride rapidly immobilized the fish, with respiratory depression, reduced heart rate, and loss of balance /motor control within 1 minute (mean). Recovery was slow, with resumed balance /motor control after 26.4 minutes. Opercular respiration movements were resumed more rapidly with a recorded mean of 1.7 minutes. Oral administration was demonstrated to be a way of immobilizing fish, for example in large aquariums, without exposing them to unwanted stress.	Hansen et al. (2003)	Rapid induction, slow recovery.
Hippoglossus hippoglossus	Halibut, Atlantic	Metomidate hydrochloride	3 mg/L	Immersion			Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Hippoglossus hippoglossus	Halibut, Atlantic	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion			Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Hippoglossus hippoglossus	Halibut, Atlantic	MS-222 (tricaine methanesulfonate)	250 mg/L	Immersion	2915 + 592 g	10	Induction to anesthesia 250–282 seconds. Dose allowed for handling and phlebotomy. Recovery time 495–649 seconds.	Malmstrøm et al. (1993)	
Paralichthys californicus	Flounder, California	Isoeugenol	45 –> 35 mg/L	Immersion	40–160 g 0.0.6		Mean anesthetic exposure time was 6 minutes and 54 seconds for wild finfish. Induction to maintenance.	Silbernagel & Yochem (2016)	
Family Scophthalmidae									
Scophthalmus maximus	Turbot	Metomidate hydrochloride	3 mg/kg	intravenous		18	Metomidate hydrochloride rapidly immobilized the fish, with respiratory depression, reduced heart rate, and loss of balance /motor control within 1 minute (mean). Recovery was slow, with resumed balance /motor control after 26.4 minutes. Opercular respiration movements were resumed more rapidly with a recorded mean of 1.7 minutes. Oral administration was demonstrated to be a way of immobilizing fish, for example in large aquariums, without exposing them to unwanted stress.	Hansen et al. (2003)	Rapid induction, slow recovery.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Scophthalmus maximus	Turbot	Metomidate hydrochloride	9 mg/L	Immersion				18	Metomidate hydrochloride rapidly immobilized the fish, with respiratory depression, reduced heart rate, and loss of balance /motor control within 1 minute (mean). Recovery was slow, with resumed balance /motor control after 26.4 minutes. Opercular respiration movements were resumed more rapidly with a recorded mean of 1.7 minutes. Oral administration was demonstrated to be a way of immobilizing fish, for example in large aquariums, without exposing them to unwanted stress.	Hansen et al. (2003)	Rapid induction, slow recovery.
Scophthalmus maximus	Turbot	Metomidate hydrochloride	7 mg/kg	Oral				18	Metomidate hydrochloride rapidly immobilized the fish, with respiratory depression, reduced heart rate, and loss of balance /motor control within 1 minute (mean). Recovery was slow, with resumed balance /motor control after 26.4 minutes. Opercular respiration movements were resumed more rapidly with a recorded mean of 1.7 minutes. Oral administration was demonstrated to be a way of immobilizing fish, for example in large aquariums, without exposing them to unwanted stress.	Hansen et al. (2003)	Rapid induction, slow recovery.
Scophthalmus maximus	Turbot	Medetomidine	0.063–420 nM	Immersion	0.25–0.80 g		Juvenile	14	Used as an antifoaling drug.	Hilvarsson et al. (2007)	Used as an antifoaling drug.
Order Salmoniformes											
Family salmonidae											
Coregonus lavaretus	Whitefish, European	Clove oil dissolved in 95% ethanol at 1:10 ratio.	3 mg/L	Immersion	31–44 g			15	Provided sedation for 6 hours without loss of equilibrium, at which time fish removed from anesthetic. Considered useful for transport. No mortality.	Hoskonen & Pirhonen (2004)	Considered useful for transport for up to 6 hours. No mortality.

Hucho hucho	Huchen	Etomidate	1.0–1.5 ml/L	Immersion		Spawners	4.5–5.0		Kazuñ & Siwicki (2012)	
Oncorhynchus kisutch	Salmon, coho	Clove oil	25 mg/L	Immersion	5.47–12.72 kg			Induction 2.5–3.5 minutes. Exposed for 10 minutes. Recovery 7.5–13 minutes. No mortality.	Taylor & Roberts (1999)	
Oncorhynchus kisutch	Salmon, coho	Ketamine	30 mg/kg	IV	1.857 ± 0.102 kg		15	Injected into dorsal aorta via cannula. Caused immediate cessation of ventilation for 10–300 seconds with loss of equilibrium. Ventilation rate recovered within 1–2 hours.	Graham & Iwama (1990)	Injected into dorsal aorta via cannula. Caused immediate cessation of ventilation for 10–300 seconds with loss of equilibrium.
Oncorhynchus kisutch	Salmon, coho	Alphaxalone-alphadolone	0.5–1.0 ml/kg	IM	2–3 kg			Sedation with partial loss of equilibrium. Able to be netted, but responsive.	Harvey et al. (1988)	Sedation with partial loss of equilibrium. Able to be netted, but responsive.
Oncorhynchus mykiss	Trout, rainbow	2-phenoxyethanol	0.2 ml/L	Immersion				Concentrations chosen so stage 3 anesthesia would be induced in 4–7 minutes.	Iwama et al. (1989)	
Oncorhynchus mykiss	Trout, rainbow	2-phenoxyethanol	0.2 ml/L	Immersion	56 ± 5 g	0.0.100	12	Fish were deeply anesthetized with 2-PE at 165 ± 22 seconds and recovered at 209 ± 26 seconds.	Soltanian et al. (2018)	
Oncorhynchus mykiss	Trout, rainbow	Alphaxalone-alphadolone	130, 150 mg/kg	ICe or ⅔ ICe+ ⅓ IM	100–500 g		10	Induction within 5–10 minutes. Doses of 18 mg/kg produced anesthesia. Lower doses only produced sedation. Recovery generally complete within 2 hours. Doses >18 mg/kg associated with apnea and prolonged recoveries (3–6 hours).	Oswald (1978)	Doses of 18 mg/kg produced anesthesia but also apnea and long recoveries. Lower doses only produced sedation.
Oncorhynchus mykiss	Trout, rainbow	Benzocaine	20 mg/L	Immersion	100–500 g		10	Provided adequate sedation within 30 seconds to permit weighing and injections.	Oswald (1978)	Provided adequate sedation within 30 seconds to permit weighing and injections.
Oncorhynchus mykiss	Trout, rainbow	Benzocaine	30 mg/L	Immersion	~400 g			Concentrations chosen so stage 3 anesthesia would be induced in 4–7 minutes.	Iwama et al. (1989)	
Oncorhynchus mykiss	Trout, rainbow	Benzocaine dissolved in ethanol at 1 gram /30 ml to make stock solution	25–40 mg/L	Immersion	2–500 g	Juvenile	Oct-13	Induction 1.25–5.5 minutes. Recovery following 15 minutes of exposure 4–16 minutes. Provided light to heavy sedation.	Gilderhus (1989)	Provided light to heavy sedation.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Oncorhynchus mykiss	Trout, rainbow	Benzocaine dissolved in ethanol at 1 gram /30 ml to make stock solution	30–45 mg/L	Immersion	0.68–2.04 kg		Adult		Induction 2.25–4.5 minutes. Recovery following 15 minutes of exposure 5.5–13.5 minutes. Provided light to heavy sedation.	Gilderhus (1989)	
Oncorhynchus mykiss	Trout, rainbow	Benozocaine (10%)	25, 65 mg/ml	Immersion	900–1000 g	0.40.0		10.1–10.4		Saunders et al. (2020)	Following multiple anesthetizations with TMS, the methemoglobin increased by 90%, 5%, and 1% in brook trout, rainbow trout, and Atlantic salmon, respectively.
Oncorhynchus mykiss	Trout, rainbow	Clove oil dissolved in ethanol at a ratio of 1:10	2–5 mg/L	Immersion	20.46 ± 0.73 g		6 months	9.1 ± 0.2	Recommended for sedation suitable for 6–8 hours of transport.	Keene et al. (1998)	Recommended for sedation and suitable for 6–8 hours of transport.
Oncorhynchus mykiss	Trout, rainbow	Clove oil (80%)	25 mg/L	Immersion	56 ± 5 g	0.0.100		12	Fish were deeply anesthetized with clove oil at 110 ± 18 seconds and recovered at 170 ± 22 seconds.	Soltanian et al. (2018)	
Oncorhynchus mykiss	Trout, rainbow	Clove oil dissolved in ethanol at a ratio of 1:10	40–60 mg/L	Immersion	20.46 ± 0.73 g		6 months	9.1 ± 0.2	Provided deep anesthesia following 3–6 minutes of exposure.	Keene et al. (1998)	
Oncorhynchus mykiss	Trout, rainbow	Clove oil	60 mg/L	Immersion	91.1 ± 3.0, 288.8 ± 9.8 g			11.5 ± 0.5	Fish exposed to MS-222 had significantly higher cortisol levels at 1 hour. These findings show that few differences exist between the anesthetic effects of clove oil and MS-222 on the physiological response of fish to stress. However, clove oil is more effective at reducing the short-term stress response induced by handling and blood sampling, and is recommended as an alternative anaesthetic.	Wagner et al. (2003)	Clove oil was more effective at reducing the short-term stress versus MS-222.
Oncorhynchus mykiss	Trout, rainbow	Clove oil	20, 30, 40, 50, 60 mg/L	Immersion	30.5 ± 11.4 g		Juvenile	15	Basal effective concentrations determined were 40 mg/L for clove oil.	Mohammadi & Khara (2014)	Recomended dose: 40 mg/L (clove oil), 150 mg/L (MS-222), 1 mg/L (ketamine), and 30 mg/L (tobacco). Fish were anesthetized more rapidly with clove oil followed by tobacco extract, ketamine, and MS-222.

Oncorhynchus mykiss	Trout, rainbow	Etomidate	0.5–1.0 ml/L	Immersion		Spawners, commerical fish	4.5–7.0		Kazuñ & Siwicki (2012)	
Oncorhynchus mykiss	Trout, rainbow	Isoeugenol	40, 60 mg/L	Immersion	2.3 ± 0.9		15.2 ± 0.4	Treatment periods 2.25–8.75 minutes for rainbow trout.	Bowker et al. (2017)	
Oncorhynchus mykiss	Trout, rainbow	Isoeugenol	20 mg/L	Immersion	754 ± 145 g	Juveniles-young adults	12 ± 2	Induction within 3 minutes. Total exposure time ≤15 minutes. Recovery within 8 minutes. Useful for basic handling procedures.	Stehly & Gingerich (1999)	Useful for basic handling procedures.
Oncorhynchus mykiss	Trout, rainbow	Isoeugenol	20 mg/L	Immersion	4.1 ± 1.4 g	Fry-fingerling		Induction within 4.1 minutes or less. Total exposure time ≤15 minutes. Recovery within 5 minutes. Useful for basic handling procedures.	Stehly & Gingerich (1999)	Useful for basic handling procedures.
Oncorhynchus mykiss	Trout, rainbow	Ketamine	0.5, 1, 1.2, 1.5, 1.7 mg/L	Immersion	30.5 ± 11.4 g	Juvenile	15	Basal effective concentrations determined were 1 mg/L for ketamine.	Mohammadi & Khara (2014)	
Oncorhynchus mykiss	Trout, rainbow	Ketamine	50 mg/L	IM	100–500 g		10	Induction generally within 5–10 minutes. Anesthesia persisted for 20 minutes at 130 mg/ and 50–80 min at 150 mg/kg. Apnea requiring assisted ventilation occurred in 30% of fish. Recovery took up to 90 minutes and was characterized by excitement and ataxia.	Oswald (1978)	Apnea in 30% fish. Recovery took up to 90 minutes and was characterized by excitement and ataxia.
Oncorhynchus mykiss	Trout, rainbow	Ketamine	30 mg/kg	IV	365 ± 26 g			Injected into dorsal aorta via cannula. Caused immediate cessation of ventilation for 10–300 seconds with loss of equilibrium. Ventilation rate recovered to preanesthesia values within 1–2 hours.	Graham & Iwama (1990)	Immediate cessation of ventilation for 10–300 seconds with loss of equilibrium. Ventilation rate recovered within 1–2 hours.
Oncorhynchus mykiss	Trout, rainbow	Ketamine	100 mg/L	Immersion	18–257 g	0.0.40		The result shows that ketamine can produce anesthesia in the fish as a water-soluble drug and it is safe and effective.	Ganjoor et al. (2021)	Ketamine produced anesthesia in the fish as a water-soluble drug and it is safe and effective.
Oncorhynchus mykiss	Trout, rainbow	Metomidate hydrochloride	5 mg/L	Immersion				Concentrations chosen so stage 3 anesthesia would be induced in 4–7 minutes.	Iwama et al. (1989)	
Oncorhynchus mykiss	Trout, rainbow	Medetomidine	5–20 mg/L	Immersion	300–400 g		10 ± 0.2	Exposure for 10 minutes. Considered to be a good sedative, but not anesthetic.	Horsberg et al. (1999)	Considered to be a good sedative, but not anesthetic.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Oncorhynchus mykiss	Trout, rainbow	Atipamezole	30–80 mg/L (6× medetomidine dose)	Immersion					Exposed to atipamezole for 7–10 minutes. Exposure to 80 mg/L atipamezole resulted in panic-like reactions.	Horsberg et al. (1999)	
Oncorhynchus mykiss	Trout, rainbow	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion	56 ± 5 g	0.0.100		12	Fish were deeply anesthetized with MS-222 at 94 ± 10 seconds and recovered at 138 ± 16 seconds.	Soltanian et al. (2018)	
Oncorhynchus mykiss	Trout, rainbow	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion			Adult			Tubio et al. (2010)	
Oncorhynchus mykiss	Trout, rainbow	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion	0.6–2 kg		Adult		70–75 ppm provides excellent anesthesia for invasive procedures.	N.D. Mylniczenko (pers. exp.)	Recommended dose: 70–75 ppm for surgical procedures.
Oncorhynchus mykiss	Trout, rainbow	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion					Concentrations chosen so stage 3 anesthesia would be induced in 4–7 minutes.	Iwama et al. (1989)	
Oncorhynchus mykiss	Trout, rainbow	MS-222 (tricaine methanesulfonate)	50, 100, 150, 200, 250 mg/L	Immersion	30.5 ± 11.4 g		Juvenile	15	Basal effective concentrations determined were 150 mg/L for MS-222.	Mohammadi & Khara (2014)	
Oncorhynchus mykiss	Trout, rainbow	Propofol 1%	2.5, 5 mg/L	Immersion	~300 g	0.0.36		15	Stage 4 anesthesia was achieved in ~5 minutes with 2.5 mg/L and in ~3 minutes with 5mg/L. Recovery time was between 3 and 9 minutes.	Prieto et al. (2017)	
Oncorhynchus mykiss	Trout, rainbow	Tobacco extract	20, 25, 30, 35, 40 mg/L	Immersion	30.5 ± 11.4 g		Juvenile	15	Basal effective concentrations determined were 30 mg/L for tobacco.	Mohammadi & Khara (2014)	
Oncorhynchus mykiss	Trout, rainbow	Carbon dioxide (CO_2)	50% (balance O_2)	Immersion					Concentrations chosen so stage 3 anesthesia would be induced in 4–7 minutes.	Iwama et al. (1989)	
Oncorhynchus nerka	Salmon, sockeye	Clove oil	50 mg/L	Immersion			Adult	9-Oct	Fish could be handled within 3 minutes for measurement, esophageal implants, and fin clips. Recovery within 10 minutes following 15 minutes of exposure.	Woody et al. (2002)	

Oncorhynchus nerka	Salmon, sockeye	Sodium bicarbonate + acetic acid	40 g + 15 ml (yielded CO_2 328–195 mg/L)	Immersion	1.5–3.5	Mature		The mean time to stage 4 anesthesia was 6.35 minutes. Mean time for recovery after removal to fresh water was 7.48 minutes. Researchers wishing to use our technique will have to modify the amount of acetic acid used to achieve stage 4 anesthesia if the pH of their water differs.	Prince et al. (1995)	
Oncorhynchus tshawytscha	Salmon, chinook	Alphaxalone-alphadolone	0.3–0.5 ml/kg	IM	3			1	Harvey et al. (1988)	
Oncorhynchus tshawytscha	Salmon, chinook	Benzocaine dissolved in ethanol at 1 gram/30 ml	25–35 mg/L	Immersion	80 g	Juvenile	Oct–13	Induction 1–3.25 minutes. Recovery following 15 minutes of exposure 2.25–18.5 minutes. Provided light to heavy sedation.	Gilderhus (1989)	Provided light to heavy sedation.
Oncorhynchus tshawytscha	Salmon, chinook	Clove oil (82%)	40 mg/L	Immersion	~350 g Female	Adult		Only exposed 3 minutes perform blood taken.	Young et al. (2019)	
Oncorhynchus tshawytscha	Salmon, chinook	Clove oil in 1:10 ratio with 95% ethanol.	20 mg/L	Immersion	40.2 ± 0.6 g	Juvenile		Provided deep anesthesia within 2 minutes.	Cho & Heath (2000)	Provided deep anesthesia within 2 minutes.
Oncorhynchus tshawytscha	Salmon, chinook	Isoeugenol	40 mg/L	Immersion	~350 g Female	Adult		Only exposed 3 minutes perform blood taken.	Young et al. (2019)	
Oncorhynchus tshawytscha	Salmon, chinook	Isoeugenol	60 mg/L	Immersion	844–1562 g		12.5 ± 2.5	Sedation with partial loss of equilibrium. Suitable for handling.	Rothwell et al. (2005)	Sedation with partial loss of equilibrium. Suitable for handling.
Oncorhynchus tshawytscha	Salmon, chinook	Isoeugenol	120 mg/L	Immersion	844–1562 g		12.5 ± 2.5	Resulted in surgical anesthesia within 10 minutes for placement of vascular cannula. Recovery within 5–8 minutes.	Rothwell et al. (2005)	
Oncorhynchus tshawytscha	Salmon, chinook	Metomidate hydrochloride	42 mg/kg	IM	9			Light sedation with partial loss of equilibrium. Directed net avoidance.	Harvey et al. (1988)	2
Oncorhynchus tshawytscha	Salmon, chinook	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion	40.2 ± 0.6 g	Juvenile		Provided deep anesthesia within 2 minutes.	Cho & Heath (2000)	Provided deep anesthesia within 2 minutes.
Oncorhynchus tshawytscha	Salmon, chinook	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	844–1562 g		12.5 ± 2.5	Resulted in light anesthesia. Recovery following 5 minutes of exposure occurred within 5 minutes.	Rothwell et al. (2005)	Resulted in light anesthesia. Recovery following 5 minutes of exposure occurred within 5 minutes.
Salmo munzuricus	Trout (novel species)	2-phenoxyethanol	0.2, 0.3, 0.4, 0.5 ml/L	Immersion	100–200 g			Most appropriate concentrations were determined as 0.4 ml/L at weights of 100–400 g.	Can et al. (2017)	Recommended dose: 0.4 ml/L (weights of 100–400 g), 0.5 ml/L (weights of 400–600 g).

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Salmo munzuricus	Trout (novel species)	2-phenoxyethanol	0.2, 0.3, 0.4, 0.5 ml/L	Immersion	200–400 g				Most appropriate concentrations were determined as 0.4 ml/L at weights of 100–400 g.	Can et al. (2017)	
Salmo munzuricus	Trout (novel species)	2-phenoxyethanol	0.2, 0.3, 0.4, 0.5 ml/L	Immersion	400–600 g				Most appropriate concentrations were determined as 0.4 ml/L at weights of 100–400 g and 0.5 ml/L at weights of 400–600 g for 2-phenoxyethanol in *Salmo munzuricus* broodstock.	Can et al. (2017)	
Salmo salar	Salmon, Atlantic	Benzocaine 20%	30–100 mg/L	Immersion	31–44 g			15	Provided sedation for 6 hours without loss of equilibrium, at which time fish removed from anesthetic. Considered useful for transport. No mortality.	Hoskonen & Pirhonen (2004)	Considered useful for transport up to 6 hours. No mortality.
Salmo salar	Salmon, Atlantic	Benzocaine	40 mg/L	Immersion	420 g	0.0.1444		~9	Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Salmo salar	Salmon, Atlantic	Clove oil dissolved in 95% ethanol at 1:10 ratio.	5 mg/L	Immersion	31–44 g			15	Provided sedation for 6 hours without loss of equilibrium, at which time fish removed from anesthetic. Considered useful for transport. No mortality.	Hoskonen & Pirhonen (2004)	Considered useful for transport up to 6 hours. No mortality.
Salmo salar	Salmon, Atlantic	Clove oil dissolved in 95% ethanol at 1:10 ratio.	8 mg/L	Immersion	44.7 ± 12.8 g		1-year-old smolt	5.4 ± 0.2	Anesthesia attained in 2.2–8.1 minutes. Exposure to 100 mg/L for >6 minutes may result in cessation of voluntary respiration.	Iversen et al. (2003)	Exposure to 100 mg/L for >6 minutes may result in cessation of voluntary respiration.
Salmo salar	Salmon, Atlantic	Clove oil dissolved in ethanol at 1:10 ratio	30–100 mg/L	Immersion	44.7 ± 12.8 g		1-year-old smolt	5.4 ± 0.2	Anesthesia attained in 2.2–8.1 minutes. Exposure to 100 mg/L for >6 minutes may result in cessation of voluntary respiration.	Iversen et al. (2003)	Exposure to 100 mg/L for >6 minutes may result in cessation of voluntary respiration.
Salmo salar	Salmon, Atlantic	Isoeugenol	5.4 mg/L	Immersion					Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Salmo salar	Salmon, Atlantic	Isoeugenol	17 mg/L	Immersion	2.39 ± 0.62	0.0.8		7.2–7.9	Not approved for food fish, but met all requirements in experiment related to fish welfare.	Erikson (2011)	Not approved for food fish, but met all requirements in experiment related to fish welfare.

Salmo salar	Salmon, Atlantic	Isoeugenol	30–100 mg/L	Immersion	44.7 ± 12.8 g		1-year-old smolt	5.4 ± 0.2	Anesthesia attained in 2.2–6.2 minutes.	Iversen et al. (2003)	
Salmo salar	Salmon, Atlantic	Metomidate hydrochloride	2–10 mg/L	Immersion	44.7 ± 12.8 g		1-year-old smolt	5.4 ± 0.2	Anesthesia attained in 3.0–17.4 minutes. Exposure to 100 mg/L for >6 minutes may result in cessation of voluntary respiration.	Iversen et al. (2003)	Exposure to 100 mg/L for >6 minutes may result in cessation of voluntary respiration.
Salmo salar	Salmon, Atlantic	Metomidate hydrochloride	3 mg/L	Immersion					Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Salmo salar	Salmon, Atlantic	Metomidate hydrochloride	1, 2, 3, 5, 10 mg/L		58, 1130 g	0.0.180, 0.0.18	Parr, adult	5, 7.7	Anesthetic was more potent in the adult salmon acclimated to sea water than in freshwater parr. Recommended concentration of 3 mg/L.	Olsen et al. (1995)	Recommended dose: 3 mg/L. Anaesthetic was more potent in the adult salmon acclimated to sea water than in freshwater.
Salmo salar	Salmon, Atlantic	MS-222 (tricaine methanesulfonate)	55 mg/L	Immersion					Concentrations based on manufacturers' recommendations.	Zahl et al. (2010)	Concentrations based on manufacturers' recommendations.
Salmo salar	Salmon, Atlantic	MS-222 (tricaine methanesulfonate)	65 mg/ml	Immersion	150 g	0.40.0				Saunders et al. (2020)	
Salmo salar	Salmon, Atlantic	Nitrogen		Immersion		0.0.4			The fish treated with nitrogen showed the strongest aversive reactions, produced the most stressed fish, and fish that did not appear to be sedated.	Erikson (2011)	The fish treated with nitrogen showed the strongest aversive reactions, lack of sedation, and the most stress.
Salmo salar	Salmon, Atlantic	Carbon dioxide (CO_2)	low 70–80, medium 180–250, high > 400 mg CO_2/L	Immersion		0.0.24			No level of carbon dioxide rendered the fish unconscious.	Erikson (2011)	No level of carbon dioxide rendered the fish unconscious.
Salmo trutta	Trout, sea	Alphaxalone-alphadolone	12–18 mg/kg	ICe or ⅔ ICe + ⅓ IM	100–500 g			10	Induction within 5–10 minutes. Doses of 18 mg/kg produced anesthesia. Lower doses only produced sedation. Recovery generally complete within 2 hours. Doses >18 mg/kg associated with apnea and prolonged recoveries (3–6 hours).	Oswald (1978)	Lower doses only produced sedation. Doses >18 mg/kg associated with apnea and prolonged recoveries (3–6 hours).

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Salmo trutta	Trout, sea	Benzocaine	50 mg/L	Immersion	100–500 g			10	Induction generally in 5–10 minutes. Anesthesia persisted for 20 minutes at 130 mg/ and 50–80 minutes at 150 mg/kg. Apnea requiring assisted ventilation occurred in 30% of fish. Recovery took up to 90 minutes and was characterized by excitement and ataxia.	Oswald (1978)	Apnea in 30%. Recovery took up to 90 minutes with excitement and ataxia.
Salmo trutta	Trout, sea	Clove oil dissolved in 95% ethanol at 1:10 ratio.	8 mg/L	Immersion	100–500 g			10	Provided adequate sedation within 30 seconds to permit weighing and injections.	Oswald (1978)	
Coregonus lavaretus	Trout, sea	Etomidate	0.5–1.0 ml/L	Immersion			Commercial	7		Kazuñ & Siwicki (2012)	
Salmo trutta	Trout, sea	Ketamine	130, 150 mg/kg	IM	100–500 g			10	Induction within 5–10 minutes. Doses of 18 mg/kg produced anesthesia. Lower doses only produced sedation. Recovery generally complete within 2 hours. Doses >18 mg/kg associated with apnea and prolonged recoveries (3–6 hours).	Oswald (1978)	Lower doses only produced sedation. Doses >18 mg/kg associated with apnea and prolonged recoveries (3–6 hours).
Salvelinus alpinus	Artic char	Carbon dioxide (CO_2)	CO_2 until near saturation (>1 h)	Immersion	478–1286 g			4.6 ± 0.2	Exposure to water saturated with CO_2 triggered aversive struggling and escape responses for several minutes before immobilization. Fish exposed to an electric current immobilized close to instant. It took 5 minutes for the fish to recover from electrical stunning. Fish stunned with CO_2 did not recover. However, the electrically stunned fish had more than double the plasma levels of cortisol compared with fish stunned with CO_2.	Gräns et al. (2016)	Exposure to water saturated with CO_2 triggered aversive struggling and escape responses and poor/lack of recovery.

Salvelinus fontinalis	Trout, brook	Isoeugenol	40 mg/L	Immersion						Durhack et al. (2020)	
Salvelinus fontinalis	Trout, brook	Eugenol + lidocaine 2%	40 mg/L + 6 mg/kg	Immersion						Lamglait & Lair (2021)	
Salvelinus fontinalis	Trout, brook	MS-222 (tricaine methanesulfonate)	60 mg/L + 6 mg/kg	Immersion	1098 ± 191 g					Lamglait & Lair (2021)	
Salvelinus fontinalis	Trout, brook	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion	25.8 ± 7.5 g	0.0.480	Juvenile		Aqui-S® and electro-immobilization may provide suitable alternatives to MS-222 for field research (which has longer clearance times).	Durhack et al. (2020)	
Salvelinus fontinalis	Trout, brook	MS-222 (tricaine methanesulfonate)	65 mg/ml	Immersion	380–770 g	16.24.0				Saunders et al. (2020)	
Salvelinus fontinalis	Trout, brook	Electric handling gloves	Electro + 6 mg/kg	Elecroanesthesia						Lamglait & Lair (2021)	Rapid immobilization, suboptimal for surgeries. Equipment: Smith-Root EFHGs.
Salvelinus fontinalis	Trout, brook	Electric handling gloves	10–14 pulses of 150 V direct current (D/C), 60 Hz frequency, and 15% duty cycle for duration of 0.20 ± 0.02 min	Elecroanesthesia						Durhack et al. (2020)	Considered appropriate for fieldwork, no withdrawal time. Equipment: PES®.
Salvelinus namaycush	Trout, lake	Isoeugenol	20–50 mg/L	Immersion	167–1399 g		Juveniles-young adult	12 ± 2	Induction in 2.5–3.9 minutes. Total exposure time ≤15 minutes. Recovery within 8 minutes. Useful for basic handling procedures. pH 8.1.	Stehly & Gingerich (1999)	Useful for basic handling procedures.
Thymallus thymallus	Grayling	Etomidate	0.5–1.0 ml/L	Immersion			Spawner	7		Kazuñ & Siwicki (2012)	
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Benzocaine	50 mg/L	Immersion	100–500 g			10	Animals were placed in benzocaine immersion for 30 seconds in to give IP/IM/IP + IM injections. Animals were reversed from brief immersion before going into induction with injected drug (5–10 minutes).	Oswald (1978)	Rapid induction to allow other anesthetic injections.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Ketamine	130, 150 mg/kg	IM		0.0.6			At 130 mg/kg, anesthesia only persisted for 20 minutes but at 150 mg/kg, it lasted between 50 and 80 minutes. The recovery period was prolonged, taking up to 90 minutes before completion.	Oswald (1978)	Dose-dependent length of anesthesia. Recovery prolonged.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Etorphine HCl/ acetylpromazine maleate(Large Animal Revivon, Reckitt)	1.25–10 mg/kg	IM or IP (unclear)		0.0.3			Rates of 8–10 mg/kg were found to be effective. Animals remained immobile for 30–60 minutes until reversal was given by deep IM (divided into two doses). Within 5 minutes of reversal regained equilibrium.	Oswald (1978)	Good anesthesia reported. Rapid reversal with diprenorphine hydrochloride. Human safety concerns.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Propanidid	80–500 mg/kg	IM or IP (unclear)		0.0.7			The optimal dosage lies between 300 and 350 mg/kg. At 300 mg/kg, the sleep time was variable, lasting from 30 to 120 minutes. At 325 mg/kg reliably produced a sleep time of 2.5 hours, with minimal respiratory effects. Highest dose produce apneic response during anesthesia (180 minutes) but animal recovered.	Oswald (1978)	Variable duration, no respiratory depression.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Xylazine HCl	100–140 mg/kg	IM or IP (unclear)					The minimal anesthetic dose was found to be 100 mg/kg and this consistently produced apnoea. Xylazine also caused gross ECG disturbances, including changes in duration of P, QRS and T waves. Atropine (0.5 mg) partially corrected this.	Oswald (1978)	Apnea, convulsive activity reported. ECG disturbances.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Alphaxalone-alphadolone	18–36 mg/kg	IM/IP		0.0.12			Fish were injected by IP or a combination of 2/3 IP, 1/3 IM. Doses of 18 mg/kg and over produced anesthesia, but lower doses produced sedation only. Sleep times ranged from 1 to 3 hours at 24 mg/kg to 4–6 hours at 36 mg/kg. Doses of 24 mg/kg and over always provoked apnoea. In most cases, recovery was complete within 2 hours.	Oswald (1978)	Duration 1–3 hours longer with higher doses.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Chlorpromazine HCl	50, 100 mg/kg	ICe		0.0.2			Ineffective.	Oswald (1978)	No effect.

Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Pentobarbitone sodium	30–72 mg/kg	ICe		0.0.4		Doses of 30 mg/kg produced sedation only, without loss of equilibrium. Recovery prolonged, with persistent ataxia noted in 48, 72 mg/kg.	Oswald (1978)	Recovery prolonged, with persistent ataxia noted in 48 and 72 mg/kg.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Lignocaine hydrochloride	0.1 ml	Spinal nerve block	120–150 g	0.0.2		A 25-gauge needle was introduced downwards from the dorsal midline surface at a point about 1 cm posterior to the occipital process. The needle tip was moved until a gap between the vertebrae was found, after which it was gently advanced until a twitch indicated contact with the spinal cord. 0.1 ml of lignocaine hydrochloride was deposited and the fish returned to water. The onset of anesthesia was very rapid, with immobilization occurring in 5 minutes.	Oswald (1978)	Rapid immobilization in 5 minutes. Recovery 45 minutes.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow and brown	Benzocaine	120 mg/kg	ICe		0.0.1		No effect.	Oswald (1978)	No effect.
Oncorhynchus mykiss, *Salmo trutta* L.	Trout, rainbow	Electroanesthesia	4–25 mA	Electroanesthesia		0.0.105		An amperage level of 16 mA produced the desired effect (category 3) most often for rainbow trout (80% of the time).		Equipment: Smith-Root Fish Handling Gloves™ desired effect 80% of the time.
Salvelinus namaycush		Electroanesthesia	5–25 mA	Electroanesthesia		0.0.105		An amperage of 25 mA produced the desired result most often for lake trout (60% of the time).		25 mA produced the desired result 60% of the time.
Order Scombriformes										
Family Scombridae										
Sarda chiliensis	Bonito, eastern Pacific	Ketamine + medetomidine	4 mg/kg + 0.4 mg/kg	IM	2.7 ± 0.6 kg		19.5–20.5	Injections placed in red lateral muscle, immediately ventral to the lateral ridge below the lateral line, posterior and dorsal to the end of the pectoral fin. Induction 8.9 ± 2.1 minutes. Anesthesia time 19.0 ± 3.8 minutes. Recovery following injection of atipamezole 7.7 ± 8.5 minutes. Mortality in fish receiving atipamezole dose <5× medetomidine dose. pH 7.8–7.9.	Williams et al. (2004)	Mortality in fish receiving atipamezole dose <5× medetomidine dose.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Sarda chiliensis	Bonito, eastern Pacific	Atipamezole	2 mg/kg	IM	2.7 ± 0.6 kg			19.5–20.5	Injections placed in red lateral muscle, immediately ventral to the lateral ridge below the lateral line, posterior and dorsal to the end of the pectoral fin. Induction 8.9 ± 2.1 minutes. Anesthesia time 19.0 ± 3.8 minutes. Recovery following injection of atipamezole 7.7 ± 8.5 minutes. Mortality in fish receiving atipamezole dose <5× medetomidine dose. pH 7.8–7.9.	Williams et al. (2004)	Mortality in fish receiving atipamezole dose <5× medetomidine dose.
Scomber japonicus	Mackerel, chub	Ketamine + medetomidine	53–228 mg/kg + 0.6–4.2 mg/kg	IM	0.33–0.40 kg			19.5–20.5	Injected placed in red lateral muscle, immediately ventral to the lateral ridge below the lateral line, posterior and dorsal to the end of the pectoral fin. Induction 4–21 minutes (mean 9 minutes) for 37 fish, 45–56 minutes for eight fish. Anesthesia time 1–52 minutes (mean 16 minutes). Recovery following atipamezole 2–12 minutes (mean 5 minutes). pH 7.8–7.9.	Williams et al. (2004)	Mortality in fish receiving atipamezole dose <5× medetomidine dose.
Scomber japonicus	Mackerel, chub	Atipamezole	5× medetomidine dose	IM	0.33–0.40 kg			19.5–20.5	Injected placed in red lateral muscle, immediately ventral to the lateral ridge below the lateral line, posterior and dorsal to the end of the pectoral fin. Induction 4–21 minutes (mean 9 minutes) for 37 fish, 45–56 minutes for eight fish. Anesthesia time 1–52 minutes (mean 16 minutes). Recovery following atipamezole 2–12 minutes (mean 5 minutes). pH 7.8–7.9.	Williams et al. (2004)	Mortality in fish receiving atipamezole dose <5× medetomidine dose.

Thunnus thynnus	Tuna, Atlantic bluefin	MS-222 (tricaine methanesulfonate)	90 mg/L	Immersion					Oxygenated water over gills at 12–20 L/min following induction until recovery. Minor surgical procedures, ultrasonographic examinations, and serial blood sampling.	Cooper et al. (1994)	
Thunnus thynnus	Tuna, Atlantic bluefin	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Induction rapid and deep. For short procedures, fish captured and dosed in vinyl bag with supplemental oxygen provided. For longer procedures fish captured in stretcher and transferred to large pool containing MS-222. Once induced, fish transferred to examination table with oxygenated anesthetic water directed over gills.	Cooper et al. (1994)	
Family Stromateidae											
Pampus argenteus	Silver pomfret	MS-222 (tricaine methanesulfonate)	10, 25, 50, 75, 100, and 125 mg/L	Immersion	11.2 ± 1.5 g	0.0.250	Fingerling/ 4 months	29 ± 0.5	Lowest effective dose established at 75 mg/L. Per author longest safe time under deep anesthesia was 10 minutes.	Yu et al. (2020)	Lowest effective dose established at 75 mg/L; per author: longest safe time under deep anesthesia was 10 minutes.
Order Scorpaeniformes											
Family Anarhichadidae											
Anarhichas lupus	Wolffish, Atlantic	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion					Physical examination, blood draw.	N.D. Mylniczenko (pers. exp.)	
Anarrhichthys ocellatus	Eel, wolf	MS-222 (tricaine methanesulfonate)	90–100 mg/L						Lower than 90 not adequate for blood draw.	T.M. Clauss (pers. exp.)	Lower than 90 not adequate for blood draw.
Family Anoplopomatidae											
Anoplopoma fimbria	Sablefish	Metomidate hydrochloride	62 mg/kg	IM	6				Light sedation with partial loss of equilibrium. Directed net avoidance.	Harvey et al. (1988)	Light sedation with partial loss of equilibrium. Directed net avoidance.
Anoplopoma fimbria	Sablefish	Alphaxalone-alphadolone	0.3–0.4 mg/kg	IM	3–5				Light to heavy sedation with some fish exhibiting directed net avoidance. Recovery within 90 minutes.	Harvey et al. (1988)	Light to heavy sedation with some fish exhibiting directed net avoidance.
Family Cyclopteridae											
Cyclopterus lumpus L.	Lumpfish	MS-222 (tricaine methanesulfonate)	100, 200, 400, 800, 1600 mg/L	Immersion	10–20, 200–400, 600–1300 g			6, 12	Deep narcosis: 200 mg/L metacaine. Lighter anesthesia: 100 mg/L can be used.	Skar et al. (2017)	Recommended dose: 200 mg/L (deep narcosis).

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Cyclopterus lumpus L.	Lumpfish	Isoeugenol	10, 20, 40 mg/L	Immersion	10–20, 200–400, 600–1300 g			6, 12	Deep narcosis: 200 mg/L metacaine. Lighter anesthesia: 100 mg/L can be used.	Skar et al. (2017)	Isoeugenol not recommended for lumpfish.
Cyclopterus lumpus L.	Lumpfish	Benzocaine	100, 200, 400, 800 mg/L	Immersion	10–20, 200–400, 600–1300 g			6, 12	Deep narcosis: 200 mg/L metacaine. Lighter anesthesia: 100 mg/L can be used.	Skar et al. (2017)	Benzocaine is less efficient than metacaine and is not suitable for larger fish >600 g.
Family Sebastidae											
Sebastes spp.	Rockfish sp.	MS-222 (tricaine methanesulfonate)	80–110 mg/L	IN					Good sedation for invasive procedures (ocular surgery).	N.D. Mylniczenko, T.M. Clauss (pers. exp.)	Good sedation for invasive procedures (ocular surgery).
Sebastes caurinus	Rockfish, copper	Gallamine triethiodide	1.0–4.0, 30 mg/kg	IM	1–3		0.0.6		Up to 2 hours until effect noted. Effect ranged from sedation (fish could be netted but were responsive) to anesthesia with marked depression of ventilation.	Harvey et al. (1988)	Up to 2 hours until effect, highly varied effects: sedation to anesthesia with marked depression of ventilation.
Sebastes caurinus	Rockfish, copper	Metomidate hydrochloride	100 mg/kg	IM	2		0.0.2		Anesthesia with marked depression of ventilation. Recovery taking several hours.	Harvey et al. (1988)	Anesthesia with marked depression of ventilation. Recovery taking several hours.
Sebastes carnatus	Rockfish, gopher	Carbon dioxide (CO_2)		Immersion					Given the prolonged recovery times of $NaHCO_3$ and CO_2, electroanesthesia is the preferable method for rapid induction, recovery, and immediate release of gopher rockfish following surgery at sea (acoustic implants).	Duryea (2014)	Given the prolonged recovery times of $NaHCO_3$ and CO_2, electroanesthesia is the preferable method for rapid induction, recovery, and immediate release.
Sebastes carnatus	Rockfish, gopher	Sodium bicarbonate ($NaHCO_3$)	2.66 g/L solutions activated with 18.95 ml of glacial acetic acid	Immersion						Duryea (2014)	Given the prolonged recovery times of $NaHCO_3$ and CO_2, electroanesthesia is the preferable method for rapid induction, recovery, and immediate release.
Sebastes carnatus	Rockfish, gopher	Electroanesthesia, pulsed direct current (pDC)	150 V, 60 Hz, 12% duty cycle, 3-s exposure	Electroanesthesia						Duryea (2014)	Given the prolonged recovery times of $NaHCO_3$ and CO_2, electroanesthesia is the preferable method for rapid induction, recovery, and immediate release.

Sebastes carnatus	Rockfish, gopher	MS-222 (tricaine methanesulfonate)	175 mg/L unbuffered solution	Immersion				Duryea (2014)	Given the prolonged recovery times of $NaHCO_3$ and CO_2, electroanesthesia is the preferable method for rapid induction, recovery, and immediate release.
Family Scorpaenidae									
Pterois sp.	(Dwarf lionfish)	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion		25	Sedation rated as good. Diagnostic examinations performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Diagnostic examinations performed.
Pterois volitans	Lionfish, red	MS-222 (tricaine methanesulfonate)	75–85 mg/L	Immersion	0.34–0.38	25	Good anesthesia, diagnostic examination, radiographs.	C.M. Burns (pers. exp.)	Sedation rated as good. Diagnostic examinations performed.
Pterois radiata	Firefish, radial	MS-222 (tricaine methanesulfonate)	60–70 mg/L	Immersion	~0.13	25	Good anesthesia, diagnostic examination.	C.M. Burns (pers. exp.)	Sedation rated as good. Diagnostic examinations performed.
Taenianotus triacanthus	Scorpionfish, leaf	MS-222 (tricaine methanesulfonate)	50–90 mg/L	Immersion		25	Provided mild to good sedation. Diagnostic examination performed. $N = 3$.	D.L. Neiffer (pers. exp.)	Provided mild to good sedation. Diagnostic examination performed.
Dendrochirus biocellatus	Turkeyfish, two-spot	MS-222 (tricaine methanesulfonate)	85 mg/L	Immersion	0.0.4	25	Good sedation for diagnostic examination and computed tomography.	C.M. Burns (pers. exp.)	Provided mild to good sedation. Diagnostic examination performed.
Dendrochirus brachypterus	Lionfish, dwarf	MS-222 (tricaine methanesulfonate)	75–90 mg/L	Immersion	0.0.2	25	Good sedation for examination.	C.M. Burns (pers. exp.)	Provided mild to good sedation. Diagnostic examination performed.
Order Siluriformes									
Family Clariidae									
Clarias gariepinus	Catfish, north African	Alphaxalone-alphadolone	24 mg/kg	IM	~1150 g	24	Preanesthetized by squirting a few milliliters of 2-PE on gills, which induced almost immediate immobility. Once alphaxalone-alphadolone injected, the gills were rinsed with fresh water. Surgical anesthesia at 26 ± 8 minutes. Artificial respiration required by pumping gills. If the investigators ensured that either the fish could reach the water surface from time to time during recovery or the fish were placed in shallow water (<15 cm), the fish survived. If these precautions were not taken, mortality occurred.	Peters et al. (2001)	

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Clarias gariepinus	Catfish, north African	Avocado pear (*Pyrus communis*) leaf extract	100, 130, 160, and 190 ml/L	Immersion	395 g	0.0.60	Adult		Aqueous extracts of avocado pear leaf at concentrations ranging from 130–190 ml/L induced general anesthesia. The effective concentration of avocado pear leaf extracts that best sustained the gonadectomy was 190 ml/L, with a recovery time of 12 minutes.	Adebayo et al. (2010)	Recommended dose: 190 ml/L.
Clarias gariepinus	Catfish, north African	Etomidate (Propiscin) 0.2%	0.5–1 ml/L	Immersion					Propiscin did not cause a change in pH or CO_2 content. Propiscin applied in a water bath can provide up to 1 hour of general anesthesia.	Kazuñ & Siwicki (2012)	
Clarias gariepinus	Catfish, north African	Propofol	2 mg/L	Immersion	300 ± 0.87 g	0.0.30	Juvenile	20 ± 0.3	Anesthesia was achieved in 5.3 ± 0.74 minutes at 2 mg/L of propofol. Recovery time in this study was recorded as 3.2 ± 0.48 minutes. Since blood studies were included, the author indicates a potential use as an anesthetic for aquaculture in the future.	Adeola et al. (2018)	
Family Ictaluridae											
Ictalurus furcatus	Catfish, blue	MS-222 (tricaine methanesulfonate)	60–120 mg/L	Immersion					Low range good for minimally invasive procedures.	T.M. Clauss (pers. exp.)	Low range, good for minimally invasive procedures.
Ictalurus furcatus	Catfish, blue										
Ameiurus nebulosus	Catfish, brown bullhead	Alphaxalone-alphadolone	24 mg/kg	IM	56–255 g			18	Injection given just behind first dorsal fin. Induction within minutes. Gradually lost balance and eventually ventilation ceased. Artificial respiration required by pumping water over gills at ~100 ml/min. Surgical anesthesia required on average 20 minutes. Time until recovery of opercular movements averaged 207 minutes.	Peters et al. (2001)	

Ameiurus melas	Catfish, black bullhead	Alphaxalone-alphadolone	24 mg/kg	IM			18	Injection given just behind first dorsal fin. Event very similar to brown bullhead above.	Peters et al. (2001)	
Ameiurus melas	Catfish, black bullhead	Clove oil	100 mg/L	Immersion	3–810 g	Juvenile to adult	26		Small (2003)	
Ameiurus melas	Catfish, black bullhead	Clove oil	100–150 mg/L	Inhalant	19.12 ± 4.32 g	Fingerling	23	No ethanol added directly to water and aerated strongly prior to addition of fish. Induction within 1 minute. Recovery following 10 minutes of exposure to 100 mg/L, recovery occurred within 4 minutes. Recovery prolonged (>10 minutes) after exposure to 150 mg/L. Exposure to 100 mg/L for >20 minutes associated with increasing mortality. Exposure to 300 mg/L for 10 minutes resulted in 50% mortality.	Waterstrat (1999)	Recovery prolonged (>10 minutes) after exposure to 150 mg/L. Exposure to 100 mg/L for ≥20 minutes associated with increasing mortality. Exposure to 300 mg/L for 10 minutes resulted in 50% mortality. pH = 7.6.
Ictalurus punctatus	Catfish, channel	Eugenol	100, 150 mg/L		1.5 ± 0.5		26.3 ± 0.3	Treatment periods 2.5–12.0 minutes for channel catfish.	Bowker et al. (2017)	
Ictalurus punctatus	Catfish, channel	Isoeugenol	2.5 mg/L	Immersion	50–75 g	Juvenile	26	Sedation achieved in all fish. No mortality with exposure from 30 minutes to 24 hours. pH 8.6.	Small (2004)	
Ictalurus punctatus	Catfish, channel	Isoeugenol	20, 40, 60 mg/L	Immersion	1.1 ± 0.04 kg	Mature	14.5	On average, all the fish lost equilibrium at 8.0, 3.9, and 3.7 minutes when anesthetized in 20, 40, and 60 mg Aqui-S®/L, respectively. Recovery time in fresh water was 2.1, 2.8, and 5.3 minutes for fishanesthetized in 20, 40, and 60 mg/L Aqui-S®, respectively.	Small & Chatakondi (2005)	
Ictalurus punctatus	Catfish, channel	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	1.1 ± 0.04	Adult	14.5	Anesthesia 4.5 ± 0.8 minutes. Fish immediately transferred to anesthetic-free water with recovery time of 1.7 ± 0.2 minutes. Survival 100% at 24 hours. Dose considered useful for basic handling procedures.	Small & Chatakondi (2005)	Dose considered useful for basic handling procedures.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Ictalurus punctatus	Catfish, channel	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	3–810 g		Juvenile-adult	26		Small (2003)	
Ictalurus punctatus	Catfish, channel	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion					Stage III sedation was attained within 120 seconds with MS-222. These results suggest that MS-222 is an appropriate anesthetic to use during the initial 5 minutes of sedation.	Smith et al. (2015)	Reduced cortisol.
Ictalurus punctatus	Catfish, channel	Metomidate hydrochloride	1.5 mg/L	Immersion	62 ± 11.3 g		Juvenile	26	Sedation achieved in all fish. No mortality with exposure from 30 minutes to 24 hours. pH 8.6.	Small (2004)	Sedation achieved in all fish. No mortality with exposure from 30 minutes to 24 hours.
Ictalurus punctatus	Catfish, channel	Metomidate hydrochloride	0.5, 1, 2, 4, 6, 8, 16 mg/L	Immersion	3–810 g		Juvenile-adult	26	The minimum desirable concentration for anesthesia, that which resulted in a total loss of equilibrium in all fish within 3 minutes, was determined to be 6 ppm. No mortalities at 8 mg/L or less. 16 mg/L had 65% mortalities.	Small (2003)	No mortalities at 8 mg/L or less. 16 mg/L had 65% mortalities.
Ictalurus punctatus	Catfish, channel	Metomidate hydrochloride	12.5 mg/L	Immersion	~12 g			26	Stage III sedation was attained within 90 seconds with metomidate hydrochloride and might be more appropriate for longer periods of sedation.	Smith et al. (2015)	Reduced cortisol. Good for longer sedation.
Ictalurus punctatus	Catfish, channel	Quinaldine	30 mg/L	Immersion	3–810 g		Juvenile-adult	26		Small (2003)	
Ictalurus punctatus	Catfish, channel	Lidocaine	100–750 mg/L	Immersion					Although both induced anesthesia, the mixture was more effective for induction and recovery, and was able to achieve the required time for the fish to be out of water (titrated at 50-mg doses).	Carrasco et al. (1984)	Lidocaine effective for anesthesia.
Ictalurus punctatus	Catfish, channel	Lidocaine-sodium bicarbonate	250 mg/L + 1 g/L	Immersion					Although both induced anesthesia, the mixture was more effective for induction and recovery, and was able to achieve the required time for the fish to be out of water (titrated at 50–mg doses).	Carrasco et al. (1984)	Lidacaine and bicarbonate combination, more effective than lidocaine alone.

Family Pangasiidae										
Pangasius sp.	Catfish, Pangasius	Isoeugenol (Aqui–S®)	20 mg/L	Immersion	335 ± 92.0 g	Juvenile-young adult	12 ± 2	Induction in 5.3 minutes. Total exposure time <15 minutes. Recovery within 8 minutes. Useful for basic handling procedures. pH 8.1.	Stehly & Gingerich (1999)	Useful for basic handling procedures.
Family Siluridae										
Kryptopterus bicirrhis	Catfish, glass	Alphaxalone-alphadolone	4.8 mg/L for induction	Immersion	2–7 g		23–27	Opercular movements disappeared after 5 minutes of exposure, at which time fish transferred to maintenance. Artificial respiration given by pumping water through mouth and across gills at 7–10 ml/min. Recovery in ~30 minutes after being placed in clean water.	Peters et al. (2001)	Recovery in ~30 minutes after being placed in clean water.
Silurus asotus	Catfish, Amur	Clove oil	200, 300, 400, 500, 600 mg/L	Immersion	50.1 ± 0.0.40 5.91, 302.1 ± 15.22 g	Larval-adult		The results showed significant relationships between the concentration of the anesthetic and the body size of the fish. Based on an optimal anesthetic time of approximately 1 minute, the preferred concentrations of the anesthetics were 500 ppm for clove oil and 600 ppm for MS-222.	Park (2019)	Recommended dose: 500 ppm (clove oil), 600 ppm (MS-222). Significant relationship between the concentration of the anesthetic and the body size of the fish.
Silurus asotus	Catfish, Amur	MS-222 (tricaine methanesulfonate)	200, 300, 400, 500, 600 mg/L	Immersion	50.1 ± 5.91, 302.1 ± 15.22 g	Larval-adult		The results showed significant relationships between the concentration of the anesthetic and the body size of the fish. Based on an optimal anesthetic time of approximately 1 minute, the preferred concentration of the anesthetic was 600 ppm for MS-222.	Park (2019)	Recommended dose: 500 ppm (clove oil), 600 ppm (MS-222). Significant relationship between the concentration of the anesthetic and the body size of the fish.
Order Syngnathiformes										
Family Syngnathidae										
Hippocampus barbouri	Seahorse, Barbour's	MS-222 (tricaine methanesulfonate)	50–60 mg/L	Immersion		Adult		Diagnostic examination.	C.M. Burns (pers. exp.)	
Hippocampus erectus	Seahorse, lined	MS-222 (tricaine methanesulfonate)	60–100 mg/L	Immersion		Adult		Low end dose adequate for radiographs and minimally invasive procedures.	N.D. Mylniczenko (pers. exp.)	Low end dose adequate for radiographs and minimally invasive procedures.

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Hippocampus erectus	Seahorse, lined	MS-222 (tricaine methanesulfonate)	5, 10, 20, 40, 60, 80 mg/L	Immersion	0.72 ± 0.08 g			26 ± 2.0	Effectively anesthetized into stage II at concentrations of 20–60 mg/L MS-222.	Qin et al. (2016)	Recommended dose: 10–30 mg/L (clove oil), 20–60 mg/L (MS-222).
Hippocampus erectus	Seahorse, lined	Clove oil	2, 5, 10, 20, 30, 40 mg/L	Immersion					Effectively anesthetized into stage II at concentrations of 10–30 mg/L clove oil.	Qin et al. (2016)	Recommended dose: 10–30 mg/L (clove oil), 20–60 mg/L (MS-222).
Hippocampus procerus	Seahorse, high-crown	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion			Juvenile-adult		Diagnostic examination, radiographs.	C.M. Burns (pers. exp.)	
Hippocampus reidi	Seahorse, longsnout	MS-222 (tricaine methanesulfonate)	50–90 mg/L	Immersion		0.0.30	Juvenile-adult		Diagnostic examination, radiographs.	C.M. Burns (pers. exp.)	
Hippocampus reidi	Seahorse, longsnout	MS-222 (tricaine methanesulfonate)	75–100 mg/L	Immersion			Adult		Good sedation for blood draw, assist feed and injectable treatments.	N.D. Mylniczenko (pers. exp.)	Good sedation for blood draw, assisted feeding and injectable treatments.
Micrognathus crinitus	Pipefish, banded	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion					Depth good for miminally invasive procedures on low end.	C.M. Burns (pers. exp.)	
Phycodurus eques	Seadragon, leafy	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion			Adult		Under 60 mg/L very light sedation and not sufficient for assisting feeding or oral examination. Above 80 mg/L occasionally noted longer recoveries.	N.D. Mylniczenko, T.M. Clauss (pers. exp.)	Under 60 mg/L very light sedation. Above 80 mg/L occasionally noted longer recoveries.
Phyllopteryx taeniolatus	Seadragon, weedy	MS-222 (tricaine methanesulfonate)	50–100 mg/L	Immersion					Same as above.	N.D. Mylniczenko, T.M. Clauss (pers. exp.)	Under 60 mg/L very light sedation. Above 80 mg/L occasionally noted longer recoveries.
Syngnathus scovelli	Pipefish, gulf	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion					Sedation rated as good. Topical treatments performed.	D.L. Neiffer (pers. exp.)	Sedation rated as good. Topical treatments performed.
Order Tetraodontiformes											
Family Balistidae											
Balistes capriscus	Triggerfish, grey	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion	~2.7			25	Good sedation to deep anesthesia.	C.M. Burns (pers. exp.)	
Balistes vetula	Triggerfish, queen	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion	0.4–1.0			25	Good sedation for diagnostic examination, treatments.	C.M. Burns (pers. exp.)	
Canthidermis maculata	Triggerfish, rough	MS-222 (tricaine methanesulfonate)	45–75 mg/L	Immersion	1.3			25	Provided mild to heavy sedation. Diagnostic examinations performed. $N = 3$.	D.L. Neiffer (pers. exp.)	
Pseudobalistes fuscus	Triggerfish, yellow-spotted (blue-line)	MS-222 (tricaine methanesulfonate)	75 mg/L	Immersion	0.19			25	Good sedation for diagnostic examination.	C.M. Burns (pers. exp.)	

Xanthichthys auromarginatus	Triggerfish, gilded (golden-edged)	MS-222 (tricaine methanesulfonate)	70 mg/L	Immersion	0.08		25	Good sedation for diagnostic examination with blood draw.	C.M. Burns (pers. exp.)
Canthidermis sufflamen	Triggerfish, ocean	MS-222 (tricaine methanesulfonate)	80 mg/L	Immersion	1.2		25	Good sedation for diagnostic examination.	C.M. Burns (pers. exp.)
Melichthys niger	Durgeon, black	MS-222 (tricaine methanesulfonate)	70–100 mg/L	Immersion	1.2		25	Good sedation, 100 mg/L induction for surgerical procedure then lowered.	C.M. Burns (pers. exp.)
Rhinecanthus aculeatus	Triggerfish, white-banded (humuhumu)	MS-222 (tricaine methanesulfonate)	50–75 mg/L	Immersion	0.07		25	Good sedation to deep anesthesia for abscess debridement.	C.M. Burns (pers. exp.)
Family Diodontidae									
Diodon holocanthus	Porcupinefish, long-spined	MS-222 (tricaine methanesulfonate)	75–80 mg/L	Immersion	0.38–1.16 kg	0.0.5		Sedative effect rated fair to good. Diagnostic examination and topical treatments performed.	D.L. Neiffer (pers. exp.)
Diodon holocanthus	Porcupinefish, long-spined	MS-222 (tricaine methanesulfonate)	100–125 mg/L	Immersion	0.38–0.42 kg			Provided surgical anesthesia for removal of fungal granulomas from integument and resection of coelomic musculature.	D.L. Neiffer (pers. exp.)
Diodon hystrix	Porupinefish, spot-fin	MS-222 (tricaine methanesulfonate)	75–80 mg/L	Immersion		0.0.2		Mild to moderate sedation. Diagnostic examination performed. $N = 2$.	D.L. Neiffer (pers. exp.)
Family Monocanthidae									
Aluterus scriptus	Filefish, scrawled	MS-222 (tricaine methanesulfonate)	50–60 mg/L	Immersion	0.44–2.35			Sedation rated as good to excellent. Diagnostic examinations performed.	D.L. Neiffer (pers. exp.)
Aluterus scriptus	Filefish, scrawled	MS-222 (tricaine methanesulfonate)	75–100 mg/L	Immersion	0.44–2.35			Heavy sedation with cessation of gilling.	D.L. Neiffer (pers. exp.)
Meuschenia trachylepis	Filefish	Clove oil in ethanol at ratio 1:5	40 mg/L	Immersion			18	Induction within 3 minutes. Recovery within 5 minutes. Sufficient for handling and measurement.	Griffiths (2000)
Monacanthus tuckeri	Filefish, slender	MS-222 (tricaine methanesulfonate)	50 mg/L	Immersion				Provided mild sedation. Diagnostic examination performed.	D.L. Neiffer (pers. exp.)
Cantherhines macrocerus	Filefish, American white-spotted	MS-222 (tricaine methanesulfonate)	70 mg/L	Immersion	0.9		25	Good sedation for diagnostic examination.	C.M. Burns (pers. exp.)
Family Ostraciidae									
Acanthostracion quadricornis	Cowfish, scrawled	MS-222 (tricaine methanesulfonate)	60–80 mg/L	Immersion	~0.4		25	Good to deep anesthesia.	C.M. Burns (pers. exp.)

(*Continued*)

Table 8.1 (Continued)

Species	Common Name	Drug		Route of Administration	Body Weight	Population	Age Class	Water Temp. (C°)	Comments	Reference	Comments
Family Tetraodontidae											
Takifugu niphobles	Puffer, grass	Clove oil	10, 20, 30, 40, 50 mg/L	Immersion	160.3 ± 37.6 g		0.0.30	20 ± 1			Recommended dose (long-term transport): 2 mg/L (clove oil) and 50 mg/L (lidocaine-HCl).
Takifugu niphobles	Puffer, grass	Lidocaine-HCl (prepared with bicarb)	500, 600, 700, 800, 900, 1000 mg/L	Immersion			0.0.30				Recommended dose (long-term transport): 2 mg/L (clove oil) and 50 mg/L (lidocaine-HCl).
Takifugu niphobles	Puffer, grass	Clove oil + lidocaine (prepared with bicarb)	30 + 800, 30 + 900, 30 + 1000, 40 + 800, 40 + 900, 40 + 1000, 50 + 800, 50 + 900, 50 + 1000 mg/L	Immersion			0.0.90				Recommended dose (long-term transport): 2 mg/L (clove oil) and 50 mg/L (lidocaine-HCl).
Takifugu niphobles	Puffer, grass	Clove oil	2, 4, 6, 8, 10 mg/L (transport)	Immersion			0.0.30		The optimum anesthetic concentrations for long-term transportation requiring more than 1 hour were 2 mg/L for clove oil and 50 mg/L for lidocaine-HCl.		Recommended dose (long-term transport): 2 mg/L (clove oil) and 50 mg/L (lidocaine-HCl).
Takifugu niphobles	Puffer, grass	Lidocaine-HCl (prepared with bicarb)	50, 100, 150, 200, 250, 300 mg/L (transport)	Immersion			0.0.30				Recommended dose (long-term transport): 2 mg/L (clove oil) and 50 mg/L (lidocaine-HCl).
Arothron nigropunctatus	Puffer, black-spotted (dogface)	MS-222 (tricaine methanesulfonate)	70–75 mg/L	Immersion					Provided mild to heavy sedation. Diagnostic examination performed. $N = 3$.	D.L. Neiffer (pers. exp.)	
Arothron nigropunctatus	Puffer, black-spotted (dogface)	MS-222 (tricaine methanesulfonate)	100 mg/L	Immersion	360 g				Provided surgical anesthesia for removal of skin lesion.	D.L. Neiffer (pers. exp.)	
Sphoeroides testudineus	Puffer, checkered	MS-222 (tricaine methanesulfonate)	70–100mg/L	Immersion	280–330 g				Variable effect from mild sedation to light anesthesia. Examinations and topical laser surgeries performed. $N = 6$.	D.L. Neiffer (pers. exp.)	

CLO, ; CT, computed tomography; D, ; DC, direct current; dpf, ; DO, dissolved oxygen; ECG, Electrocardiogram; EFHG, ; GABAA, GABAa receptor; HR, Heart rate; IC, Intracardiac; ICe, Intracoelomic; IM, intramuscular; IP, Intraperitoneal; IV, intravenous; LA, Left arm; MS-222, Tricaine Methyl-Sulfate; OA, ; OpR, Opercular respirations; 2-PE, 2-phenoxyethanol; PE, phenoxyethanol; PES, ; phd, ; PhE, Phenylalanine; PO, per os; ppm, parts per million; ppt, parts per thousand; QS, ; RR, respiration rate; S4, ; YT, yellowtail.

dosages used in salmon smolts may not be effective in ocean ranging adults.

Regardless of available information, the anesthetic regimen for an untested species should be tried using one or a small group of fish. Start at the low end of the recommended dosage range and work up to the desired effect (Harms 1995; Neiffer & Stamper 2009; Ross 2001; Stetter 2001). However, in a species whose anesthetic tolerance is known, using a high dosage for a smoother and more rapid induction is most appropriate. Once induced, a lower immersion maintenance dosage is recommended (Harms 1999). Rapid capture or in-enclosure anesthesia will reduce stress and facilitate smoother inductions. Utilizing graded anesthesia (high induction, low maintenance dose) is a stress-reducing method of anesthesia (Matsche 2011).

Preanesthetic Preparations and Considerations

Whenever possible, the following should be performed prior to induction:

1) Baseline behavioral parameters (i.e., ventilation, caudal fin stroke rate, and overall activity level) should be recorded for comparison during anesthesia.
2) Although aspiration pneumonia is not a concern, it is not uncommon for fish to regurgitate material that clogs gill rakers and contributes to water quality degradation. Additionally, if the regurgitant is fine and covers the gill lamellae, then suffocation can theoretically occur (sestonosis). Fasting for 12–24 hours (one feeding cycle) limits regurgitation and decreases nitrogenous waste production (Harms & Bakal 1995; Stetter 2001).
3) Containers with adequate water for transportation, induction, maintenance, and recovery should be available (Harms 1999; Stetter 2001). This is particularly important when water is used for immersion anesthesia. If the procedure occurs next to the animal's tank it can be used for recovery. This assumes monitoring is possible and other specimens will not traumatize or predate the fish during recovery.
4) The physical (e.g., temperature) and chemical (e.g., pH, salinity) variables of all water used should be matched to those of the fish's source water. Smaller water volumes used for anesthetic procedures will warm or chill to the temperature of the room air, thus water temperature should be monitored during the procedure and maintained as consistently as possible. Dissolved oxygen is maintained >5 ppm (mg/L) with 6–10 ppm ideal (Harms 1999; Stetter 2001); in the authors' practices, 9–12 ppm is a targeted range.
5) For out-of-water procedures, it is important to prevent drying of the skin, fins, and eyes. This can include coverage with clear plastic drapes, bubble wrap, soft cloth (chamois or microfiber), and regular rinsing of tissues with water from a syringe or a small portable atomizer (Harms 1999; Ross 2001).
6) Capture techniques should be considered and the procedure discussed with all staff involved, especially with large fishes.

Immersion (Waterborne, Bath or Inhalant) Anesthesia

Immersion anesthesia via immersion in the water is analogous to gaseous anesthesia in terrestrial animals. The anesthetic in solution is ventilated by the fish, enters the bloodstream through the gills, accessory respiratory organs, and the skin, and passes rapidly to the central nervous system. When returned to drug-free water, drugs or their metabolites are excreted mostly via the gills and presumably accessory respiratory organs. Some elimination also occurs through the kidneys, liver, and presumably the skin (Ross 2001; Walsh & Pease 2002). Unlike in terrestrial vertebrates, any water-soluble drugs or metabolites excreted from fish will be continuously absorbed through the body surface and gills, while being simultaneously metabolized and eliminated (Oikawa et al. 1994). This is problematic for assessing dosage effects and performing pharmacokinetic studies unless flowthrough systems or closed systems with inline carbon filters are utilized. This is significant when considering reusing the same water for multiple fishes. It is unknown how much drug is metabolized per volume of anesthetic water; it is in the authors' experience that with multiple animals, there is degradation of water quality and as a result, inductions are longer. This is highly variable though and based on the number of fish, size of the animals, and volume of water used.

Immersion drugs must be water-soluble or utilize a water-soluble solvent as a vehicle. For simple, short procedures the required drug concentration is made up in an aerated container to which fish are transferred or drugs are added directly to the water containing the fish. In the latter situation, a buffer (e.g., sodium bicarbonate or carbonate) is added. It is always preferable to use water from the fish's environment to make the anesthetic solution prior to drug administration to minimize acute drops in pH or other water-quality parameters (Harms 1999; Ross 2001).

For large fish, where immersion is impractical or dangerous to handlers, drugs in solution may be applied directly to the gills. Inexpensive plastic pump spray bottles (e.g., unused bug sprayers) are ideal for this application. When used by divers, the addition of a harmless dye (e.g., food coloring) helps identify distribution of the anesthetic.

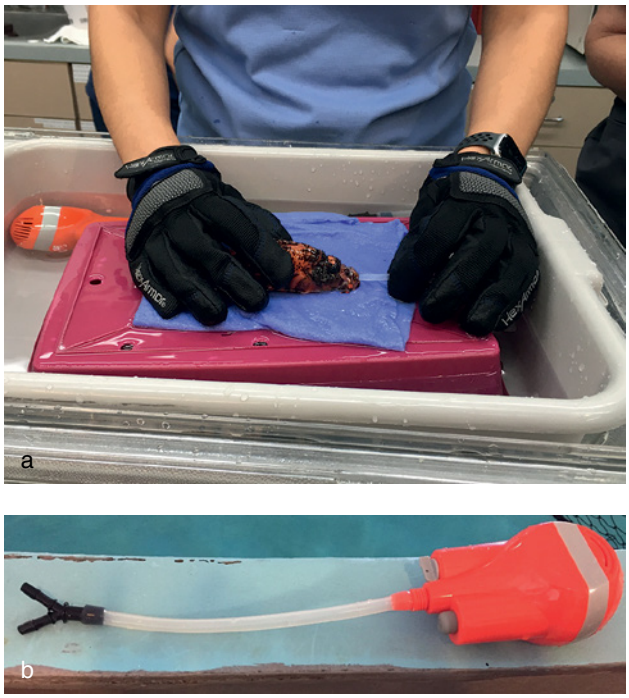


Figure 8.7 (a) A dwarf lionfish (*Dendrochirus brachypterush*) ventilated with an outdoor submersible camp shower (behind the tub). (b) An outdoor submersible camp shower, rechargeable and submersible for ventilation of fishes in a recirculating system.

Regardless of application, anesthetic solutions are most accurately made using a measured volume of a standard stock solution. However, preparing stock solutions of expensive powdered anesthetic drugs (e.g., MS-222) is not economical if used infrequently because potency decreases over time (Ross 2001). Alternatively, preweighed drug packets are recommended. Waterproof quick reference charts and known volume containers are useful for procedure set up. More importantly, they enable quick modification of drug dosage level.

Ventilation, even in animals that are apparently ventilating on their own, is an important standard of practice. It is akin to providing oxygen to sedated mammals. Simply, a syringe and plastic tubing can ventilate each side of the animal's gills. Otherwise, an aquarium pump with flow control or modified camp shower pump will work (Fig. 8.7). With longer procedures (>10 minutes), debilitated fish, species that are slow to recover, and all but the shortest out-of-water procedures, an artificial ventilation system should be used (Fig. 8.8). The animal is placed in shallow water or on a fenestrated surface in lateral recumbency or in dorsal recumbency in a soft holder (foam, soft cloth, sponge).

Aerated anesthetic solution is delivered across the gills from a bifurcated pipe or mouthpiece placed in the buccal cavity (Fig. 8.9) using a nonrecirculating or recirculating system. In its simplest form, a nonrecirculating system uses an intravenous (IV) fluid bag and drip set. Resealable bags are easier for preparation but used sealed bags with an opening cut in the end will suffice. Flow rate is controlled by the drip set valve. Aeration of the anesthetic water with an air stone in the IV bag ensures near saturation of oxygen and removal of dissolved CO_2. Used water is collected, but not recycled (Harms 1999; Ross 2001; Stetter 2001). This system is suitable for small to medium-sized fish depending on reservoir volume, drip set tube diameter, and the rate at which fluid can be delivered.

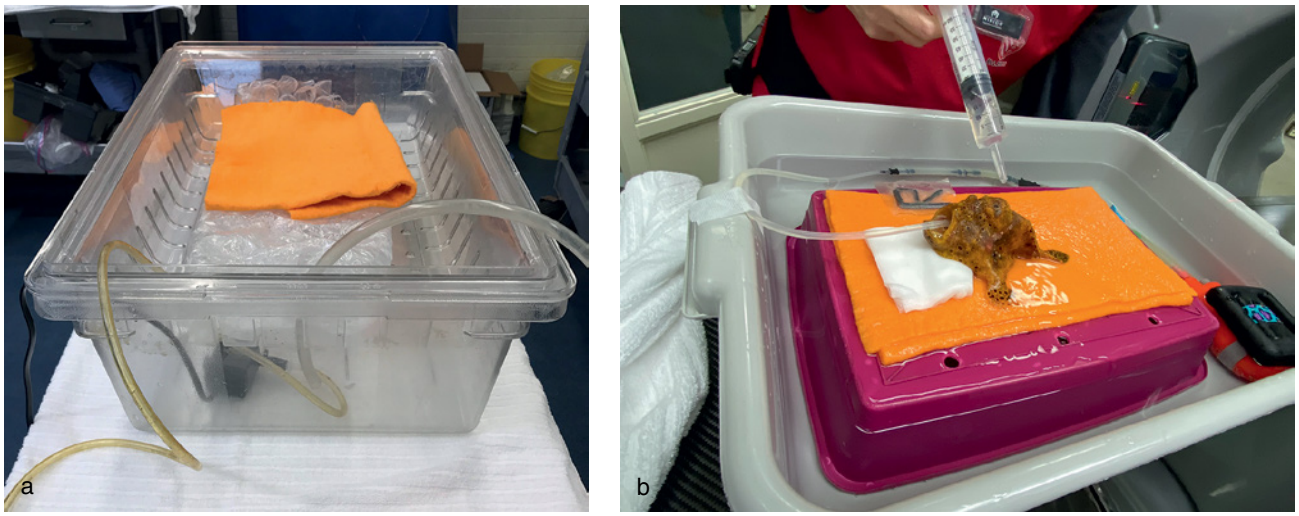


Figure 8.8 (a) A simple recirculating system which enables delivery of anesthetic water from a reservoir to the gills and recycling of the effluent back to the fish by use of a submersible pump. (b) A simple recirculating system which elevates the patient, a frogfish (*Antennarius maculatus*), out of water for CT scan.



Figure 8.9 Goliath grouper (*Epinephelus itajara*) positioned in dorsal recumbency in a foam holder during anesthesia with MS-222. Note the bifurcated (Y) mouthpiece being placed in the oral cavity for delivery of oxygenated anesthetic water to both sets of gills.

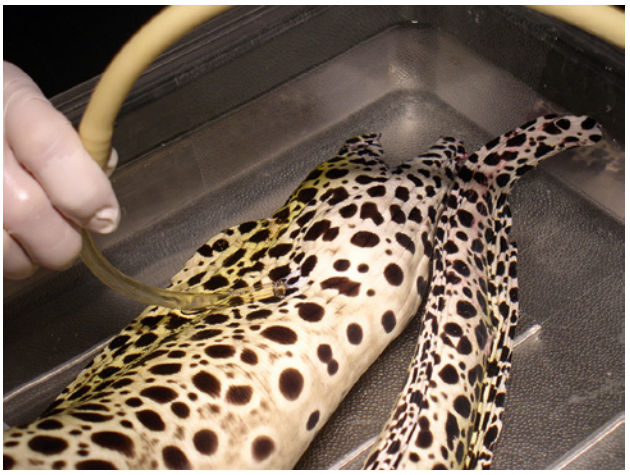


Figure 8.10 Retrograde flow over through gill slit in a laced moray eel (*Gymnothorax favagineus*) that is having oral surgery.

Recirculating systems enable delivery of anesthetic water from a reservoir to the gills and recycling of the effluent back to the fish. This recycling is either done manually (refill elevated reservoir with collected effluent) or with a submersible pump. When using pumps, electrical safety for the operator must be considered. Flow rate can be controlled by a valve on the tube leading to the mouth. Minimum effective flow rate during fish anesthesia has not been determined; 1–3 L/min/kg seems appropriate. Low delivery rates fail to keep the gills on both sides wet, thereby reducing gas exchange. High flow rates similarly prevent gas exchange and can result in alimentary anesthetic delivery and gastric dilatation, which may also occur due to depth of anesthesia and low sphincter tone. Both scenarios can be alleviated with the use of a "Y" or "T" plastic piece that equally distributes water over both gill arches. Oxygenation is provided as described above. Recirculating systems are used in large fish where cost and wastewater concerns make conservation of anesthetics and water paramount (Harms 1999; Ross 2001; Stetter 2001).

Regardless of the method used, adjusting the delivered drug concentration in response to anesthetic depth is difficult. One option is to prepare measured volumes of anesthetic-free water and concentrations of anesthetic solution. These solutions are placed in separate reservoirs and used in either recirculating or nonrecirculating systems. Alternatively, a syringe or turkey baster is used to rapidly deliver small amounts of fluid directly to the gills without disconnecting the fish from the system (Harms 1999).

The flow is usually normograde to achieve optimal gas and anesthetic exchange. During oral surgery, flow can be reversed if needed to allow for surgical access. However, retrograde flow nullifies the normal countercurrent exchange mechanism and may damage the gills, but in some circumstances may be required (oral surgery). The size or anatomy of some fish (e.g., filefish [Monocanthidae], triggers [Balistidae], or eels [Muraenidae]) (Fig. 8.10) make placement of a bifurcated buccal tube difficult. In these species, some retrograde flow is used to ensure all gill tissue is adequately perfused.

In some circumstances, whole-tank anesthesia is required to move fishes out of their systems. When this occurs, sufficient supportive staff for induction, transport, and recovery will be necessary. Using lower doses that tranquilize the animals enough for safely moving into transports would be sensible versus full sedation, but this will be species-specific not animal-specific (individual temperament, disease state, and size). This method has been shown to result in the least amount of stress when compared to capturing animals out of the tank and transferring to an induction tank (Tubio et al. 2010).

Enteral and Parenteral Anesthesia

In addition to immersion, anesthetics are delivered orally, intravenously, intramuscularly, and intracoelomically. Oral administration is rarely used because precise dosing is difficult and the rate and degree of absorption is uncertain (Harms 2003). However, a few examples of successful use of oral drugs exist (Hansen et al. 2003; Harms & Bakal 1995; Harvey et al. 1988; Raines & Clancy 2009; Steers & Sherrill 2001). IV injection is the fastest delivery method, with rapid induction and usually short duration of effect. However, this route has limited clinical use because it requires either manual restraint or prior administration of

drugs by another route to allow IV access (Fleming et al. 2003; Hansen et al. 2003).

Intramuscular (IM) delivery is the most common parenteral route. The major consideration with this route is that muscle is composed of both red and white muscle, with the white muscle taking up a majority of the muscle mass. In comparison to white muscle, the red muscle is aerobic and fast twitch, most likely the ideal set of muscles for appropriate metabolism and pharmacokinetics. However, because of location and low percentage of muscle mass, it is unlikely that an injection will be in the correct location, particularly if it needs to be administered quickly. Additionally, not all fish have both types of muscle; some species have all white muscle. Scale presence, size, and shape are also considerations with IM delivery. Intracoelomic (ICo) delivery has an increased risk of visceral damage and drugs must pass through the serosal surface, making induction time erratic. Both IM and ICo routes are used in larger fish because many are kept in large-volume aquariums or pens where adding waterborne anesthetics is impractical and because injection-site trauma is less problematic in larger specimens (Harms 1999; Harvey et al. 1988; Williams et al. 1988). Sedated fish will stop swimming and begin to drop through the water column with or without obvious gilling. However, when approached by divers with a net, they will often arouse and swim with directed movement, which signifies that more time is needed for the drug to have full effect and/or supplemental drug injections may need to be administered. Regardless of ease of capture, parenteral anesthetics are unpredictable and often do not provide adequate sedation or anesthesia, requiring supplemental anesthesia. Additionally, hypoxemia during induction is a concern as ventilatory ability is compromised. Ventilatory support is necessary during maintenance of parenteral immobilization drugs and particularly during recovery if prolonged (Harms 1999), but there is a period where safety for the staff and anesthetic depth are not always compatible. Injections are delivered by hand syringe, pole syringe (or modified pole syringe, Fig. 8.11), or a darting system (Runnells & Mylniczenko 2014).

Examples of darting systems include a modified Hawaiian sling (Fig. 8.12), pneumatic spear guns, a traditional dart gun system (Dan Inject Dart Guns, Austin, TX, US, https://dan-inject.com/) and a laser-aimed underwater gun (Harms 1999; Harvey et al. 1988; Runnells & Mylniczenko 2014; Williams et al. 1988).

The latter propels darts from a distance of 1–2 m (4–7 feet) that inject pneumatically on impact and remain attached after jettisoning the lightweight spear shaft. Hawaiian sling and pneumatic spear guns should be used with caution. They are used mostly for euthanasia as they

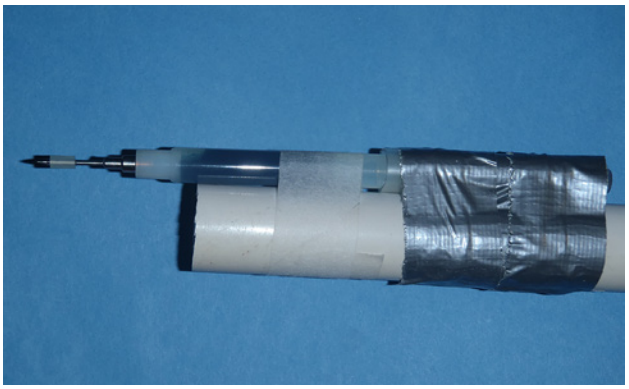


Figure 8.11 "Handmade" pole syringe system using an air charged dart capable of injecting 5 ml. The dart is backed into a plastic case that is taped to a polyvinyl pipe. The setup is secured with paper tape that will easily fall off after the animal is injected. Filtered food dye has been added to the contents of the syringe so injection success can be judged.

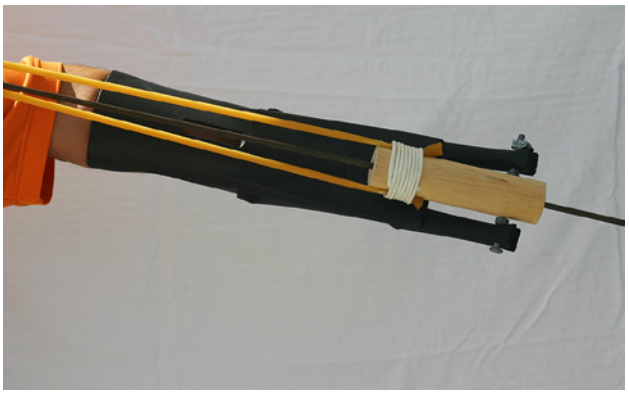


Figure 8.12 An example of a Hawaiian sling. It is recommended that this only be used for long distances or euthanasia by skilled users. Special thanks to Forrest Young, Dynasty Marine Associates, Marathon, FL.

are very powerful and it is difficult to control the force of the impact on the animal. Dart guns can be used from the surface, but skill is required to adequately propel and aim the dart. Both barbless and barbed needles are used for large, active, and heavily scaled or sluggish fish (Harvey et al. 1988). A complication of dart use is injection-site trauma and scale loss, with some fish requiring local or systemic wound treatment. IM injections will often result in leakage of some injected drug as the needle falls out or is withdrawn and the surrounding muscles contract (Harms 1995; Peters et al. 2001). Some scaled fish have very large and/or thickened scales that can deflect a dart or result in incomplete needle insertion. Consideration to injection volume is important as fish cannot retain much fluid due to muscle inelasticity. A final thought is that when divers are underwater, there is refraction between the diver's mask and the water, thus affecting the aim.

If the fish is in hand for injection, the needle is placed directly on the dorsal midline between epaxial muscles, and then laterally inserted into a muscle bundle to reduce drug loss (Harms 1995). Filtered food dye can be added to the contents of the syringe so injection success can be judged. Alternatively, fluorescein stain or methylene blue dye is used (Harvey et al. 1988).

A first consideration when using parenteral anesthetics is human safety. The large dosages and drug volumes required make accidental injection a possibility for handlers (Harvey et al. 1988). The authors recommend reference to drug exposure protocols for hoofstock when using doses that may be large enough to adversely affect the handler.

Monitoring

Anesthetic Depth

Various schemes are used to describe anesthetic depth in fish with no consensus (Detar & Mattingly 2004; Myszkowski et al. 2003; Oikawa et al. 1994). This makes comparison of regimens between and within species difficult when reviewing the literature. Common criteria used in defining anesthetic depth or level include activity, reactivity to stimuli, equilibrium (righting reflex), muscle tone, and respiratory and heart rates. Broad stages include sedation, narcosis or loss or equilibrium, and anesthesia; each stage is subdivided further into light and deep planes (Harms 2003; Stetter 2001). Depending on the species, drug, and dosage used, some stage components are unrecognized (Harms 1999; Neiffer & Stamper 2009; Stetter 2001). Conversely, some signs attributed to drug effects are instead responses to stress. For example, Gulf sturgeon (*Acipenser oxyrinchus desotoi*) often turn into a ventral/dorsal position when stressed (Fleming et al. 2003). Therefore, loss of the righting reflex is not used to determine the anesthetic stage in this species.

For most fish, induction occurs in 5–10 minutes with immersion drugs, but may be prolonged when using other routes. During induction, swimming, respiratory rate, and reaction to stimuli decreases. As the fish becomes anesthetized, there is loss of equilibrium and response to stimuli. At a surgical anesthetic plane, there is total loss of muscle tone and a further decrease, but not cessation, in respiratory rate. A firm squeeze at the base of the tail or insertion of a needle into the peduncle is used to determine response to stimuli; if the animal does not respond, general anesthesia has been achieved (Harms 2003; Stetter 2001; Storms & Mylniczenko 2004). Some species go through excitement during immersion induction and may traumatize themselves (Harms 1999; Stetter 2001).

Cardiopulmonary

Respiratory and cardiac rate changes are useful in assessing anesthetic depth. Both usually decrease with increased anesthetic dosage and anesthetic time. Respiratory rates are determined in the perianesthetic period by observing opercular movement (Harms 1999, 2003; Stetter 2001). However, in some species (e.g., scombrids) opercular movement is minimal to nonexistent, and potentially nondetectable in some species due to anatomy (frogfish, cowfish, etc.). Additionally, passage of oxygenated water over the gills of any anesthetized fish with ceased opercular movement will maintain adequate ventilation, at least in the short term. This is accomplished because of the large differential between respiratory and cardiac arrest. The heart will still supply fresh arterial blood to the gills, allowing for adequate gas exchange.

In species with thin pliable body walls and proportionally large hearts, the heartbeat may be observed directly, but for most it is neither visible nor palpable (Harms 1995, 1999). In these species, heart rate is monitored using cardiac ultrasonography, Doppler flow probes, or electrocardiography (Harms 1995, 1999; Ross 2001). During cardiac ultrasonography the probe is placed into the opercular slit of medium to large fish, or directly over the heart in smaller or small scaled/scaleless species (Fig. 8.13). Doppler probes



Figure 8.13 Ultrasonography is a useful tool for monitoring heart rate in fish. In this goliath grouper (*Epinephelus itajara*) the probe is placed directly over the heart in smaller specimens or small scaled/scaleless species.

are placed in the same locations (Fig. 8.14). Regarding electrocardiograms, electrodes can be clamped lightly to the surface of the fins, with the pectoral and anal fins being a good combination (Ross 2001). Subcutaneous placement of needle electrodes minimizes skin trauma, reduces the chance of grounding out the ECG signal by contact with a wet external surface, and improves signal quality (Harms 1999). In some species, use of human electrodes may work as well (Fig. 8.15). Pulse oximetry is not effective for measuring hemoglobin saturation in fish (Harms 1999; Ross 2001).

If the animal is stable, respiratory and heart rates are measured and recorded every 5 minutes. Trends are key because normal rates are not known for most species. Additionally, assessing quality of the rhythm and, if using ultrasound, contractility can be helpful, particularly if a baseline has been observed. Anesthetized fish generally have slower heart rates than terrestrial animals of similar size (Stetter 2001).



Figure 8.14 Doppler flow is also used for monitoring heart rate in fish. This figure demonstrates placement of the probe onto the area of the heart in a laced moray eel (*Gymnothorax favagineus*).



Figure 8.15 While not always practical, is it possible to monitor the ECG of fish as with this laced moray eel (*Gymnothorax favagineus*).

Other variables that are visually or palpably monitored include equilibrium, jaw tone, color of fin margin (pallor = hypoxemia, hypotension or peripheral vasoconstriction), response to touch or surgical stimuli, and gill color (pallor = hypoxemia, hypotension, hypovolemia, or asystole) (Harms 1995, 2001; Stetter 2001). Because of the relatively low blood pressure of fishes, blood pooling can occur normally and often occurs in the dependent portions of the body, particularly when animals are not in the water, where hydrostatic forces keep this pooling from occurring (Sandblom & Axelsson 2007).

An effective way to monitor respiratory efficiency is periodic blood gas sampling to determine lactate, carbon dioxide, and pH. Venous samples are easier to collect and useful information about physiological trends is obtained. Other blood variables used to assess metabolic status include HCT, bicarbonate, and glucose. Lactate is a critical metabolite that has been instrumental in evaluating fish responses to hypoxia and exertion (Heming 1989; McDonald & Milligan 1992). Point-of-care units are convenient but limited in their accuracy for some of these parameters (Harrenstein et al. 2005). There are species variations in tolerance of both hypoxia and exertion that must be taken into account; regardless, changes in blood gas values indicate a potentially unstable anesthetic event, depending on the degree of derangement. Small size or debilitation may prohibit collection of even a single blood sample from some individuals.

Water Quality

After cardiorespiratory function, water quality monitoring is critical to reducing anesthetic morbidity and mortality. Assuming aeration, DO, and temperature are appropriate and constant, ammonia concentration is of greatest concern. Ammonia concentrations will rise and buffering capacity will decrease during prolonged procedures and when multiple fish are sequentially anesthetized in the same system. Marine systems have an alkaline water pH, which enhances ammonia toxicity. Ammonia concentrations are easy to measure with tank side kits. Another indicator of deteriorating water quality is surface foam formation due to increased protein from fish "slime" or the mucus coat (Harms 1999). Some species (e.g., Gulf toadfish, *Opsanus beta*) are facultatively ureotelic and ureogenic. In contrast to most teleosts, which are obligate ammonioteles, the toadfish switches to ureotelism in response to moderate stressors (e.g., anesthesia),

excreting the majority of its nitrogenous waste as urea (Gilmour et al. 1998). Consequently, ammonia level measurement as a guide to water quality is inaccurate for this and similar species.

Declining water quality during anesthesia is corrected with a partial water change. The handler either adds water containing a known anesthetic concentration or, when reducing anesthetic depth, a known volume of clean water to the system.

Recovery

Recovery from immersion anesthesia begins when the fish is placed in drug-free water (Ross 2001). Even when using oral or parenteral drugs, moving to clean water is important as some of these drugs and their metabolites may be excreted into the water and be reabsorbed across the gills and/or skin. The recovery water is aerated with the fish's mouth oriented toward water flow. In an artificial ventilation system, clean drug-free water is passed over the gills until spontaneous ventilation and movement return. Alternatively, if the fish is not spontaneously ventilating it can be pulled forward through the water with its mouth open, but assisted ventilation is preferred. Dragging the animal backwards through water may cause gill damage and should be avoided. Most fish recover within 5–15 minutes from immersion anesthetics when the procedure is short, but this duration can be highly variable. Recoveries extending >10 minutes indicate either excessive anesthetic dosage or a medically compromised animal (Ross 2001; Stetter 2001). In comparison, recovery from parenteral agents is often greater. The time is dependent on route, rate of drug metabolism, and if a reversal agent is available and used. As the fish recovers, respirations increase, muscle tone returns, fin movements start, and the fish swims with progressively less ataxia until full equilibrium is regained. Some fish go through an erratic porpoising phase and escape from the tank must be prevented (Harms 1999). Certain individuals may need to be manually restrained during this period to prevent damage to eyes and body.

Resuscitation

Marked hypoventilation or apnea is usually not alarming. If cardiac output is maintained and oxygenated water is flowing appropriately over the gills, tissue gas exchange is probably adequate. Decreasing the anesthetic concentration or moving the fish to anesthetic-free water until respirations resume (Stetter 2001) are recommended. If involved in a major procedure (e.g., exploratory coeliotomy), the latter is not possible. In either scenario, the anesthetist takes advantage of the buccal flow/heart rate reflex: increasing water flow through the buccal cavity accelerates heart rate. The subsequent increase in gill blood flow more rapidly eliminates immersion drugs and hastens recovery. However, too rapid a flow may not allow adequate exchange, thus a balance must be achieved. Unresponsive fish are given standard mammalian emergency drugs such as doxapram, corticosteroids, and fluids. The authors' have observed positive responses to doxapram administration (5 mg/kg IV, IM [or both at the same time], ICe or even over the gills) in several cases of erratic respirations or respiratory arrest. Controversy over the use of epinephrine versus norepinephrine in fish exists and is an area in need of further investigation. At this time, epinephrine appears to be an effective drug for critical situations.

Anesthetic Drugs

General Comments

Anesthesia is "a biological state induced by an external agent which results in the partial or complete loss of sensation or loss of voluntary neuromotor control through chemical or non-chemical means" (Bressler & Ron 2004).

Rather than listing a few cross-taxa dosage recommendations for several commonly used drugs, the authors have taxonomically arranged cited and anecdotal dosages for representative species from most orders (Table 8.1).

Immersion (Waterborne, Bath or Inhalant) Drugs

Tricaine Methanesulfonate (MS-222, TMS)

Tricaine methanesulfonate (MS-222) is a benzocaine derivative with a sulfonate radical, which accounts for its water solubility and increased acidity over the parent compound (Harms 1999; Oikawa et al. 1994; Topic Popovic et al. 2012). It is absorbed through gills and skin and is metabolized in the liver, kidneys, blood, and muscle. The main action is by blocking sodium channels in muscle and potassium pathways in nerve membranes (Priborsky & Velisek 2018). It is cleared primarily through the gills as free and acetylated forms, with additional metabolites eliminated in urine and bile (Harms 1999). Tricaine powder is directly mixed into the anesthetic chamber or administered as a stock solution of 10 g/L (10,000 mg/L). The latter is unstable in light and is kept in a dark container. Oily residues in buffered stock solutions indicate the presence of a de-sulfonation product and decreased potency.

MS-222 is acidic and is more effective and safe in its neutralized form. Solutions are buffered to the pH of the holding water before immersing the fish. Although sodium bicarbonate has been used most predominantly, other buffers include imidazole, sodium hydrogen phosphate, sodium hydroxide, and calcium carbonate. Sodium carbonate was recently found to be a better medium than bicarbonate for buffering (Waxman et al. 2021). Exact amounts of buffer can be measured out or the powdered buffer incrementally mixed into the anesthesia chamber until the solid no longer dissolves and saturation is reached (Harms 1999; Oikawa et al. 1994; Roubach et al. 2001; Stetter 2001). The latter can cause supersaturation and may result in blood gas abnormalities (author's personal experience), so measuring precise amounts of buffer is strongly encouraged.

There has been some dispute in the literature regarding the susceptibility of some sturgeon to MS-222, suggesting they are refractory to standard doses (Fleming et al. 2003), however other groups have used MS-222 with no resistance at typical inductive doses (Feng et al. 2011; Hernandez-Divers et al. 2004; Matsche 2011). The reasons for this discrepancy can include subspecies variations and environmental parameters (e.g., temperature) which may affect metabolism. In one study of sturgeon anesthesia, it was found that when compared to medetomidine/ketamine and even clove oil, MS-222 resulted in much higher negative physiologic effects (Di Marco et al. 2011).

The margin of safety is narrower with young fish in warm, soft water, and there are species variations (Harms 1999; Topic Popovic et al. 2012; Roubach et al. 2001). In all age groups, MS-222 can be associated with hypoxemia resulting from drug-induced hypoventilation (Davis & Griffin 2004; Harms 1995; Oikawa et al. 1994). MS-222 is a suspected carcinogen (Detar & Mattingly 2004) and in fish and humans may cause reversible retinal deficits (Berstein et al. 1997). A chronically exposed ichthyologist developed decreased vision, photophobia, and photopsia that resolved after terminating MS-222 contact for 7 months (Berstein et al. 1997). Personnel with regular occupational exposure should wear personal protective equipment to prevent systemic absorption of this retinotoxic drug.

MS-222 is the only US Food and Drug Administration (FDA)-approved anesthetic for fish in the United States and consequently is widely used in aquaculture. However, there is a 21-day withdrawal period prior to human consumption or release to the wild. This makes its use impractical or incompatible with some farming operations and field work (Detar & Mattingly 2004; Sladky et al. 2001; Waterstrat 1999).

Benzocaine

Benzocaine, the parent compound to MS-222, is similar in pharmacology, but is much less water soluble. Consequently, a stock solution in ethanol or acetone (100 g in 1 L) or propylene glycol is prepared prior to its use. The stock solution is kept in a dark bottle and held at room temperature (Harms & Bakal 1995). Its relative insolubility may account for its usefulness in species sensitive to MS-222. For example, striped bass (*Morone saxatilis*) are very sensitive to MS-222 but are effectively anesthetized in benzocaine solutions (55–80 mg/L) (Hseu et al. 1998).

Other advantages include low toxicity to humans at the concentrations used, and it can be removed from aquaculture facility effluents using activated carbon filtration. Even if not filtered, breakdown in water is approximately 4 hours, making it less likely to cause environmental contamination. Exposure also does not impair fish growth or reproductive capacity (Gomes et al. 2001; Hseu et al. 1998).

Efficacy and sensitivity to benzocaine are species and dosage related (Gomes et al. 2001; Heo & Shin 2010), and it can stimulate the stress response as discussed previously. The only other major concern is its fat solubility, which may result in prolonged recovery in older and gravid fish. It is one of the few drugs shown to be effective for safe anesthesia of arapaima (Honczaryk & Inoue 2009). A paper in Crucian carp (*Carassius carassius*) noted it to be a safe rapid agent with low increases in stress biomarkers (glucose and cortisol) (Heo & Shin 2010). In Atlantic cod, induction and recovery times were found to increase with increasing body weight. Additionally, it was found that recovery times were longer with benzocaine versus MS-222, even at half the dose of MS-222. In combination with metomidate, however, induction times did decrease (but not as much as metomidate and MS-222) (Zahl 2009). In a recent study it was found that methemoglobin levels increase in several salmonids when anesthetized with both MS-222 and benzocaine at varying levels with no obvious clinical effects (Saunders et al. 2020).

Lidocaine Hydrochloride

Anesthesia with lidocaine baths showed moderate species differences in dose and effect (Carrasco et al. 1984). Lidocaine is a Na^+ channel blocker with local and central action reported. In 10 mg/L sedation was noted in zebrafish with parallel reduction of brain acetylcholinesterase (de Abreu et al. 2019). In immature black ruby barbs 80–100 mg/L was considered optimum (Priyangika et al. 2007). Surgical anesthesia was achieved in zebrafish at 325 mg/L but had a low margin of safety at 350 mg/L (Collymore et al. 2014). In carp it produced reliable, rapid induction and fast recoveries for short procedures at 100 mg/L (Cagiltay et al. 2017).

Clove Oil, Eugenol, Isoeugenol, and Aqui-S® 20e

Clove oil is a mixture of compounds, of which the phenol, eugenol, comprises 85–95%. Isoeugenol and methyleugenol make up the remaining 5–15% of active ingredients. Commercially available clove oil has approximately 84% eugenol, but it is possible to purchase 100%, even at local natural product stores. There are several modes of action: inhibiting voltage dependent ion channels, potentiation of gamma-aminobutyric acid A (GABA) receptors, and inhibition of N-methyl-D-aspartate (NMDA) receptors (Javahery et al. 2012; Zahl et al. 2012).

Clove oil and isoeugenol are "generally recognized as safe" (GRAS) by the FDA as a food additive for humans. Eugenol is similarly approved for use in animal feeds and is used in dental cement for temporary fillings (Harper 2003). However, clove oil, any component of clove oil, and Aqui-S® (isoeugenol, no longer available in the US) are not approved for use as a fish anesthetic in food fish in the United States due to concerns of carcinogenicity in a few animal models (Silbernagel & Yochem 2016). Aqui-S® 20e is currently an Investigational New Animal Drug (https://www.fws.gov/fisheries/aadap/inads.html).

Clove oil and eugenol are incompletely water soluble, particularly at cold temperatures. A 1:10 mixture in 95% ethanol yields a 100 mg/ml stock solution. Concentrations are wide and range from 25 to 120 mg/L (the contribution of ethanol to the anesthetic effect is nil at these concentrations) (Harms 2003; Silbernagel & Yochem 2016). Aqui-S® 20e is completely water soluble, pH neutral, and has no foaming effects as reported with Aqui-S®. Doses for Aqui-S® 20e are 25–55 mg/L with mortalities occurring in several teleost species at >75 mg/L; the reader should review the literature for available species-specific effective doses and if not available, the authors recommend starting at 25 ppm and increasing as warranted by level of sedation achieved (see Table 8.1 for some recommendations).

For tide pools and reef surveys, a section is covered with a mesh net covered in turn by a nylon cloak. A solution of clove oil mixed with ethanol is then pumped into the netted area to temporarily immobilize all fish (as a reminder, clove is not an FDA-approved drug). This application of clove oil may be of use in managed exhibits, which often have elaborate rock or coral work, making removal of fish for medical or maintenance reasons difficult.

Clove oil at doses of >75 mg/L had mortalities in some species (*Astyanax altiparanae*) (Pereira-da-Silva et al. 2009). This may be a function of the physical properties of eugenol oil, increased duration of exposure, or peri-anesthetic management (ventilation, capture stress, etc.). As an oil, eugenol coats anatomic structures and its persistence on gill epithelia may block gaseous diffusion (Sladky et al. 2001). In addition, mild gill necrosis due to repeated exposure to low-dose eugenol (9 mg/L) has been reported (Afifi et al. 2001). With Aqui-S® and Aqui-S® 20e there appears to be a wider safety margin than other clove oil products and fewer mortalities (Bowker et al. 2017; de Oliveira et al. 2019; Gladden et al. 2010; Silbernagel & Yochem 2016; Tennant et al. 2019).

Clove oil has also been used for long-term transports (up to 48 hours) in the cichlid, *Haplochromis obliquidens,* with some mortalities at the higher end (Kaiser et al. 2006). Aqui-S® 20e and eugenol have been effectively used in transports (Cupp et al. 2017). Compared to other immersion anesthetics, clove oil results in more rapid induction times and consistent anesthesia (Abdulrahman et al. 2018; Balamurugan et al. 2016; Bressler & Ron 2004; Detar & Mattingly 2004; Sladky et al. 2001). Additionally, it is less aversive than anesthetics like MS-222 (Wong et al. 2014). In the authors' experience this tends to be true with many anesthetics. In beluga sturgeon (*Huso huso*) that were exposed to clove oil at doses of 500–3000 mg/L it was noted that cortisol, glucose, and lactate levels were lower at the higher dosages with faster inductions (Hoseini et al. 2011). The stress response is variable with suppression in some cases and activation in others, and the reader is directed to the literature (Small & Chatakondi 2005; Wagner et al. 2003) for more detail.

A more practical approach has been to utilize clove powder rather than oil. In sturgeon, the powder has been used in juvenile beluga sturgeon from 175 to 350 mg/L with negative side effects being limited to increases in hematocrit, hemoglobin, and total erythrocyte count but with a return to normal within 24 hours (Mohammadizarejabad et al. 2010). In common carp (*Cyprinus carpio*), 190 mg/L (range 120–230 mg/L) was considered a safe and effective dose with no adverse side effects (Abdulrahman et al. 2018). In convict cichlid (*Amatitlania nigrofasciata*), both clove powder and lavender essential oil successfully worked as anesthetics, however the overall effect was different between the two methods (Raisi et al. 2020).

Although the analgesic effects of eugenol in humans result from the inhibition of prostaglandin H synthase (Keene et al. 1998), proof of analgesia in fish does not exist (Sladky et al. 2001). In red pacu (*Piaractus brachypomus*), fish anesthetized with eugenol were more likely to react to a hypodermic needle puncture than fish anesthetized with tricaine methanesulfonate raising the question of appropriateness of clove oil or related compounds for invasive or markedly noxious procedures. The effect of clove oil and its components on the stress response is variable, with suppression in some cases and activation in others. There has been recent interest in the potential of other essential oils to expedite zero withdrawal for market fish such as basil, thyme, mint, rosemary, lavender, citronella, verbena,

eucalyptus, and camphor as sedatives and anesthetics in different fish species (Aydin & Barbas 2020; Soldatov 2021; Souza et al. 2019) but more research is needed.

Alfaxalone

A combination steroid anesthetic, Alfaxalone (alphaxalone)/alphadolone (A/A), was marketed as Saffan™ and found to induce surgical anesthesia in fish when used as an immersion anesthetic (Peters et al. 2001). It mainly depresses central nervous system (CNS) activity while leaving the integumentary sensory system operational. This makes it very valuable for research in sensory physiology, including mechanoreceptors (Peters et al. 2001). Unfortunately, the main solvent in the drug, Cremophor EL, was associated with histamine release in cats and dogs and subsequently removed from the market (Sear 1996). A newer formulation of alfaxalone has been released without alphadolone, Alfaxan™ (alfaxalone); it is a controlled substance. Alfaxan™ is solubilized in hydroxypropyl-beta cyclodextrin and has not been associated with histamine release.

Alfaxalone has been studied as an immersion anesthetic in goldfish (*Carassius auratus*) (Bauquier et al. 2013; Leonardi et al. 2019), koi (*Cyprinus carpio*) (Minter et al. 2014), and Oscar fish (*Astronotus ocellatus*) (Bugman et al. 2016). Similar to A/A, species and individual variation should be anticipated with the use of alfaxalone (Zellar et al. 2018). In a comparison between MS-222 and alfaxalone of two fish species, black spot barbs (*Puntius filamentosis*) had significantly faster induction times when treated with both drugs, and a faster recovery time from 5 mg/L alfaxalone compared to peacock cichlids (*Aulonocara* spp.). However, shorter induction and longer recovery times were observed for both species treated with 5 mg/L alfaxalone, compared to MS-222 (Zellar et al. 2018). In zebrafish (*Danio rerio*), it produced similar anesthetic results as MS-222 (Farry et al. 2019) and another study in goldfish found it to reach an appropriate level of anesthesia with no adverse effects (Fernández-Parra et al. 2017).

Metomidate and Etomidate

Metomidate and etomidate are nonbarbiturate imidazoles that act through modulation of the inhibitory GABA type A receptors (Martins et al. 2019). Metomidate is labeled currently as Aquacalm™ (Syndel, WA) at doses of 0.1–1.0 mg/L (sedation) and 1.0–10.0 mg/L (anesthesia). It is readily water soluble and is stored in tight, light-protected containers. In addition to immersion, the drug can be given orally (Hansen et al. 2003; Harvey et al. 1988). Etomidate is not widely used in teleost fishes, possibly because of its overall availability and because it is an aqueous solution, requiring ethanol dilution to use. It has been suggested as the best anesthetic for zebrafish, a popular research fish (Readman et al. 2013), and recent use in perch (*Perca fluviatilis*) suggests it is appropriate for this species (Rożyński et al. 2018).

Metomidate and etomidate suppress cortisol response to anesthesia in many (not all) fishes. They block adrenocorticotropic hormone stimulation of steroidogenesis, even when exogenous ACTH is injected intracoelomic. This occurs by a direct effect on the interrenal gland and the mitochondrial cytochrome P_{450}-dependent enzymes that catalyze the synthesis of cortisol (Davis & Griffin 2004; Small & Chatakondi 2005). Cortisol synthesis blockade may cause the immobilized fish to transiently turn very dark. This may be due to reduced cortisol production terminating the negative feedback loop on ACTH synthesis. As ACTH synthesis is linked to melanocyte-stimulating hormone production, both compounds increase with the associated color change occurring (Harms 1995, 1999).

In addition to sedation and anesthesia for minor procedures, metomidate is useful for limiting transport trauma. Fish transported while immobilized can sustain damage if in contact with the container sides and bottom. Metomidate dosages that suppress the cortisol stress response still allow maintenance of equilibrium (Davis & Griffin 2004; Harms 1999; Kilgore et al. 2009).

Metomidate is a hypnotic that more technically induces a sleep-like state rather than general anesthesia. This is reflected in maintenance of opercular respiration for twice as long at the effective concentration as other immersions (Mattson & Riple 1989). Additionally, muscle fasciculations occur at low dosages, indicating incomplete relaxation (Harms 1999). Metomidate is probably a poor analgesic and should not be used alone for major surgical or noxious procedures (Hansen et al. 2003; Harms 1999). It was recently evaluated for use as a euthanasia agent as it shows no aversive effects to exposure of the drug at 100 mg/L, but several caveats were iterated: cessation of reactivity to stimuli and not cessation of ventilation after 30 minutes of exposure and buffering, and higher doses were required in some species (Yanong 2021).

In some marine species, metomidate has a wider therapeutic range compared to benzocaine (Hansen et al. 2003). Among freshwater tropical fish, three-spot gouramis (*Trichogaster trichopterus*) are very sensitive to metomidate and its use in cichlids (Cichlidae) in water of pH <5 is contraindicated (Harms 1999). As a result of the gourami study, it has been recommended not to use this product in air-breathing fishes (Martins et al. 2019). In Atlantic cod, recovery times were found to increase with increasing body weight, but not induction times. When metomidate was used in combination with MS-222 or benzocaine, overall

reduction of dose of both MS-222 and benzocaine was possible with marked reduction of both induction and recovery time (Zahl et al. 2009). The authors have found that while the drug is useful for light sedation, induction times and depth of anesthesia (or sleep) did not show an advantage over other immersion drugs other than a consideration for the low cortisol response in published species and lack of aversion to this drug (Weber et al. 2017).

Quinaldine and Quinaldine Sulfate

Quinaldine sulfate (QS) is a strongly acidic, highly water-soluble powder that must be buffered. Rather than adding powder directly to the water, QS is administered as a stock solution (10 g/L). Its parent compound, quinaldine, is a yellowish oily liquid and must be dissolved in acetone or alcohol prior to mixing in water. Due to high lipid solubility, quinaldine tends to accumulate in the brain more than QS (Harms 1999; Hseu et al. 1998; Ross 2001). Like MS-222 and most immersions, quinaldine and QS depress the CNS sensory centers. Unlike MS-222, neither drug is metabolized by fish and is excreted entirely unchanged (Harms 1999; Hseu et al. 1998).

Though not approved for use in the United States (Harms 1999), QS is common in aquaculture elsewhere because of its relatively low cost. This has also made quinaldine a popular tool for collection of fishes from tidal pools and small lagoons (Ross & Ross 1984). Other reported advantages include effectiveness at very low concentrations, purported low toxicity and wide safety margin, and short fish recovery time (Kumlu & Yanar 1999).

Despite claims of safety, mortality occurs in some species. For example, in gilt-head seabream low-dosage QS (15–20 mg/L) resulted in 30–100% mortality (Kumlu & Yanar 1999). In addition, quinaldine can be an irritant and has caused corneal damage in salmonids (Harms & Bakal 1995; Ross & Ross 1984). Also of importance are studies that demonstrate that fish exposed to quinaldine or QS alone retain a strong reflex response to being touched, even when they have totally lost equilibrium and are deeply anesthetized. This, along with the potential lack of analgesia makes it inappropriate for transportation, handling, and surgical or similarly noxious procedures (Cullen 1996; Harms 1999; Kumlu & Yanar 1999).

To reduce toxicity, and increase efficacy and analgesia, some researchers have combined diazepam with QS. As demonstrated in gilt-head seabream, sea bass (*Dicentrarchus labrax*), and cichlids, addition of diazepam to the QS bath results in fish entering a deeper anesthetic plane at lower QS dosages. This occurs with lower to no mortality, improved muscle relaxation, and reduced excitement in confined spaces (e.g., transport boxes) (Kumlu & Yanar 1999; Yanar & Kumlu 2001; Bircan-Yildirim et al. 2010). Nondepolarizing neuromuscular blocking agents (gallamine triethiodide, tubocurarine chloride, and pancuronium bromide) IM eliminate the reflex responses in fish anesthetized by quinaldine alone (Kumlu & Yanar 1999). However, these combinations do not provide analgesia. Given the more advantageous properties of other immersives, this drug is not in favorable use in most managed-care situations, but is being investigated in other countries.

2-Phenoxyethanol

2-phenoxyethanol (2-PE) is a clear or straw-colored oily liquid. It has a faintly aromatic odor and is moderately water soluble. The mode of action is related to inhibition of NMDA receptors, which have been related to analgesic effects but analgesia appears to be incomplete (Martins et al. 2019). 2-PE was used initially in aquaculture to treat ichthyophonus and other fungal, bacterial, and parasitic diseases. Historically less expensive than many anesthetics, 2-PE has been widely used for sedation, particularly in fish transportation, as well as general anesthesia (Hseu et al. 1996, 1997; Martins et al. 2019; Priborsky & Velisek 2018; Ross 2001). Another advantage is that it causes no pH change when added to seawater (Hseu et al. 1998).

In addition to the poor analgesic properties, 2-PE also produces hypoventilation (Oswald 1978). Additionally, 2-PE may not completely cease involuntary movements, so muscle twitching is possible. Other negative aspects to the drug include no block of the stress response and cardiovascular activity is significantly reduced (Fredricks et al. 1993; Molinero & Gonzalez 1995) although low doses (such as for light sedation and transport) showed no effect on cortisol secretion (Martins et al. 2019). Also, sustained and regular exposure to 2-PE solution causes a neuropsychological syndrome in some handlers (Hseu et al. 1998) although a recent article shows it to be relatively safe (Dreno et al. 2019).

Over 102 species (30 families) of a variety of sizes and ages of fish were moved from one aquarium to another using 2PE exclusively at an average dosage of 0.15 ml/L with maintenance in the immersion for up to 330 minutes. In general, the procedure was smooth, with very little excitation noted in most of the species (Vaughan et al. 2008).

Isoflurane

There are limited published studies evaluating chlorofluorocarbon-based anesthetics in fish, and they have limited applicability (Cagiltay et al. 2017). Isoflurane is considered safe and effective in freshwater and marine fish at concentrations ranging from 0.4 to 0.75 ml isoflurane/L H_2O for induction and 0.25 ml isoflurane/L H_2O for maintenance (Stetter 2001). Isoflurane liquid is vaporized and bubbled

through the water or is directly added to the anesthetic chamber. The latter involves spraying the drug through a 25-gauge needle beneath the surface of the anesthetic chamber. This allows small drug droplets to be distributed in the water (Stetter 2001). Anesthetic depth is difficult to control and, due to insolubility in water, localized areas of higher concentrations may occur, resulting in overdosage. In addition, volatilization and difficulty in scavenging waste gas is a hazard to personnel (Harms 1999; Ross 2001). This is addressed, to some extent, by attaching a funnel system to a standard scavenging system and placing it immediately above the anesthetic chamber (Stetter 2001). Given the disadvantages associated with its use, a number of researchers and clinicians recommend use of isoflurane or similar drugs only as a last resort anesthetic, for euthanasia, or not at all (Harms 1999; Ross 2001). A recent study utilized emulsified gas anesthetics compared to propofol, finding that isoflurane and sevoflurane when emulsified induced general anesthesia in Amur carp (*Cyprinus rubrofuscus*), with faster recovery times compared to propofol (Natalini 2021). In zebrafish isoflurane bubbled into a concentration of 0.5 ml/L resulted in mortalities without providing stage 3 anesthesia (Collymore et al. 2014). Using isoflurane and halothane in carp at 1.5 mg/L resulted in deaths in the isoflurane group of small fish in the study (Cagiltay et al. 2017).

Propofol

Propofol produced anesthesia when used as an immersion in goldfish at 5 and 10 mg/L. Anesthetic needs were similar following repeated exposure and it was safe, but it was not suitable to test MAC reduction (Balko et al. 2017). Propofol has been used as an immersion anesthetic in other species, including silver catfish (*Bagrus bajad*) (GholipourKanani and Ahadizadeh 2013), Nile tilapia (*Oreochromis niloticus*) (Gressler et al. 2012; Goncalves and Giaquinto 2020), koi (Oda et al. 2014, 2018), Persian sturgeon (*Acipenser persicus*) (Adel et al. 2016), and goldfish (Valenca-Silva et al. 2014) with reported efficacy.

In goldfish, a concentration of 1 mg/L resulted in sedation but not anesthesia while 2.5–10 mg/L resulted in dose-dependent decreases in induction times and conversely longer recoveries (Balko et al. 2017). In another study, a dose-dependent response was similarly seen, but body size also influenced induction and recovery times (larger fish had longer induction and faster recoveries) (Obirikorang et al. 2020). Dose of 2 mg/L was effective in African catfish (*Clarias gariepinus*) with no adverse effects on hematologic parameters (Adeola et al. 2018).

Ketamine, Xylazine, and Telazol

Traditionally used intramuscularly or intravenously, the drugs ketamine and xylazine can also be used as an immersion. In a study conducted by Hamdani et al. (2010), these drugs utilized in various combinations as a bath for carp resulted in smooth inductions with sufficient anesthetic time to perform minor procedures. In rainbow trout, 100 mg/L ketamine was considered safe and easy (very water soluble) (Ganjoor et al. 2020). Conversely, in Persian sturgeon there were no clinical effects at 500 and 750 mg/L; even with doses of 5000 mg/L, induction was still long (>5 minutes) (Adel et al. 2016). In addition to species variable responses, other disadvantages are the cost and DEA regulations. In a study on grass carp, xylazine was more effective in deep anesthesia and recovery times compared to benzocaine (Shakeri et al. 2016).

Medetomidine

Medetomidine is an antifouling agent used for barnacle control (Koning et al. 2021). The drug is incorporated into marine paints and prevents the settling of barnacle and tubeworm larvae on surfaces coated with the paint. To assess the potential for effects on nontarget species in the vicinity of such paints, studies have been performed with low-dose long-term immersion baths. In one of these studies, 0.5–50 nM medetomidine baths were used; mostly fry was affected and side effects noted were body paleness, decreased oxygen consumption, and decreased respirations (Lennquist et al. 2010). Sedative effects were not noted as it was not the scope of the study, but all side effects were reversible when animals were removed to clean water.

Carbon Dioxide

Carbon dioxide for immobilization is obtained from three sources: CO_2 gas, sodium bicarbonate ($NaHCO_3$), or carbonic acid (H_2CO_3) (Gelwicks et al. 1998; Prince et al. 1995). Use of carbon dioxide gas involves diffusing compressed CO_2 gas through air stones into water. The $NaHCO_3$ (baking soda) method involves mixing a specific amount of the drug with water to release CO_2. Carbonic acid immobilization involves mixing equal volumes of sulfuric acid (H_2SO_4) and $NaHCO_3$ solutions in water to form carbonic acid and liberate CO_2 (Gelwicks et al. 1998; Prince et al. 1995).

Carbon dioxide gas and $NaHCO_3$ methods are popular, but cumbersome for many field applications (Gelwicks et al. 1998; Prince et al. 1995). In comparison, the materials needed for carbonic acid immobilization are compact and concentrations are easily controlled, making it more applicable to field work (Gelwicks et al. 1998). The carbonic acid method has its own disadvantage in that $NaHCO_3$ and H_2SO_4 solutions are designed to react completely and accuracy is essential. If one solution is mixed incorrectly, water chemistry (i.e., pH) will be significantly affected. Safe handling of concentrated H_2SO_4 requires protective gloves, clothing, and glasses, and work should be performed under

a fume hood (Gelwicks et al. 1998). The acid is added to the water, not the reverse.

Regardless of method, CO_2 use has many disadvantages. Concentrations in water are difficult to control and oxygen must be maintained at high levels. Blood gases and acid-base balance are markedly altered (Harms 1999; Prince et al. 1995). To address the latter concern, some handlers use $NaHCO_3$ with CO_2 gas for its buffering effect (Prince et al. 1995). Alternatively, some handlers mix $NaHCO_3$ with glacial acetic acid to yield carbon dioxide concentrations sufficient for immobilization while limiting acid-base shifts (Prince et al. 1995).

Following immersion in water with a high CO_2 concentration, there is a rapid decrease in blood pH and increase in blood CO_2 concentration. Low blood pH results in less efficient oxygen transport to tissues, including the brain. The resulting cerebral hypoxia causes an overall inhibition of spontaneous activity of the CNS and the observed "anesthetic" effect (Gelwicks et al. 1998; Harms & Bakal 1995). When fish are returned to freshwater, CO_2 diffuses out of the gills, blood pH rapidly returns to normal levels and fish recover. One may expect these changes in blood pH and subsequent cerebral hypoxia to produce morbidity. However, rainbow trout appear tolerant of these changes in blood pH. Recent studies provide conflicting evidence regarding the effectiveness and safety of carbonic acid (Gelwicks et al. 1998).

Although touted to decrease the stress response, CO_2 has questionable analgesia (Prince et al. 1995; Ross 2001) and is not appropriate for invasive procedures. Additionally, fish are aversive to CO_2 in their environment (Robb et al. 2000; Tix et al. 2018).

In the United States the primary advantage of using CO_2 is that it is "generally regarded as safe, and there are no restrictions on its use, which is appealing to both aquaculture and field work" (Gelwicks et al. 1998; Harms 1999). However, many handlers feel it should be used for immobilization or euthanasia as a last resort (Harms 1999).

Other Immersion Agents

There are more esoteric plant-based essential oils that have been tried in fishes, with a dearth in the extant literature (for a review, see Aydin & Barbas [2020] and Table 8.1). This is owing to financial reasons, lack of residues (no withdrawal), availability, and ease of use. Of additional interest is the use of diazepam as an immersion anesthetic, and while not overtly sedative, it does show evidence of anxiolytic effects which may prove useful in other combinations (Bencan et al. 2009; Grebauer et al. 2011). Similarly, many psychoactives (e.g., gabapentin, tramadol) are trialed in fish due to wastewater exposure (Cunha et al. 2019) but these are not at doses that would likely be used for sedation or anesthesia.

Some historical drugs include chloral hydrate, urethane, chlorobutanol, and diethyl ether, none of which are recommended for use in fish any longer (McFarland & Klonz 1969).

Oral Anesthetics

Metomidate

In addition to being used as an immersion, metomidate has been administered orally by high-pressure syringe as a supplement in fish partially immobilized by remote injection (Harvey et al. 1988) and to turbot (*Scophthalmus maximus*) via stomach tube for rapid and complete immobilization (Hansen et al. 2003).

Diazepam

In addition to being combined with QS for immersion anesthesia (Yanar & Kumlu 2001), diazepam-impregnated pellets have been fed to American shad (*Alosa sapidissima*), resulting in a slow anesthetic induction (Harms & Bakal 1995). The authors regularly use oral diazepam as an oral pre-sedative in larger fishes at dosages of 0.5–4.0 mg/kg.

Ketamine

Ketamine, when gavaged orally to goldfish and hybrid striped bass, showed notable sedative effects and animals allowed themselves to be netted; furthermore, an arapaima sedated by this method tolerated slinging (Raines & Clancy 2009).

Tiletamine-Zolazepam

Though designed to be used as an injectable drug combination, successful sedation and translocation of >70% of a population of captive yellowtail jacks (*Seriola lalandi*) was performed using per os tiletamine-zolazepam. The powder was packed in gelatin capsules and placed in food items. Mortalities did occur and were attributed to anesthetic overdosage from fish consuming more than one medicated food item (Steers & Sherrill 2001).

Injectable Anesthetics

Alfaxalone

In a collection of marine and freshwater species A/A was effective IM, but not consistent for capture of free-swimming individuals (Harvey et al. 1988). In several catfish species, IM A/A provided surgical anesthesia lasting several hours (Peters et al. 2001). In rainbow and brown trout, A/A produces similar long sleep times, but it is difficult to give a dose that simultaneously abolishes locomotion yet preserves ventilation (Oswald 1978). With the new formulation of alfaxalone, immersion works well, but

intramuscular dosages of 1.0–10.0 mg/kg were tested in koi with variable responses (mostly inadequate sedation at the low doses) and 33% mortality in the 10 mg/kg dosage (Bailey et al. 2014).

Ketamine Hydrochloride

Ketamine is used alone or in combination with alpha-2 agonists (Harms 1999). Intramuscular injection is the most common route and requires high dosages in teleosts and sturgeons when used alone (Bruecker & Graham 1993; Fleming et al. 2003; Williams et al. 1988). When available in the lyophilized form, a concentrated solution permitting a smaller volume IM injection can be prepared (Oswald 1978). IV administration, though rarely reported, uses dosages a third to a half of those used IM.

Ketamine has been used for capture and manipulation of a number of marine and freshwater species (Williams et al. 1988) and for short-duration procedures and transport (Bruecker & Graham 1993; Oswald 1978). Ketamine IV in coho salmon (*Oncorhynchus kisutch*), rainbow trout, and Midas cichlids (*Heros citrinellum*) reduces the oxygen demand during handling (Bruecker & Graham 1993; Oswald 1978). Tested protocols of IM ketamine (K), dexmedetomidine (D), and midazolam (M) in red porgy (*Pagrus pagrus*) and black sea bass (*Centropristis striata*) showed variable and poor (fatal consequences) responses in porgy but were effective in black sea bass (see Table 8.1 for doses) (Christiansen et al. 2014).

Regardless of administration route, ketamine alone has a species-specific effect in fish often characterized by incomplete anesthesia, periods of apnea, and prolonged recovery with excitement (Bruecker & Graham 1993; Graham & Iwama 1990; Oswald 1978). To reduce dosage and apnea, and improve anesthesia, ketamine is often combined with the reversible alpha-2-adrenergic agonist medetomidine. This combination provides safe and effective anesthesia in some species (Williams et al. 2004), but respiratory depression, bradycardia (Fleming et al. 2003) and incomplete immobilization are noted in others. For the latter reason, either ketamine or a ketamine/medetomidine (K/M) combination is more appropriate as an aid to restraint, rather than as a substitute for immersion anesthesia during major procedures. K/M can be useful in capture of fish from large-volume aquaria. Following reduction of reflexes or sedation with K/M, staff are able to net the fish and transfer them to an MS-222 bath for maintenance and evaluation. In sturgeon (*Acipenser* hybrids), IV medetomidine 0.04 mg/kg and ketamine 4.0 mg/kg had slower inductions and longer recoveries than MS-222 or cove oil, but interestingly had fewer physiologic effects than the MS-222 or clove oil (Di Marco et al. 2011).

Lidocaine

Lidocaine is suggested as an effective injectable local anesthetic in fish, with some question recently on actual analgesic properties (see Chatigny et al. 2017; Harms & Bakal 1995; Park et al. 2011; Sneddon 2012). It has been reported in several fishes as the primary local anesthetic with rare instances of novocaine addition (Chatigny et al. 2017). Immersion at a low dose is suggested for analgesia at 2.0–5.0 mg/L in a postoperative holding aquarium but there are confounding factors and interpretation of success is left to the reader; theoretically topical and possible central effects are possible, but dose and species dependent (Schroeder & Sneddon 2017). At the very least, there have been mortalities reported with local use up to doses of 15.0 mg/kg (see review in Chatigny et al. [2017]).

Medetomidine and Dexmedetomidine

Medetomidine is usually combined with ketamine and reversed with atipamezole. However, it can be used alone as an immersion in rainbow trout to produce sedation, but not analgesia. Bradypnea was observed during immobilization, with an increase in respiration occurring after addition of atipamezole to the recovery water at six times the medetomidine concentration (Horsberg et al. 1999). One of the authors (Mylniczenko) found that in black pacu (or tambiqui), *Colossoma macropomum*, medetomidine (100.0 ug/kg IM) in combination with midazolam (1.0 mg/kg IM) and butorphanol (1.0 mg/kg IM) did not produce ataxia or adequate anesthesia to allow any invasive testing or significant animal manipulation, but it did allow sedation for removal into a small transport. Dexmedetomidine has been used with mixed results (see Table 8.1) (Christiansen et al. 2014).

Propofol

Propofol IV has been used successfully for rapid induction in Gulf of Mexico sturgeon, but caused significant respiratory depression. This complication was addressed by ventilating the fish via the passage of oxygenated water across the gills. In addition to respiratory depression, uncomplicated bradycardia was noted (Fleming et al. 2003). At one facility, propofol in an African lungfish (*Protopterus annectens*) was associated with mortality. It is not certain if this was directly drug related or due to an obligate air-breathing fish being recovered in water that was too deep to allow surface access (Mylniczenko et al. 2014).

Tiletamine-Zolazepam

IM administration of tiletamine-zolazepam (TZ) was used in one study at dosages of 5.0–20.0 mg/kg in multiple saltwater species (not noted in the abstract). Even at dosages of 60.0 mg/kg this group did not experience any mortalities.

At higher dosages, animals had prolonged recoveries, some up to 72 hours (Garcia-Parrage et al. 2007). The greatest advantage of using TZ was lower volumes of drug required as the drug is purchased as a powder and can be reconstituted to high concentrations with good effect and no supersaturation.

Xylazine

In rainbow and brown trout the lowest effective dose of xylazine (100.0 mg/kg) consistently produced apnea. Convulsant activity occurred during induction and recovery, making it difficult to ensure artificial ventilation because the convulsions frequently dislodged the water supply. In addition, gross ECG disturbances were detected. Consequently, xylazine is not recommended in salmonids (Oswald 1978). Given the proven usefulness of medetomidine in other teleost species, xylazine is not the preferred alpha-2 agonist for any fish.

Miscellaneous Drugs

Gallamine triethiodide IM has been used for capture and handling of large tank fish, providing a smooth induction of paralysis following injection (Harvey et al. 1988). If used it is suggested for noninvasive procedures or as an adjunct to other anesthetic agents. A combination of etorphine-acetylpromazine (Large Animal Immobilon™) has been used in trout for anesthesia but given the human accidental exposure risks (Oswald 1978) and availability of other agents, its use is not recommended. Ethanol is an anesthetic of last resort. Anesthetic depth is variable and difficult to control. However, in nonclinical situations or for euthanasia, ethanol is sometimes available when other drugs are not (Harms & Bakal 1995).

Nonchemical Anesthesia

Electroanesthesia (galvanonarcosis) is a common fisheries tool for group immobilization to tag, survey, or remove animals from an area. Anesthesia may not be an accurate descriptor as animals are not truly anesthetized. The process results in electronarcosis or stunning, but when the intensity of the current is too high, it can result in severe muscle tetany and spinal injuries (Schreck et al. 1976). There are two main methods currently used to sedate fish using electricity: (1) lower-voltage, nonpulsed-DC fish-handling gloves (EFHGs), which tend to only sedate fish while the gloves are touching the animal, and (2) a comparatively high-voltage, pulsed-DC portable electrosedation system (PES) that leads to galvanonarcosis (Abrams et al. 2018).

Electroanesthesia can be used appropriately and successfully, with reports of shorter induction and recovery times (Hudson et al. 2011; Roth et al. 2003), however results have indicated that physiological responses are often varied between species and individuals (Abrams et al. 2018) and there are a few deleterious effects. One author (Mylniczenko) has experienced long-term immunocompromise and resulting secondary infections in animals collected by PES. Additionally, the acute effects can be very dramatic and mimic exhaustive exercise. Finally, this method does not have much practical application for the aquarium but may be a tool used to collect specimens coming into quarantine or utilized during field work. A study comparing EFHGs with immersion anesthesia found that a lower plane of anesthesia and inconsistent immobilization made surgeries with EFHGs more challenging to perform than surgeries conducted using immersion anesthesia (Lamglait & Lair 2021). Lastly, there should be caution for human safety when using electricity in water and for collateral damage of nontarget animals in the vicinity of the shock.

Hypothermia is not an appropriate method of anesthesia but has been used historically to induce light anesthesia and for transport; the physiologic effects are too great for its consideration as an anesthetic.

Analgesia

The importance of animal welfare and whether fish feel pain has received increased attention over recent years. The topic of analgesia is beyond the scope of this chapter but the reader is referred to the numerous contemporary articles on the topic of analgesia in fishes (Chatigny 2019; Chatigny et al. 2018; Martins et al. 2019; Sneddon et al. 2018; Sneddon 2019; Woodruff 2018). Most sources define analgesia as the absence of pain in the presence of stimuli that would normally be painful without the loss of consciousness. The less-used definition seems more universally acceptable as it includes absence of noxious stimulation as well as pain in the definition (Blood & Studdert 1988; Thurmon et al. 1996). Putting aside the question of pain perception, fish have pain receptors throughout the brain, making it reasonable to expect some effect of treatments in fish experiencing noxious stimuli (Harms et al. 2005). Additionally, beneficial effects on behavior and physiologic parameters have been reported in many instances, especially associated with morphine administration (Chatigny et al. 2018). The empirical evidence in fish demonstrates that pain-related behaviors are conserved across vertebrates and that fish experience pain. Additionally, where tested, the lack of adverse effects in those drugs does not put the clinician in a risky situation with their patient. Thus, it is important to minimize and

alleviate pain or noxious stimuli in fish whenever possible (Chatigny 2019; Sneddon 2019).

Euthanasia

Euthanasia can be difficult in fishes as determination of death can be difficult. Cessation of opercular movement and cardiac movement are not always sufficient to correlate to brain (telencephalon) death (Louis et al. 2020). As such a secondary method is always recommended (severing the spinal cord from the brain). Typically, overdosage of an immersion immobilization drug is used. However, the most recent AVMA euthanasia guidelines (Leary et al. 2020) for immersion euthanasia recommend that "finfish should be left in the anesthetic solution for a minimum of 10 minutes after cessation of opercular movement" and state that an MS-222 "concentration of 250–500 mg/L, or 5 to 10 times the anesthetic dosage, is effective for most species." MS-222 is most common but injectable agents can also be used. However, several papers recently have shown that MS-222 at five to 10 times the anesthetic dosage may be ineffective at euthanizing certain species. Up to 96% of goldfish exposed to higher doses and longer exposure periods than the current recommended guidelines made complete recoveries with no signs of morbidity or mortality. Additionally, myocardial contractions continued for up to 4 hours in decapitated goldfish and immersion in propofol at a concentration of 25 mg/L for 30 minutes did not reliably euthanize goldfish (Balko et al. 2018). Other studies have evaluated other substances for teleost euthanasia but are out of scope for discussion here (Chu et al. 2020; Collymore et al. 2016; Louis et al. 2020; von Krogh et al. 2021; Yanong 2021).

Many fish in large exhibits require induction first with parenteral drugs (e.g., medetomidine/ketamine), then euthanasia in an MS-222 bath. Alternatively, in fish too large for a bath, the solution is poured directly over the gills (Harms & Bakal 1995). Cessation of opercular movement sometimes indicates a fish has expired but is not definitive and should not be used as the sole parameter for confirmation of death. Cardiac asystole usually lags behind brain death since fish myocardial cells utilize local glycogen stores for energy and do not need blood glucose (Stetter 2001). Use of Doppler flow probes, ultrasonography, or electrocardiography is recommended to confirm asystole. To be certain, additional anesthetic drugs, KCl or pentobarbital are administered IV into the heart or caudal vein (Louis et al. 2020; Ross 2001). Alternatively, cranial concussion, decapitation, spinal transection, or exsanguination may be performed once the fish is deeply anesthetized (Harms & Bakal 1995). These physical forms of euthanasia can result in instantaneous death when applied correctly, thus it is imperative to use the proper equipment and trained personnel who are regularly monitored for proficiency (Leary et al. 2020).

While euthanasia with baking powder or Alka Seltzer™ tablets has been utilized, CO_2 release is very aversive and may not be ideal for the welfare of the fish without a multimodal anesthetic protocol. The reader is directed to review euthanasia principles for fish in other documents (Leary et al. 2020; Posner et al. 2019; Kilgore et al. 2009; Yanong 2021). Unacceptable methods of euthanasia include asphyxiation and hypothermia. Though there are reports of success using these methods, variability has been reported (Wallace et al. 2018) and the animal welfare implications are unknown at this time.

Field Immobilization

Immobilization of fishes in the field is a commonplace event. Considerations for immobilizing fish in remote areas include having portable equipment that can connect to car batteries or portable generators/batteries. It is important to consider guidelines for approved drugs (US Fish and Wildlife Service, The Aquatic Animal Drug Approval Partnership 2022) and to observe withdrawal periods. Alternatively, there are tags available that state "do not consume" that are affixed to the fish. Typically for field procedures, unless invasive, animals are not anesthetized with chemicals and are only physically restrained. Hook and line, net, trawl, and electroanesthesia fishing are methods used to capture free-range fish. Each technique carries its own risk to the animal, including hypoxia, trauma, exhaustion, and major physiologic disturbances. These must be considered for long-term management or survival of the animals.

When using source water, clarity must be considered as some water bodies may have turbid water, algal blooms or high tannins. This can complicate visualization of induction or recovery in these animals. Temperature shifts throughout the course of the day will greatly modify temperatures in holding vats. Manual restraint and air exposure can also affect physiology (see earlier comments in this chapter).

Postanesthetic Challenges

Once animals are placed into recovery water, ensuring adequate ventilation is critical. The authors prefer using an electronic pump to facilitate oxygenated water flow over the gills, but many aquarists prefer moving the animal through the water column. Determining when to release the animal requires skilled staff that are aware of

normal swimming behavior. Staff should be prepared to retrieve the animal if it falls to the bottom of the water column (or if aggressed upon) rather than showing normal behavior or swimming away and recovering. Observation of the animal for the next 24–48 hours is recommended for observing any morbidity or mortality associated with the procedure. As with all anesthetic procedures in animals, restraining a compromised animal with either manual or chemical methods carries a risk for increased morbidity or mortality.

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9

Amphibians

Amy B. Alexander and Eric Baitchman

Introduction

Amphibians are native to all continents, except Antarctica, and occupy a wide variety of aquatic, semi-aquatic, and terrestrial habitats. Amphibians are found from the equatorial rainforest to Canada, where they may remain frozen through the winter. There are more than 6800 species within the Orders Anura (frogs and toads), Caudata (salamanders and newts), and Gymnophiona (caecilians) (IUCN 2020). Although new species of amphibians continue to be discovered, amphibians are considered the most threatened class of vertebrates, with one-third being listed as threatened. Threats include infectious disease, particularly chytrid fungus, *Batrachochytrium dendrobatidis* (Bd), as well as climate change and habitat destruction, which can also exacerbate susceptibility to infectious diseases (Catenazzi 2015; IUCN 2020; Pessier 2018). There is significant concern about worldwide amphibian decline and its implications for global ecosystem health.

Amphibians are routinely maintained in human care as pets, in laboratories, and in zoos for education, as well as conservation and reintroduction projects. Veterinarians are most likely to be involved with anurans or caudates. It is not uncommon for amphibians to require sedation or anesthesia for diagnostics, surgery, or research.

Anatomy and Physiology

Amphibians have several unique and clinically relevant anatomical characteristics. The first is that many go through metamorphosis and change from strictly aquatic larval forms (i.e., tadpoles) to terrestrial adults. These metamorphoses include dramatic anatomical changes; growth of legs, loss of gills, resorption of tails (anurans), and formation of lungs. As a completely aquatic tadpole with gills they have very similar respiration to fish.

The respiratory physiology of amphibians is unlike that of any other animal taxa. Four different types of respiration are employed: branchial, cutaneous, pulmonary, and buccopharyngeal. All species utilize branchial respiration (gills) as larvae, and some paedomorphic species, such as axolotl (*Ambystoma mexicanum*), mudpuppies (Proteidae), and sirens (Sirenidae), retain gills as adults (Duellman & Trueb 1994). All adult amphibians utilize cutaneous respiration to varying degrees and this may account for a significant portion of an animal's total oxygen exchange.

The largest family of salamanders, the Plethodontidae or lungless salamanders, perform nearly all respiration via cutaneous gas exchange. Even those caudates that do possess lungs primarily utilize cutaneous gas exchange (Baitchman & Herman 2015; Duellman & Trueb 1994). A unique adaptation in cryptobranchid salamanders (hellbenders and giant salamanders) is intradermal capillaries concentrated along lateral skin folds that increase surface area for gas exchange (Baitchman & Herman 2015; Pessier 2018).

Adult anurans and caecilians possess lungs, but the majority of oxygen intake is usually via pulmonary exchange, while the cutaneous route still accounts for the majority of carbon dioxide exchange (Clayton & Mylniczenko 2015; Duellman & Trueb 1994; Hillman et al. 2009; Wright & Whitaker 2001). Lungs are inflated by positive pressure ventilation achieved through buccal pumping. Small amounts of gas exchange may also occur across buccopharyngeal mucus membranes. Central respiratory drive to increase respiratory frequency or tidal volume is stimulated by either a decrease in PO_2 or increase in PCO_2 (Branco & Glass 1995; Fonseca et al. 2012; Hillman et al. 2009).

Amphibian skin is highly permeable and well vascularized. In addition to respiratory gas exchange, it is the primary route of water exchange and actively participates in electrolyte balance. Smooth-skinned animals, adapted to moister environments, have higher permeability and are

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Figure 9.1 Ventral pelvic region of a grey tree frog, *Hyla versicolor*. Note the verrucae hydrophilicae, or granular sculpturing, of the skin providing increased surface area for water absorption. This region can have application for drug absorption as well.

susceptible to dehydration through insensible water loss. In most species the ventral pelvic region, often referred to as the pelvic patch or drink patch, is the area of highest water uptake. It is especially well developed in terrestrial species, showing increased surface area and vascularity in this region (Fig. 9.1).

Vascular Access and Injection Sites

Vascular access is limited by animal size. Fine-gauge needles or catheters (24-gauge or smaller) may be needed. Useful access sites include the ventral abdominal vein on the caudal ventral midline (Fig. 9.2), the femoral vein behind the stifle, the axillary venous plexus (Fig. 9.3), the sublingual plexus, and the ventral tail vein in caudates. Other sites, such as the brachial vein or lateral abdominal veins, may be accessible in larger species. Transillumination is a useful technique for highlighting the pathways of major vessels (Fig. 9.4).

Intramuscular injections can be administered in the large muscles of the hind limbs. However, as amphibians have a renal portal system, injections are ideally administered in the cranial limbs to prevent possible first-pass effect. Subcutaneous injections should be considered intralymphatic/intravascular in anurans, as the subcutaneous space along the dorsum consists of extensive lymphatic

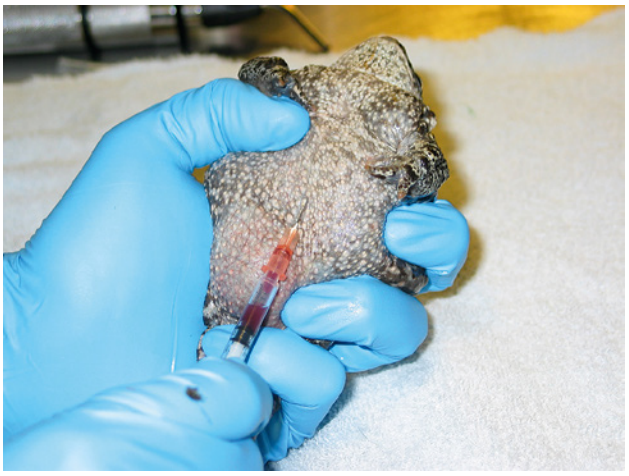


Figure 9.2 Collecting blood from the ventral abdominal vein in a western toad, *Anaxyrus boreas*.



Figure 9.3 Collecting blood from the axillary plexus in a bullfrog, *Rana catesbeiana*.

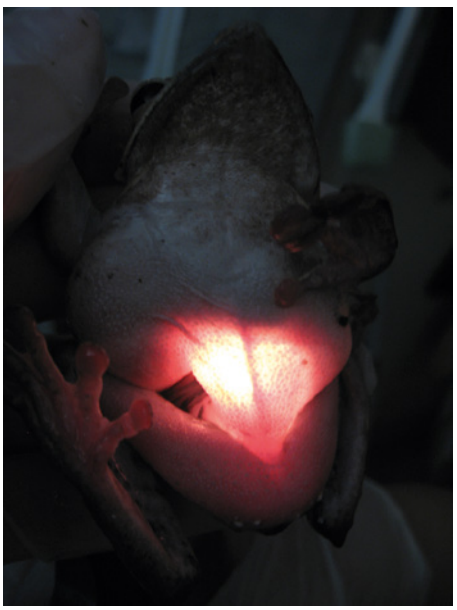


Figure 9.4 Transillumination technique highlighting the ventral abdominal vein in a Borneo eared frog, *Polypedates otilophus*.

sacs. In caudates, the dermis is firmly adhered to the underlying tissue, limiting subcutaneous access (Pasmans & Martel 2019; Pessier 2018).

General Anesthetic Considerations

The aquatic nature and skin permeability of amphibians makes topical use of anesthetic agents a convenient means of achieving systemic effects. Amphibian anesthesia is very similar to fish anesthesia in the methodology and drugs used (Stetter 2001). Anesthetic compounds may be delivered in water and absorbed across the animal's skin or gills. Inhalant anesthetic agents may be used either topically or in solution. When gas anesthetics are delivered into a chamber or bubbled through water, induction can be prolonged or unsuccessful. Some amphibians can be intubated awake and administered an inhalant anesthetic for induction. Parenteral or injectable anesthetics are often unreliable, have a low margin of safety, may be associated with prolonged recovery, and have species-specific doses (Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). Caution is recommended when using an anesthetic agent in a new species.

Aquatic amphibians can be kept out of water for extended periods of time if the skin is kept moist to prevent damage or dehydration and ensure dermal respiration is maintained (Wright & Whitaker 2001). When working with entirely aquatic species (e.g., African clawed frog, *Xenopus laevis*), tank water from the animal's environment is used to prevent abrupt environmental changes (e.g., temperature, pH, etc.). All water used for anesthesia is tested using standard reagent test kits to ensure there are no elevated deleterious variables such as ammonia (Wright & Whitaker 2001). Toxin-free (dechlorinated) water within the animal's preferred body temperature range (usually 15–23°C, 59–73°F) is used (Wright & Whitaker 2001). Bottled spring water at room temperature is often convenient to use or amphibian Ringer's solution may be prepared.

The container used as an anesthetic chamber must be thoroughly cleaned and rinsed. Since amphibians absorb chemicals across their skin, cleaning solutions or other chemicals left in a container can be toxic. In addition, some amphibians secrete toxins from their skin and it is important to rinse containers well between patients. Sealable plastic bags are efficient containers for anesthetic bath induction chambers and can be discarded when the procedure is complete. Other potential induction chambers include small plastic containers with lids or small fish aquariums. Many amphibians exhibit an excitement phase during induction, making it important to have a closed container to prevent the patient leaping out. The interior should be smooth and padded, if possible, to prevent injury (Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). When a water bath is being used for anesthetic application, there should be an interface with the air at the surface (i.e., do not fill the container completely to the lid). Animals with lungs should be positioned with nostrils elevated out of the water to prevent aspiration during induction.

When using a bath solution to induce anesthesia, the induction dose received is dependent on the surface area of the animal, that is, smaller animals with greater surface area are exposed to larger amounts of anesthetic than larger animals with smaller surface area relative to body size. Consideration should be given to adjusting solution concentrations based on body size (Goulet et al. 2010, 2011).

Moistened gloves are worn when handling amphibians to protect their skin as well as to protect the handler from potentially toxic secretions (Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). Rinsed nonlatex, nonpowdered gloves are recommended for handling adults, and only washed vinyl gloves have been found safe for handling amphibian larvae. Mortality was seen in tadpoles exposed to latex, nitrile, and unwashed vinyl gloves (Cashins et al. 2008; Gutleb et al. 2001). Small towels moistened with tank water can help restrain aquatic species, as well as prevent damage to their mucus layer.

Amphibians are not commonly fasted prior to anesthesia. Their larynx remains tightly closed even under general anesthesia and the chance of aspiration is low (Wright & Whitaker 2001). Regurgitation or gastric prolapse has been reported in studies using isoflurane or eugenol in *Xenopus laevis* or eugenol in *Rana pipiens* (Goulet et al. 2011; Lafortune et al. 2001; Smith & Stump 2000). Regurgitation was also observed in a lesser siren (*Siren intermedia*) during induction via alfaxalone bath (D. Heard, pers. comm.). While no lasting adverse effects were appreciated in those animals, consideration might be given to fasting for 24 hours when feasible, particularly if the amphibian's diet includes large prey items or if the anesthetic procedure is to include coelomic surgery.

Respiratory ventilation is usually reduced or absent during amphibian anesthesia. The dermis is kept moist to allow for efficient dermal respiration. Cutaneous oxygen exchange, however, may be low in some species (Hillman et al. 2009) and supplemental oxygen should be considered to avoid hypoxemia and acidemia (Andersen & Wang 2002). While some amphibians can tolerate anoxia for long periods, reoxygenation is a significant stress and risks free-radical injury to tissues (Bickler & Buck 2007). For long surgical procedures the patient can be placed in a shallow water bath with oxygen bubbled into it. Intubation is also a safe option to provide supplemental oxygen (G. Crawshaw & D. Mader, pers. comm.). Small species

may be intubated with modified intravenous catheters or noncuffed Cole tubes may be used in larger species. The larynx is usually tightly closed, even in anesthetized animals, and the tube may need to be gently forced (G. Crawshaw, pers. comm.). The trachea is very short and the tip of the tube should be placed just past the larynx (Stetter 2003). Amphibian lungs are composed of thin-walled membranes and manual or mechanical ventilation must be done gently. Larger species can be ventilated at a pressure of 5 cmH_2O, with a breath every 10 seconds (D. Mader, pers. comm.).

Monitoring

The skin under the mandible and along the ventral cervical region is the gular region; movement in this area is a primary means of respiration. As a patient becomes anesthetized, gular respirations decrease and there is a diminished withdrawal reflex (Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). Light anesthesia is associated with loss of righting reflex and an absence of abdominal respirations. Surgical anesthesia is indicated by a loss of withdrawal reflex and cessation of gular respiration (Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). When the patient has ceased movement and appears to be anesthetized, the animal may be placed in dorsal recumbency to assess righting reflex. For procedures requiring light anesthesia (e.g., blood sampling, radiographs, physical examinations, etc.) the patient is removed from the container and quickly rinsed with anesthetic-free water before the procedure begins. If surgical anesthesia is required, an aggressive toe pinch of the rear leg will help determine if there is loss of withdrawal reflex and nociception.

Anesthetized amphibians usually become apneic; abdominal and gular respirations cease. This can be very disconcerting for the anesthetist who relies on respiratory rate for assessing anesthesia. Consideration should be given to intubation or other means of supplementing oxygen, as discussed above.

Heart rate is a useful indicator for anesthetic monitoring (Crawshaw 2003; Wright & Whitaker 2001). In most anesthetized patients in dorsal recumbency, the heart is seen contracting on the midline just caudal to the pectoral girdle. Direct visualization, a Doppler monitor, or ultrasound is used to measure heart rate (Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). Although normal heart rates for species are not extensively published, a significant decrease in baseline heart rate is of concern and indicates excessive anesthetic depth. Pulse oximetry has not been validated in amphibians, but may show trends in hemoglobin saturation for long procedures and can assist with monitoring pulse (Fig. 9.5). Intermittently monitoring withdrawal reflex will determine if the patient is transitioning from surgical to light anesthesia. A patient that regains its withdrawal reflex, or gular respirations, requires supplementation if a surgical plane of anesthesia is still required. For supplementation, a 10–50% concentration of the induction solution is applied topically via syringe or partial water bath (Fig. 9.6). When the animal reaches an adequate level of anesthesia the application is discontinued.

During recovery, animals should be kept moist and well oxygenated, ideally at the preferred optimal temperature for the species. Recovery is considered complete when the

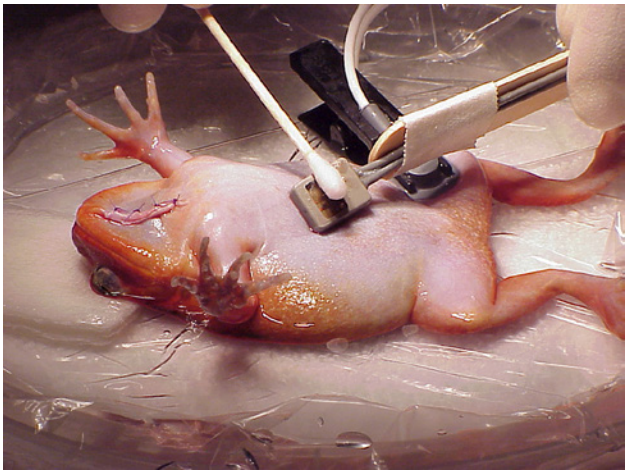


Figure 9.5 A tomato frog, *Dyscophus insularis*, under surgical anesthesia in a liquid anesthetic bath, being monitored by Doppler and pulse oximetry. Note the nostrils are elevated above the water line with gauze pads.

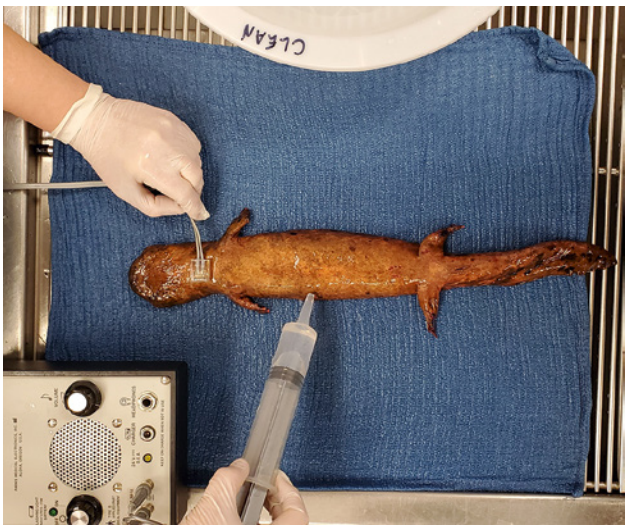


Figure 9.6 Anesthetic supplementation to maintain surgical plane of anesthesia in an adult Ozark hellbender (*Cryptobranchus alleganiensis bishopi*). Note the diluted MS-222 being applied to the lateral folds. Photo credit: Christian Burmeister, St. Louis Zoo.

animal is responsive, respiring normally, and has regained all reflexes (Wright & Whitaker 2001).

Analgesia

Excellent discussions on nociception in amphibians can be found in Machin (1999) and Stevens (2011). Amphibians share the same array of nociceptive afferent nerves, spinal cord neurotransmitters, and endogenous opioid peptides as mammals. While the perception of pain in an amphibian is unknown, all the same nociceptive pathways are conserved as in higher phylogenetic classes of vertebrates. Analgesia should be considered for any noxious procedures in amphibians.

Analgesic drugs and dosages are summarized in Table 9.1. Anesthetic drugs and dosages are summarized in Table 9.2.

Opioids

All mammalian opioid receptors, mu, delta, and kappa, are present in the central nervous system of amphibians. While receptor selectivity is less than in mammals, the relative analgesic potency mu > delta > kappa, is the same (Stevens 1996, 2004). In a study comparing alfaxalone-butorphanol versus alfaxalone-morphine via immersion in oriental fire-bellied toads (*Bombina orientalis*), only the group that received morphine had adequate antinociception. Both groups had cardiac and respiratory depression, but recoveries were smooth. Irrigation with naloxone did not speed recovery (Adami et al. 2016a). In general, opioid dosages tend to be much higher in amphibians compared to mammals and onset to peak analgesic effect is longer at 60 minutes or greater when given systemically (Stevens et al. 1994). Planning analgesia for procedures should take this delay of onset into account.

Alpha-2 Adrenergic Agonists

In amphibians, alpha-2 adrenergic agonists provide analgesia without sedation. Normal movement, including righting, corneal, and hindlimb withdrawal reflexes, all remain intact. Onset of effect is rapid and long lasting, with peak effect occurring by 60 minutes and lasting for 6–8 hours or more (Brenner et al. 1994). In *Bombina orientalis*, the addition of dexmedetomidine to an alfaxalone immersion protocol did provide some analgesia, but seemed to lighten the anesthetic depth, making the combination unsuitable for surgical anesthesia in this species (Adami et al. 2016b).

Nonsteroidal Anti-inflammatory Drugs

Although often used empirically, little data exists to support the use of nonsteroidal anti-inflammatory drugs (NSAIDs) for analgesia in amphibians. Flunixin meglumine is reported

Table 9.1 Analgesic drug dosages for amphibians.

Drug	Dosage	Route	Duration	Comments
Fentanyl	0.3–0.8 mg/kg	SC	>4 hours	ED_{50} = 0.5 mg/kg in *Rana pipiens*[a]
Morphine	18–33 mg/kg	SC	>4 hours	ED_{50} = 25 mg/kg in *Rana pipiens*[a]
Buprenorphine	27–79 mg/kg	SC	>4 hours	ED_{50} = 50 mg/kg in *Rana pipiens*[a]
	50 mg/kg	IC	NE	Shortened time to normal behavior following surgery in *Notophthalmus viridescens*[b]
Butorphanol	0.5 mg/L	72 hours Bath	NE	Shortened time to normal behavior following surgery in *Notophthalmus viridescens*[b]
Dexmedetomidine	120 µg/kg	SC	>8 hours	*Rana pipiens*[c]
Meloxicam	0.1 mg/kg	IM	NE	Reduced PGE2 in *Rana catesbeiana*; analgesic effect not examined[d]
Ketoprofen	1 mg/kg	SC, Topical	24 hours	Plasma concentration in *Leptodactylus pentadactylus*[e]

ED_{50}, effective dose in 50% of test subjects; IC, intracoelomic; IM, intramuscular; NE, not examined; PGE2, prostaglandin E2; SC, subcutaneous.
[a] Stevens et al. (1994) (ranges based on 95% confidence interval of ED_{50}).
[b] Koeller (2009).
[c] Brenner et al. (1994).
[d] Minter et al. (2011).
[e] Balko et al. (2018).

Table 9.2 Anesthetic drug dosages for amphibians.

Drug	Dosage	Route	Comments
Tricaine methanesulfonate			Add buffer until neutral pH when using tricaine
	0.1–0.5 g/L	Bath	Larvae and paedomorphic species
	1.0–2.0 g/L	Bath	Adults
	0.25–0.5 g/L	Bath	Hellbender adults[a,b]
	1 g/L	Bath	Caecilian adults[c]
Eugenol	350 µL/L	Bath	Using 99% pure eugenol oil; see text for comments using clove oil
Isoeugenol	20 µL/L	Bath	*Litoria ewingii* tadpoles[d]
Isoflurane	2–3 mL/L	Bath	
	0.025–0.035 mL/g BW	Topical gel	3 mL isoflurane, 1.5 mL water, 2.5 mL water-based gel
	0.03–0.06 mL/g BW	Liquid	Use absorbent pad with plastic backing to apply to dorsum
Sevoflurane	0.0375 mL/g BW	Topical gel	Applied to dorsum in *Bufo marinus*; sedation but prolonged recovery[e]
Benzocaine	0.2–0.3 g/L	Bath	Pure benzocaine will require dissolution in ethanol first, up to 1% ethanol in final solution
Alfaxalone	20–30 mg/kg	IM	Sedation in *Litoria* spp.[f]
	10–17.5 mg/kg	IM	Sedation in *Lithobates catesbeiana*[g]
	0.2 g/L	Bath	Sedation in *Bombina orientalis*[h]

BW, body weight; IM, intramuscular.
[a] Junge (2012).
[b] O'Brien (pers. comm.).
[c] Barbon et al. (2017).
[d] Speare et al. (2014).
[e] Stone et al. (2013).
[f] Sladakovic et al. (2014).
[g] Posner et al. (2013).
[h] Adami et al. (2015).

to provide significant analgesia. The dosages used in two studies, however, are extremely high (25 mg/kg) compared to typical doses in other taxa, and one animal that died during the trial had histopathologic evidence of renal congestion and inflammation (Coble et al. 2011). Meloxicam reduced circulating prostaglandin E2 in *Rana catesbeiana*, implying it can suppress the inflammatory response and may therefore provide an analgesic effect (Minter et al. 2011). No significant analgesic effect was seen, however, when using meloxicam in trials with *Xenopus laevis* (Coble et al. 2011). Plasma concentrations of meloxicam were not reliably detectable after subcutaneous or topical administration in smoky jungle frogs (*Leptodactylus pentadactylus*). Ketoprofen administered subcutaneously and topically did have detectable plasma concentrations for at least 24 hours, with the subcutaneous route having the more predictable plasma concentrations (Balko et al. 2018). Mild analgesia is reported from a study with two uncommon NSAIDs, indomethacin and ketorolac (Stevens et al. 2001).

Anesthetic Drugs

Tricaine Methanesulfonate (Ms-222 Or Finquel®)

This is the most commonly used anesthetic for amphibians (Cooper 2003; Crawshaw 2003; Downes 1995; Stetter 2001; Wright & Whitaker 2001). It is effective in all species and all developmental stages, and it has a wide margin of safety.

Tricaine methanesulfonate is a white powder that readily dissolves in water. Its mechanism of action, like other local anesthetics, is as a sodium channel blocker inhibiting nerve conduction. Used systemically, it creates anesthesia via central nervous system depression (Cakir & Strauch 2005). In aqueous solution, it is very acidic, especially at higher concentrations and with waters that have a low buffering capacity (Crawshaw 2003; Downes 1995; Stetter 2001; Wright & Whitaker 2001). This acidic solution is not only irritating to the patient, but the drug is also in a more ionized form and

therefore less effective as an anesthetic at low pH levels. It is important to buffer the solution to keep the pH at 7.0–7.4 (Crawshaw 2003; Downes 1995; Stetter 2001; Wright & Whitaker 2001). This is easily accomplished by adding sodium bicarbonate to the mixture. Common baking soda (powdered sodium bicarbonate) is added to the solution until saturation (powder no longer dissolves) is achieved, usually a 1:1 ratio. Amphibian ringer's solution also provides some buffering capacity as it contains sodium bicarbonate. Since the patient is being induced in an anesthetic water bath, rather than a dosage based on body weight, the anesthetic solution concentration is determined by the level of sedation or anesthesia required along with relative life stage (larvae vs. adult) and species of amphibian (Crawshaw 2003; Downes 1995; Stetter 2001; Wright & Whitaker 2001). In general, lower concentrations are required for younger larval stages, species with external gills, and the more aquatic frogs compared to the terrestrial toads. Hellbenders are unique in that they also require lower concentrations (Junge 2012; S. O'Brien, pers. comm.). Skin disease is common in amphibians, with lesions including ulceration and hyperkeratosis, which can affect anesthetic absorption, osmoregulation, cutaneous respiration, and metabolism. These lesions should be taken into consideration when determining an anesthetic plan, as concentrations may need to be adjusted. Refer to Table 9.2 for general recommendations of concentrations.

For a desired volume of solution, the exact amount of tricaine methanesulfonate is weighed out, dissolved in water, and the buffer is added until neutral pH is achieved. The solution is not stable over long periods of time and is discarded after each use. Anesthetic solution is added to the induction chamber at a level sufficient to cover approximately the ventral half of the patient's body. Additional anesthetic solution can be diluted to 10–50% of the induction concentration to be used as a maintenance solution for longer procedures. Specific areas to focus supplementation for more rapid effect are the ventral drink patch in anurans and the lateral folds in hellbenders.

Although induction times are variable, initial effects can be seen within a few minutes, with a surgical plane of anesthesia achieved in up to 30 minutes. The general comments in the above sections apply to induction and monitoring in tricaine anesthesia. Loss of gular respiration is expected at a surgical plane of anesthesia and excessive anesthetic depth will cause cardiac depression on a dose-dependent basis (Cakir & Strauch 2005).

Eugenol

Eugenol is the active compound in clove oil, wherein eugenol concentration can vary widely, from 47% to 88% (Chaieb et al. 2007). It is worth noting that when dosing clove oil, the percentage of eugenol may not be known, nor is the possible presence of other active or inactive compounds. Interpretation of published dosages of clove oil as an anesthetic should take this variability into consideration. Simple side-by-side comparison of protocols using clove oil is not straightforward. Purified eugenol can be obtained for use as an anesthetic, allowing more accurate and consistent dosing. As more published reports using purified eugenol are produced, species and dosage comparisons can be made more easily. The terms "clove oil" and "eugenol" are not used interchangeably in this chapter.

Eugenol has been used as a topical anesthetic in humans, as well as a general anesthetic in invertebrates, fish, and amphibians. Its mechanism of action is as a local anesthetic, creating analgesia and anesthesia by blocking sodium voltage-gated channels as well as vanilloid receptor TRPV1 and activating inhibitory $GABA_A$ receptors (Goulet et al. 2010).

Eugenol or clove oil induction is most effective via an immersion bath solution. Eugenol solutions do not need to be buffered. Surgical anesthesia has been reliably achieved in multiple reports with *R. pipiens* and *X. laevis*. Regurgitation or gastric prolapse has been observed in these studies as a fairly common side effect during induction or recovery, though apparently without adverse consequence (Goulet et al. 2011; Guenette et al. 2007; Lafortune et al. 2001). Clove oil anesthesia has been reported in one caudate species, *Ambystoma tigrinum*, where a surgical plane of anesthesia was achieved in 67% (8/12) at a higher dose than required for *R. pipiens* (Mitchell et al. 2009).

Toxicity studies in *Xenopus* indicate that smaller animals have a higher incidence of toxic effects. Smaller animals have a higher surface area and therefore are likely to absorb anesthetics at a higher dosage per body weight relative to larger animals in the same bath concentration. Smaller *Xenopus* are also less mature than larger animals, so the mechanism of toxicity could be either dose- or age-dependent (Goulet et al. 2010, 2011). Histopathologic findings in small animals (28.2 ± 13.7 g) 24 hours after receiving anesthetic doses (350 μL/L) of eugenol included apoptosis of distal tubular cells in the renal medulla, followed by regeneration 1 week after anesthesia. Animals that were anesthetized daily for three consecutive days had tubular apoptosis ranging from mild to severe, followed by tubular regeneration, massive hepatic necrosis, and hemorrhage of coelomic fat bodies 1 week later (Goulet et al. 2011). Large female *Xenopus* (111.7 ± 18.3 g) showed no histopathologic abnormalities 24 hours after anesthesia in the same bath concentration (Guenette et al. 2007). Cardiovascular depression is also seen with smaller animals in a surgical plane of anesthesia, but not in larger animals (Goulet et al. 2010; Guenette et al. 2007). Cutaneous necrosis has been reported in *Xenopus* receiving topical applications of

eugenol at concentrations of 60 mg/mL or greater (Ross et al. 2006).

Isoeugenol (Aqui-S®), an isomer of eugenol, has been used as an anesthetic in fish and produces similar anesthetic effects as eugenol, but at lower concentrations. Southern brown tree frog tadpoles (*Litoria ewingii*) were safely anesthetized using 20 µL/L immersion and the animals did not show signs of irritation or excitement and recovered uneventfully. Repeated dosing and histopathology were not performed (Speare et al. 2014).

Inhalant Agents

Isoflurane is a safe and effective anesthetic in amphibians and may be familiar and useful to the practitioner who does not keep tricaine methanesulfonate in stock (Barbon et al. 2019; Stetter 2001). Topical applications of liquid isoflurane or bath immersion in isoflurane solution are the most reliable means of induction. Isoflurane gas can also be delivered in the traditional vaporized form via a chamber or by bubbling vaporized isoflurane and oxygen from an anesthetic system into a water bath (Barbon et al. 2019; Crawshaw 2003; Stetter 2001; Wright & Whitaker 2001). In both cases a sealed container is used to minimize human exposure and increase isoflurane concentrations in the induction chamber. While these methods can be effective in some cases, they are associated with slow induction times and rapid recoveries once the patient is removed from the chamber. Frogs in a gas induction chamber can cease ventilation, thereby significantly increasing induction times (Barter et al. 2007). The aquatic frog *Xenopus* was not anesthetized by bubbling vaporized isoflurane into a water chamber (Smith & Stump 2000). Intubation and maintenance of large amphibian patients with isoflurane gas may be performed with an uncuffed endotracheal tube (Wright 2006). Mountain chicken frogs (*Leptodactylus fallax*) were induced with isoflurane via chamber induction and removed once they lost their righting reflex. They were then intubated with a modified cuffed endotracheal tube (2.5–3.5 mm) and manually ventilated at 2% isoflurane to achieve and maintain a surgical anesthetic plane. Manual ventilation with room air was continued until the animals regained the righting reflex (Rodrigeuz 2019).

The most effective and longest lasting methods of isoflurane anesthesia are application of concentrated liquid isoflurane to the skin or immersion in an isoflurane bath solution (Stetter 2001). For the immersion bath, a syringe is used to add the liquid isoflurane directly into the water. The syringe tip is placed below the surface of the water and the isoflurane liquid is injected and mixed into the bath. A concentration of 2–3 mL/L is most commonly used (Crawshaw 2003; Stetter 2001).

When applying concentrated liquid isoflurane directly to the skin, a carrier solution or barrier is created to increase dermal contact time prior to the isoflurane evaporating. A gel mixture is created using 3 mL of liquid isoflurane, 1.5 mL of water, and 3.5 mL of K-Y® Jelly (Stetter 2001). These three ingredients are placed in a 10 mL empty serum vial and vigorously shaken until a uniform gel is established. This isoflurane gel can now be applied to the patient's dorsum at dosages of 0.025–0.035 mL/g body weight (Stetter 2001). Lower dosages are used for more aquatic species and higher dosages for thicker-skinned terrestrial species (e.g., toads). After the isoflurane gel is mixed in the vial the indicated volume is withdrawn through a syringe and needle and the gel deposited on the patient's dorsum. Once applied, the patient is placed in a small sealed container until induction is complete. After induction, the anesthetic gel preparation should be rinsed from the patient's skin. Patients anesthetized with topical isoflurane gel will remain under anesthesia for 45–80 minutes. Shorter anesthetic times with a more rapid recovery are seen with the liquid isoflurane in water method (Stetter 2001), or the isoflurane and water solution can be dripped on the skin at a rate needed to maintain anesthetic depth, similar to the method for maintenance with tricaine methanesulfonate.

Topical application of concentrated isoflurane liquid was successful for anesthetizing *Xenopus* frogs using an absorbent pad with a plastic backing. Isoflurane at 0.03–0.06 mL/g body weight is used to saturate the absorbent pad, which is cut to size to cover the animals' dorsum and placed against the skin with the plastic backing facing up (Smith & Stump 2000).

Sevoflurane, compounded into a gel as described above, has shown good absorption across skin in *Rana catesbeiana* and reliable loss of righting reflex in *Bufo marinus* (Ardente et al. 2008; Stone et al. 2013). When applied topically as compounded gels to American green tree frogs (*Hyla cinerea*), both isoflurane and sevoflurane had similar induction rates, but the sevoflurane-anesthetized animals had a more rapid return of the righting reflex, with the isoflurane frogs taking 4.5 times longer to recover (Zec et al. 2014). Cane toads (*Rhinella marina*) were induced in a chamber with isoflurane, sevoflurane, or desflurane, which has a lower tissue solubility. All three anesthetics had similar induction rates, but the recovery rate was approximately twice as long with isoflurane and sevoflurane compared to desflurane (Morrison et al. 2016).

Adverse complications are few when using isoflurane by the above methods. In the study comparing topical compounded isoflurane and sevoflurane gels in *Hyla cinerea*, skin lesions and death secondary to septicemia were noted in some of the isoflurane-treated frogs. The dose used in the

study was significantly higher than what is recommended in this chapter, reinforcing that caution is always required when using anesthetic drugs in different amphibian species (Zec et al. 2014). The dose of sevoflurane was also significantly higher than in a previous study in *Bufo marinus*, which may indicate a wider safety margin for sevoflurane (Stone et al. 2013; Zec et al. 2014). Regurgitation was observed in *Xenopus* frogs fed within 1 day of isoflurane induction. Injectable administration of isoflurane (intracelomic, subcutaneous, or intramuscular) is not recommended due to variable results and high mortality (Smith & Stump 2000).

Human exposure to vaporized volatile gas anesthetics is of concern during protocols involving these drugs in their liquid form. Procedures should be performed within a fume hood or beneath an active scavenging system.

Miscellaneous Topical Anesthetic Drugs

A variety of drugs traditionally used for local analgesia in mammals have been evaluated for general anesthetic use in amphibians. Benzocaine has been used with good results in a variety of anuran and caudate amphibians (Andersen & Wang 2002; Cakir & Strauch 2005; Crawshaw 2003; Wright & Whitaker 2001). Benzocaine powder is not readily soluble in water and should be dissolved in ethanol first. The volume of ethanol in the final anesthetic solution should not exceed 1% (Wright & Whitaker 2001). A commercially available topical gel product, Orajel®, containing 10–20% benzocaine, has been successfully utilized topically in caudates and anurans in its original form and in solution as an immersion bath (Brown et al. 2004; Cecala et al. 2007; Guenette & Lair 2006). At least one study found unexpected mortality in *Bufo fowleri* with a 1 g/L Orajel® bath (equivalent to 0.2 g/L benzocaine; Cecala 2007). No mortality, however, was seen in another bufonid, *Bufo marinus*, using 1 g/L pure benzocaine dissolved in ethanol and water (Andersen & Wang 2002).

A topical xylocaine spray (10% solution) produced satisfactory anesthesia in two *Rana* species (Garcia Aguilar et al. 1999). High mortality was seen in *Rana pipiens* exposed to a commercial product containing lidocaine 2.5% and prilocaine 2.5% cream (Guenette & Lair 2006). Lidocaine administered subcutaneously in bullfrogs (*Lithobates catesbeianus*) resulted in dose-dependent sedation, with respiratory depression and loss of righting reflex, but did not provide local antinociception at the hindlimb injection site (Williams et al. 2017).

Injectable Anesthetic Drugs

Alfaxalone is a neuroactive steroid that potentiates GABA receptors. There have been a few studies in recent years evaluating its use as an anesthetic in amphibians. Generally, only sedation and light anesthesia are achieved, with intramuscular administration having more consistent results than immersion. As there are no antinociceptive properties, alfaxalone alone may be useful for restraint or noninvasive procedures, such as radiographs or blood collection, but is not appropriate as a single agent for surgical procedures (Adami et al. 2015; Posner et al. 2013; Sladakovic et al. 2014). A surgical anesthetic plane via immersion was achieved in oriental fire-bellied toads (*Bombina orientalis*) when morphine was added to alfaxalone in an immersion bath, and this combination could be considered in other species (Adami et al. 2016b). Surgical anesthesia via immersion was also described in a case report in an axolotl. Induction in a 5 mg/L immersion bath was followed with maintenance by irrigation of the external gills with the same solution, supplemented as necessary with additional drops of 10 mg/L solution (McMillan & Leece 2011). Most studies found that alfaxalone was safe and did not significantly affect heart rates. The most common adverse effects were decreased respiration and prolonged recoveries, particularly with higher doses (Adami et al. 2013; Posner et al. 2013; Sladakovic 2014). An increase in heart rate was observed in bullfrogs (*Lithobates catesbeianus*) administered intravascular and intramuscular alfaxalone (Williams et al. 2018).

Propofol is a short-acting intravenous anesthetic in mammals and reptiles that also potentiates GABA receptors. In amphibian species, intravenous administration is a challenge and the effects of propofol when given by alternate routes are highly variable. In *Rana pipiens* 10 mg/kg perivascularly in the sublingual plexus produced brief and light anesthesia following a short induction time (Lafortune et al. 2001). *Xenopus laevis* were induced to a brief light plane of anesthesia in an 88 mg/L immersion bath, but all animals died when exposed to bath concentrations of 175 mg/L or higher (Guenette et al. 2008). Surgical anesthesia was not achieved in either of these studies. Intracoelomic administration of 35 mg/kg in *Ambystoma tigrinum* did produce very brief surgical anesthesia after prolonged induction times (Mitchell 2009). Given the variability of reported dosages and routes of administration, and potential mortality at higher concentrations, recommendations for its use in amphibians are not possible. Differences in GABA receptor density between species may introduce further variability in the effect of these drugs among amphibians (Guenette et al. 2008).

Alpha-2 adrenergic agonists such as medetomidine and dexmedetomidine do not produce sedation in amphibians. Dexmedetomidine, when added to an alfaxalone immersion protocol, did provide some analgesia, but resulted in lightening of the anesthetic depth in

oriental fire-bellied toads (*Bombina orientalis*) (Adami et al. 2016b). Imidazole-based, nonbarbiturate hypnotic drugs, metomidate and etomidate, have been shown to achieve anesthesia in amphibians, but complications such as extremely prolonged recoveries in *Rana pipiens* and pruritus, myoclonus, and prolonged recoveries in *Bombina orientalis* make these drugs unsuitable as a sole anesthetic agent in these animals (d'Ovidio et al. 2015; Doss et al. 2014). They may be effective in gilled animals, as etomidate does produce anesthesia in fish and *Xenopus laevis* tadpoles (Plumb et al. 1983; Paris et al. 2007).

A variety of other injectable anesthetic agents, including ketamine, tiletamine/zolazepam, and various barbiturates, have been used. These agents are not recommended because they are less reliable than the topical and inhalant anesthetic agents. They are associated with large species variability in effect and produce significantly higher mortality rates.

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10

Tortoises, Turtles, and Terrapins (Chelonians)

Alessio Vigani and Darryl Heard

Introduction

The order Chelonia includes almost 300 species of tortoises, turtles, and terrapins. They inhabit many different habitats, from tropical rain forests to deserts, from freshwater swamps to oceans. The wide variety of environments, dietary preferences, and activity levels explains the substantial differences in metabolic rate among chelonian species. They also differ significantly in body size, from the 0.1-kg adult Cape tortoise (*Homopus* spp.) to the 1000-kg adult leatherback sea turtle (*Dermochelys* coriacea) (Raphael 2003). Most tortoises are generally shy, harmless animals, but there are differences in temperament among chelonians. Many aquatic species are natural predators and often respond with aggression to potential threats. These species can be dangerous and require caution when handled.

Interventions in the field for research purposes and the management of patients in the hospital setting represent the main conditions where sedation and general anesthesia are needed. It follows the choice of the anesthetic protocol will depend on the invasiveness of the procedure and the environment where it will take place. Collection of diagnostic samples in the field generally only requires mild to moderate sedation and, ideally, wild animals should return to the wild without the risk of any residual anesthetic effect. For this purpose, sedative protocols that include short-acting and reversible agents are particularly suitable.

Invasive surgical procedures should be performed under general anesthesia in the controlled environment of a veterinary hospital. The facility should be equipped with specific anesthesia equipment and monitoring devices. Prior to anesthesia the patient should be thoroughly evaluated and acclimatized, homeostasis should be restored, and thermoregulation should be supported to optimize the response of the patient to the anesthetic. Appropriate analgesia should be provided to any patient that is to undergo a painful procedure. New information on the ability of reptiles, chelonians included, to feel pain underlines the responsibility of every veterinarian to properly prevent and manage pain in these species.

Furthermore, independently from the operative setting, prerequisites to the design of a safe anesthetic protocol are a good knowledge not only of the anatomy and physiology, but also of the species-specific differences in response to anesthetic drugs and dosages. Multiple studies have evaluated the efficacy of a variety of single or combined anesthetic and analgesic drugs in different chelonian species.

The perfect anesthetic agent does not exist for any species. There is no anesthetic drug devoid of side effects and even the most recently marketed agents produce dose-related toxicity. For this reason the use of combinations of small doses of multiple drugs has become popular in anesthesia (Turner et al. 2021). This anesthetic technique is referred to as *balanced anesthesia* and has been shown to be superior to single-agent anesthesia in humans and many veterinary species (Kushiro et al. 2005; Sanders et al. 2008). The explanation of its success is that the use of small doses summates the advantages, but not the disadvantages of the individual components of the mixture. It follows that the safety of the anesthetic protocol largely depends on the right choice of drugs, used at the adequate dose for the patient.

Anatomy and Physiology

Cardiovascular

The cardiovascular system is characterized by many morphological and functional peculiarities. The heart is three-chambered and valentine-shaped. It is located within the pericardial sac, at midline, above the cranial portion of the plastron, immediately cranial to the liver. The large right and left atria are distinct and open independently into an anatomically single but functionally divided ventricle. The

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right atrium receives deoxygenated blood from the systemic venous circulation via a preatrial muscular, thin-walled chamber called the *sinus venosum*. The latter represents the confluence site of blood from the left and right precaval veins, the postcaval vein, and the left hepatic vein.

The cardiac muscle constituting the *sinus venosum* acts also as the pacemaker of the heart. This electrical activity is detectable on the electrocardiogram by the presence of an "SV wave" preceding atrial depolarization.

The left atrium receives oxygenated blood from the pulmonary circulation via the left and right pulmonary veins. The ventricular muscle is internally organized in a series of ridges that divide the ventricle into three functional chambers: *cavum pulmonale*, *cavum venosum*, *and cavum arteriosum*. Blood coming from the right atrium enters first the *cavum venosum* and then the *cavum pulmonale*, which has a direct pulmonary arterial output into the pulmonary trunk. Left atrial blood enters the *cavum arteriosum* and secondarily the *cavum venosum*, which opens into the systemic arterial systems via the left and right aortas (Farrell et al. 1998). It follows the *cavum venosum* receives both deoxygenated (directly from right atrium) and oxygenated blood (indirectly from the left atrium), with the potential for mixing of the two.

The ventricular anatomy is such that, in physiologic conditions of normal ventilation, there is a high degree of separation between the systemic and pulmonary circulations, with minimal mixing between venous and arterial blood. During ventilation, systemic ventricular output matches with the pulmonary ventricular output and intracardiac shunting is low. With the animal at rest, the physiological cardiac shunting in is bidirectional with coexistence of right-to-left and left-to-right components (Farrell et al. 1998).

The extraordinary adaptability of chelonians is fully displayed during apnea. The dive reflex induces complex physiologic changes, including modulation of intracardiac shunting (Hicks & Malvin 1992). During breath holding, the arterial tension of oxygen progressively decreases. This induces vasoconstriction of the pulmonary arterial vasculature and causes a substantial decrease in pulmonary blood flow (Crossley et al. 1998). During apnea in turtles, the increased pulmonary arterial pressure causes the systemic venous return to be preferentially directed into the systemic circulation (R-L shunt), bypassing the lungs. This mechanism produces an oxygen-sparing effect in the lungs (Jackson 2000). Aquatic, and to a lesser extent terrestrial, chelonians have been shown to develop right-to-left intracardiac shunting in hypoxic conditions (Hicks et al. 1996). During ventilatory periods, the cardiovascular changes are the reciprocals of those occurring during apnea: the heart rate increases, the pulmonary vascular resistance falls, and pulmonary blood flow is maximized. Blood flow measurements indicate a net formation of a left-to-right shunt during ventilation which increases hemoglobin oxygen saturation of pulmonary arterial blood (Shelton & Burggren 1976). Low rates of elimination of inhalant anesthetics, such as isoflurane or sevoflurane, can be expected whenever cardiac shunting exists.

Hypoxemia and the subsequent right-to-left shunt trigger a generalized hypometabolic state (Hicks & Wang 1999). This hypometabolic condition significantly decreases the hepatic function with a potential detrimental effect on the clearance of drugs (Platzack & Hicks 2001). Therefore, it is important to provide ventilation and oxygenation during anesthesia to maintain a steady cardiovascular and metabolic state. Once cardiac shunting is present, it may be difficult to provide oxygen supplementation.

The direction (right-to-left vs. left-to-right) and size of shunting in chelonians are influenced by multiple factors that control cardiac function. These include both adrenergic and cholinergic innervation. Stimulation of the vagus nerve in tortoises results in an increase in pulmonary arterial pressure and net formation of right-to-left shunt (Hicks & Comeau 1994). In contrast, epinephrine or the stimulation of the cardiac sympathetic nerves abolish right-to-left shunting and induce vasodilation of the pulmonary vasculature. In *Trachemys scripta* it has been shown the infusion of epinephrine increases the blood flow in the pulmonary circulation (left-to-right shunt) and eliminates the systemic venous admixture in the aortic arches (Hicks & Malvin 1992).

An additional important factor that modulates cardiac shunting is thermoregulation. Variation of body temperature from the physiologic optimal conditions has major effects on the circulatory system (Krosniunas & Hicks 2003). At normal body temperature the intracardiac shunting is relatively stable, with a small right-to-left shunt. Interestingly, both heating and cooling result in the development of an increased R-L intracardiac shunt (Galli et al. 2004). The ability to selectively shunt blood flow away from the pulmonary circulation is likely the cause of prolonged recoveries from inhalant anesthesia. Therefore, during anesthesia the maintenance of steady physiologic thermal conditions is important to provide optimal gas exchange, including inhaled anesthetics.

The renal portal system (RPS) maintains sufficient blood flow to the renal tubules at times when a decreased effective circulating volume generates a low glomerular blood flow. The portal vein is a large vessel that enters the kidney and originates at the confluence of the epigastric and external iliac veins. It contains muscular valves capable of shunting blood from the caudal half of the body directly to

the kidney. Hydration status seems to play a primary role in the activity of the RPS and affects the degree of shunting. Dehydration causes an increased diversion of blood. The blood in the RPS is exposed to the renal tubular surface and this may result in increased clearance of drugs normally excreted through the tubules into the urine. Angiographic studies have also shown a large amount of venous blood from the hindlimbs is directed to the liver (Holz et al. 1997b), therefore renal and hepatic levels of some drugs injected into the caudal limbs may be unpredictable. It has been demonstrated, however, that the injection site is unlikely to have any influence over the activity of most drugs and the caudal half of a chelonian is available for drug administration (Holz et al. 1997a). For example carbenicillin, a drug largely excreted by tubular secretion, was injected into the hindlimbs of turtles. The systemic blood levels of the drug obtained were just slightly lower compared to the forelimb injection (Holz et al. 1997b). Whether the same scenario applies to drugs injected into the dorsal venous sinus of the chelonian tail remains unclear. In green iguanas (*Iguana iguana*), the venous flow from the tail was found to directly enter the kidney through the renal portal circulation (Benson & Forrest 1999). Until adequately investigated, it is advisable not to use the dorsal venous sinus for drug administration in dehydrated chelonians.

Respiratory System

Chelonians are obligate nasal breathers. Open-mouth breathing indicates decreased airflow through the nasal cavities, possibly due to pathology. The external nares open into a keratinized vestibule divided symmetrically by a cartilaginous septum into right and left nasal chambers. The nasal chambers lie above the hard palate and extend aborally into the oropharynx through a ventral recess. Turbinates, sinuses, and soft palate are absent. The glottis is located at the base of the tongue, with species-specific differences in morphology. In aquatic species in particular, it is characterized by a strong muscular component needed to provide efficient sealing of the distal airways during immersion. The trachea is composed of complete rings, is relatively short, and bifurcates in paired bronchi at the level of the mid-cervical region (McArthur et al. 2004). It is therefore easy to unilaterally intubate most chelonians.

The lungs are located dorsally in the coelomic cavity and their dorsal surface is attached to the carapace. All chelonians have multichambered lungs with paired unbranched intrapulmonary bronchi reinforced by cartilage over their entire length. In sea turtles, the intrapulmonary bronchi are supported by cartilaginous rings, are broad cranially, and taper caudally. In other chelonians, the bronchi are uniform in diameter for their entire length, and the supporting cartilage forms a network instead of separate rings. Each bronchus opens into three to 11 chambers from which multiple subcompartments, referred to as "niches", originate. The chelonian analogues of mammalian alveoli are termed "faveoli", "ediculae", and " trabeculae" and represent the parenchymal gas exchange units (Perry 1998).

The presence of the carapace impedes the costal component of ventilation, therefore muscle-induced movements of the viscera and limbs are responsible for alterations in intrapulmonary pressure. Chelonians do not possess a functional muscular diaphragm. A horizontal septum, or pseudodiaphragm, separates the lungs form other intracoelomic organs. In some chelonians, such as sea turtles, the horizontal septum is extensive and attaches the liver and stomach to the ventral surface of the lung. This attachment maximizes the transmission of the movement of the body wall and limb girdles through the visceral mass to the lungs. Limb movements stretch the septum downward, causing expansion of the lungs. The lung expansion generates a negative intrapulmonary pressure and facilitates the passive inflow of air during inspiration. The "muscle pump" mechanism is abolished by immobility; subsequently ventilation is profoundly depressed during anesthesia. Ventilatory artificial support by intermittent positive pressure ventilation (IPPV) is therefore always recommended in anesthetized chelonians. IPPV can be provided either manually or mechanically with a ventilator.

Chelonians are unable to cough and lack effective ciliary clearance of respiratory material. This explains why their ability at clearing secretions and foreign material from their lower respiratory tract is very poor. Consequently, inflammatory exudates tend to accumulate in dependent area of the lungs with severe effects on respiratory function and gas exchanges. The innate resilience of chelonians, however, allows them to withstand extreme physiologic perturbations, such as severe hypoxemia or hypercapnia, and clinical signs of respiratory distress occur late in the course of the primary disease (McArthur et al. 2004).

Reptiles, compared to avian and mammalian species, have a relatively large lung volume which is distributed a relatively small respiratory surface area. The multichambered lungs of chelonians, however, represent the advantage of a more complex surface elaboration compared to the single-chambered lungs of other reptiles. Studies in red-eared sliders (*Trachemys scripta*) showed the septa that divide the pulmonary chambers provide a 40% larger surface area used for gas exchanges compared to the outer wall of the lungs. This yields effective gas exchange to cover metabolic requirements (Perry 1998).

Respiration is characterized by intermittent breathing patterns with ventilatory periods alternated with nonventilatory

pauses. The respiratory cycle in terrestrial species consists of a passive inspiratory followed by an active expiratory phase. The latter is reversed in aquatic species. These peculiarities, along with the high compliance values of chelonian lungs, produce a significantly lower work of breathing compared to mammals. In regard to anesthesia, however, the chelonian highly compliant lungs are extremely easy to inflate and hence highly sensitive to barotrauma (Herman et al. 1997). It is therefore recommended that low peak inspiratory pressures be used during IPPV.

The need to maintain the low-energy requirements of ventilation is also reflected by the adaptive mechanisms that chelonians operate in response to increased metabolic stress. Increasing tidal volume is ineffective and represents a major energy expense in chelonians. This explains why most tortoises and turtles during activity increase their minute ventilation by increasing respiratory rate and not tidal volume. In regard to the diving mechanisms of ventilation, hypoxemia and hypercarbia affect the length of respiratory cycles differently. Hypoxemia induces bradypnea while hypercapnia causes tachypnea. The explanations of these opposite effects are oxygen preservation and the elimination of carbon dioxide, respectively. Conversely, the artificial induction of either hyperoxia or hypocapnia independently from one another causes persistent cessation of spontaneous ventilation (Wang et al. 1998). Therefore, the maintenance of blood gas variables within physiologic range is critical during anesthesia to avoid long-lasting alteration of ventilatory function.

Many chelonians can perceive a low oxygen environment and develop a cardiorespiratory response similar to the dive reflex described in mammals. They become apneic, bradycardic, and convert to anaerobic metabolism. These physiological changes, combined with cardiac shunting, facilitate diving and hibernation, but complicate the use of inhaled anesthetic agents. The alterations in respiratory circulation typical of the chelonian dive reflex can affect the uptake and excretion rates of inhalant anesthetics.

Pain and Nociception

Pain and nociception are often mistakenly considered synonymous. Pain is inherently subjective, and in animals is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain represents the interpretation by the cerebral cortex of a noxious stimulus and consciousness, therefore, is a prerequisite to feel pain. Nociception instead refers to the physiologic or neuroanatomical components necessary to sense and transmit the noxious stimuli to the brain (IASP 1994). Any organism that has developed these neuroanatomical structures is defined as sentient. In a sentient animal, therefore, nociception persists during unconsciousness and anesthesia unless analgesic interventions are provided (Giordano 2005).

Multiple studies in different reptile species have demonstrated the presence of the neuroanatomical apparatus for sentience and nociception (Liang & Terashima 1993; ten Donkelaar and de Boer-van Huizen 1987). It has been shown that environmental stimuli elicit impulse transmission from sensory receptors, through the spinal cord, to the animal's brain. Furthermore, the reptile cerebral structures are operationally sophisticated enough to convert the impulses into perceived sensations (Giordano 2005). The opioid receptor gene family is highly conserved across multiple vertebrate orders, and new information is now available on opioid receptors and their modulation in chelonians (Reiner 1987; Li et al. 1996). For example, mu (μ) and delta (δ) opioid receptors are located throughout the brain in aquatic turtles, with δ opioid receptors being more abundant than μ opioid receptors (Xia & Haddad 2001). With respect to endogenous opioid related neurotransmitters, proenkephalin and other neuropeptides (i.e., neuropeptide FF) are present in the brain of turtles with a distribution similar to that in mammals and birds (Munoz et al. 2008). New information is also now available on the role of the different opioid receptors in nociception and analgesia in chelonians (Sladky et al. 2009). For example, kappa (κ) opioid receptors are significantly less involved in nociception and pain compared to μ opioid receptors. κ receptor agonists do not produce any detectable analgesic effect in turtles whereas agents with μ agonist activity significantly increase the nociceptive threshold (Wambugu et al. 2010).

In nonverbal species, suffering is expressed in the form of behavioral changes that are often not obvious to the observer (Holton et al. 2001; Holsti et al. 2008). Chelonians are not an exception. It follows, independently from the inability of these animals to show evident expressions of pain, veterinarians should consider chelonians are capable of suffering when a noxious stimulus in applied, and therefore they should be provided with appropriate analgesia.

Perianesthetic Considerations and Patient Management

Preanesthetic Assessment

A complete history provides crucial information regarding the patient's environment, husbandry, and diet, and helps to determine duration and severity of clinical signs of the medical condition. The observation of the unstressed patient is important to determine the level of activity of the patient unbiased by any restraint.

Ideally, prior to anesthesia, the patient should be acclimatized to the new environment and the room temperature and humidity should be set within the ideal range for the species. This obviously does not apply to emergency cases where immediate intervention is required. As with all ectotherms, chelonian body temperature is reliant on the environmental temperature. The preferred optimal temperature zone (POTZ) refers to the ideal environmental temperature range selected by a particular species. Each species has its own POTZ and it is only when the animal is in its POTZ that its physiology is functioning at its best. For most chelonians, data regarding optimal environmental temperature and humidity can be found in the literature. If the specific POTZ is uncertain, exposure to a room temperature range of 24–28°C during preanesthetic stabilization seems to be appropriate for most chelonian species (McArthur et al. 2004).

Body temperature should be measured prior to anesthesia. Oscillations in body temperature in ectothermic species are common and it is important to identify and correct wide variations from the normal range. All chelonians have what is referred to as an active temperature range (ATR). This is the body temperature range where they are capable of normal, voluntary activity. Each species has a different ATR (McArthur et al. 2004). Critically ill patients are often hypothermic and the prompt restoration of normothermia is of critical importance to maximize the chance of patient stabilization. On the other hand, overheating should also be carefully avoided. Hypothermia and hyperthermia have significant effects on metabolic rate (drug clearance), acid base status, intracardiac shunting (respiratory gas exchanges and inhalant anesthetic uptake and clearance), and inhalant agent potency (decreased minimum alveolar concentration [MAC] during hypothermia). Therefore, attention to maintaining normothermia in the perianesthetic period is a priority for the anesthetist.

The preanesthetic physical examination consists of the assessment of systems and organs, and should include a preliminary visual examination aimed at determining body condition, nutritional and hydration status, and presence of trauma. Body weight must be recorded to ensure accurate dosing of anesthetics.

A basic assessment of the cardiovascular system of the patient should be performed prior to anesthesia. Heart rate and pulse rate and strength can be evaluated noninvasively with a Doppler flow detector. Pencil and flat probes are selected based on the size of the animal and the location where the probe must be placed. For cardiac auscultation a pencil probe can be placed lateral to the neck at the level of the coelomic (thoracic inlet) (Fig. 10.1). For pulse assessment, a flat probe can detect blood flow in vessels directly beneath the probe. Suitable arteries for pulse assessment are the carotid and femoral artery (McArthur 2007). Several formulas to determine the normal heart rate based on body



Figure 10.1 (a) Appropriate positioning of a Doppler pencil flow probe in the coelomic inlet to assess blood flow and heart rate in a semi-awake wood turtle (*Glyptemys insculpta*). (b) An anesthetized freshwater turtle with a Doppler pencil flow probe placed in the coelomic inlet for continuous blood flow and heart rate monitoring. Note also the use of a soft mouth gag and a portable ECG.

weight in reptiles have been given by different authors. However, the absence of validation studies and the significant physiologic differences between species often make those equations clinically inadequate for predicting heart rate.

Baseline respiratory rate and depth are measured before induction. Identification of even mild signs of respiratory disease should be considered as an expression of potentially severe respiratory illness. Chronic respiratory disease is fairly common, and chelonians are able to withstand extensive injury to the respiratory system before showing signs of distress.

Ideally when planning elective procedures, a venous blood sample should be collected prior to anesthesia for hematologic and plasma biochemical evaluation. Blood should be collected into lithium heparin tubes as EDTA causes lysis of reptilian erythrocytes. As a general rule, the sample size should not be larger than 1% of the body weight of the subject. Abnormalities in the laboratory variables of special interest for the anesthesiologist are represented by, but not limited to, the presence of anemia or hemoconcentration, hypoproteinemia, hypoglycemia, hyperuricemia, and electrolytes and acid-base imbalances. The presence of any of the above abnormalities warrants further investigation to identify the underlying cause and properly treat prior to anesthesia.

The patient's hydration status should be assessed based on history, physical examination, and laboratory findings. At present, however, the evaluation of hydration status is still somewhat subjective. Indications of dehydration are sunken eyes, reduced skin turgor, and hematological and plasma biochemical alterations such as hemoconcentration and hyperproteinemia (McArthur 2004). Ion pump activation and significant fluid reabsorption by the lower urinary and digestive tracts complicate the use of many variables as indicators of hydration. In most reptiles, approximately 75% of body weight is water. In chelonians, the presence of the carapace reduces the value closer to that found in mammals, which is approximately 66%. However, in contrast to mammals, the total body water is equally distributed between the intra- and extracellular fluid compartments and 30% of the extracellular fluid volume exists in the intravascular space (Smits & Kozubowski 1985). These differences should be considered to accurately plan and administer fluids to chelonians.

Differences in response to various inhaled and injectable sedatives and anesthetics have also been shown between chelonian species. The drugs and doses effective and safe in one species may not apply to other chelonians.

Handling of Dangerous Chelonians

Chelonians generally do not need significant restraint during examination and most herbivorous animals can be handled with no real risk of danger to the personnel. However, aggressive and potentially dangerous species represent exceptions. Snapping turtles (*Chelydra* spp.), soft-shell turtles (*Trionyx* spp.), and marine chelonians may show unpredictable, aggressive reactions and these large animals can inflict serious injuries with their beaks and claws. These species should be handled with extreme caution. Wearing heavy-duty gloves is recommended, but serious bite injuries can still occur despite their use. These animals can be examined more safely after they have bitten or locked on nontraumatic objects such as a PVC pipe. Alternatively, a suitably sized container can be placed over the head to prevent biting when injecting into the pectoral muscles. When working with aggressive species, the help of an assistant is often necessary.

Smaller marine, snapping, and soft-shell turtles can be held with a hand on either side of the carapace, with the head directed away from the operator and other people (Fig. 10.2). Turtles of the genera *Chelydra* and *Trionyx* are able to extend their head up to the level of their hindlimbs. It is important to determine the "safe zone" around the animal. Medium-sized (10–40 kg) marine and snapping turtles are better controlled with one hand around the nuchal scute (cranial carapace above the neck) and the other on the caudal carapace (Fig. 10.3). Very large individuals of these species are capable of incredible strength and stretchers or canvas slings should be used during maneuvering procedures. Marine chelonians should never be picked up by their flippers. This is due to the risk of causing luxations and fractures. The handler should also be prepared for a



Figure 10.2 Appropriate physical restraint of a medium-size (15 kg) alligator snapping turtle (*Macrochelys temminckii*). Note the position of the hands on either side of the shell. The use of reinforced gloves provides additional protection from the claws.



Figure 10.3 Physical restraint of a large (30-kg) alligator snapping turtle (*Macrochelys temminckii*). The animal is controlled with one hand on the nucal scute and the other on the caudal carapace. The head of the animal is directed away from the operator.

rapid burst of struggling and flipper flapping when a marine turtle is first lifted out of water or its enclosure.

While necessary in some cases, chemical immobilization should be considered as a last resort in a simple physical examination procedure. Whenever sedation is used, an aquatic animal must not be reintroduced into water until it is fully recovered to avoid the risk of drowning.

Venipuncture and Intravenous Catheterization

Venipuncture and venous catheterization for phlebotomy and drug or fluids administration purposes are difficult. The diversity in morphology of turtles and tortoises precludes any single dependable venipuncture site for all species. Therefore, it is important to know the location of multiple potential sites and select the most appropriate for the individual species. Venipuncture sites previously described include the jugular veins, dorsal cervical sinus, subcarapacial (subvertebral) sinus, and the dorsal coccygeal vein (Lloyd & Morris 1999). Other peripheral venipuncture sites, where only small blood samples can be obtained, are the radio-humeral venous plexus and the femoral vein. These sites may be more yielding in larger animals.

It is recommended blood collection be from the jugular veins when possible. Samples taken from the jugular site are least likely to be lymph diluted (Jacobson et al. 1992). The external and internal jugular veins are located on either side of the neck in many chelonian species. The external jugular veins lie higher on the neck compared to mammals. Either can be used for venipuncture. The external jugular vein is larger and located in a lateral to dorsolateral position. It runs approximately in a line from the dorsal edge of the tympanic membrane parallel to the dorsal plane of the neck in the direction of the thoracic inlet (Fig. 10.4). Extension of the neck is needed to allow the jugular vein to be raised and seen. This is possible in many small chelonians, but in large individuals (>10 kg) or aggressive species such as snapping turtles, it is often impossible without adequate chemical restraint. Should the jugular site prove impractical, the subcarapacial sinus or the dorsal coccygeal vein may represent good alternatives, particularly for intravenous (IV) drug administration.

The subcarapacial venous sinus can be easily accessible in small chelonians (<10 kg) (Fig. 10.5). It is located under the carapace, on the dorsal midline, at the junction of the common intercostal and the caudal branch of the external jugular veins, just cranial to the eight cervical vertebra (Hernandez-Divers & Hernandez-Divers 2002). Although the presence of clear liquid in the syringe at this site has often been attributed to lymph, it is most likely to be cerebrospinal fluid. Consequently, the subcarapacial vein is not recommended for injection of anesthetic drugs, except for euthanasia (Quesada et al. 2010).

The dorsal coccygeal vein is a safe and dependable venipuncture site in snapping turtles (Fig. 10.6). The dorsal coccygeal vein runs in the dorsal midline from the tip of the tail to the carapace. Blood samples from this site can be unpredictably lymphodiluted, therefore, when clear fluid

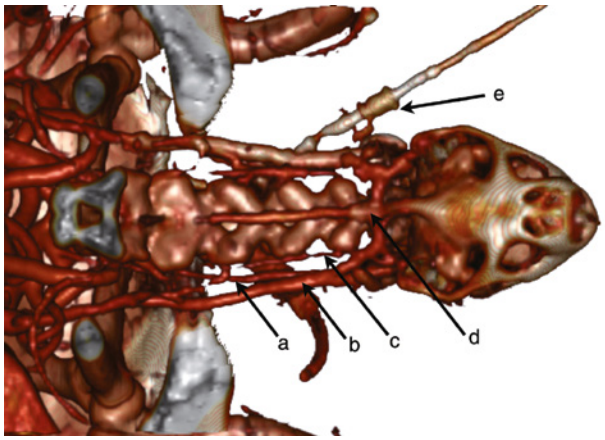


Figure 10.4 CT-scan 3D reconstruction of the neck of the Gopher tortoise (*Gopherus polyphemus*). The vascular structures are identified as follows: (a) carotid artery, (b) external jugular vein, (c) internal jugular vein, (d) occipital venous sinus. (e) indicates an intravenous catheter placed in the left external jugular vein.

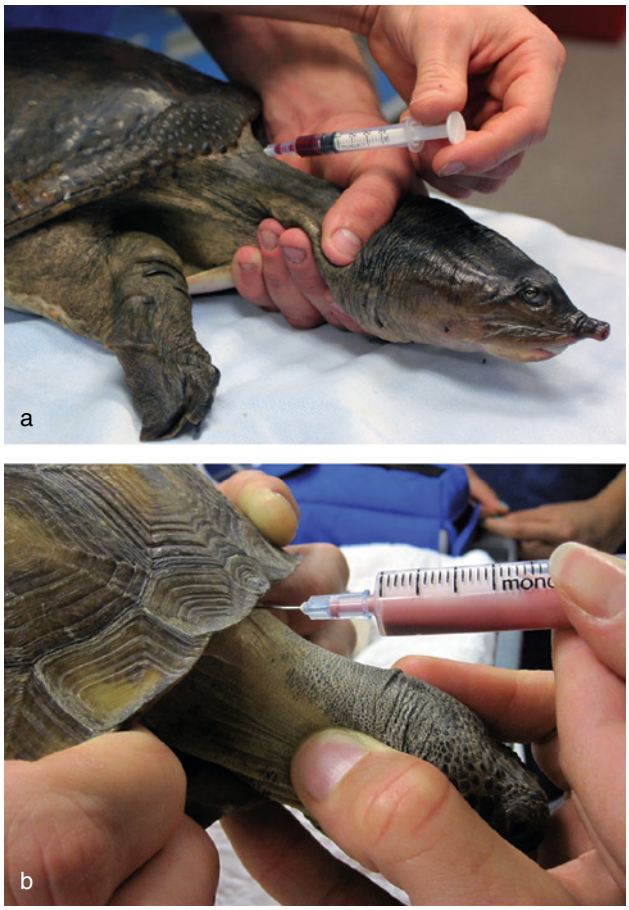


Figure 10.5 Use of the subcarapacial venous sinus for (a) blood withdrawal in a Florida soft-shell turtle (*Apalone ferox*) and (b) intravenous injection of propofol in a gopher tortoise (*Gopherus polyphemus*). The needle is inserted on the midline of the neck, at the junction between the skin and the carapacial nucal scute. The needle is advanced caudally while maintaining gentle negative aspiration on the syringe until blood is flowing into the chamber.

is sampled, another attempt should be made at a different site. The vessel is occasionally more superficial then expected and a needle which is inserted between the vertebrae too deep has the potential to enter the vertebral canal, therefore accurate disinfection of the skin of the tail is mandatory before attempting venipuncture.

In marine turtles the dorsal cervical sinus is a reliable venipuncture site and it is popular with those working with these chelonians. It is useful both for blood withdrawal and IV injections. The paired sinuses are parallel to the midline and are located on either side, 0.5–1 cm away from the dorsal spinous processes of the proximal cervical vertebrae. They are found 0.5–3 cm deep depending on the size of the animal.

Suitable anatomical locations for IV catheter placement are limited; the jugular veins are usually the only option.



Figure 10.6 Venipunture in an alligator snapping turtle (*Macrochelys temminckii*) using the dorsal approach to access the dorsal coccygeal vein. The main advantage of this venipuncture site is represented by its location in the "safe zone" around the animal. For safety, an assistant should restrain the animal during the venipuncture procedure.



Figure 10.7 A single-lumen jugular catheter placed in the external jugular vein of a green sea turtle (*Chelonia mydas*). The catheter was inserted using an over-the-wire technique. The winged proximal portion is secured to the skin with sutures.

Jugular catheter placement can be performed with either a venous cut-down or percutaneously. Prior sedation is recommended and often necessary for a successful catheter placement. In general, over-the-needle, 22–18-gauge, 2–4-cm long IV catheters can be used for short-term placement. When long-term venous access is required, indwelling polyurethane or silicon central venous catheters should be used (Fig. 10.7). This author (A. Vigani) recommends the use of the standard Seldinger technique (over-the-wire) for percutaneous placement of long-term catheters (Fig. 10.8) (Pardo & Divers 2016).



Figure 10.8 Placement of a long-term jugular catheter in an Aldabra tortoise (*Aldabrachelys gigantea*). In the anesthetized animal, the external jugular vein is identified by palpation of the dorso-lateral aspect of either side of the neck. A hollow needle is advanced through the skin until blood is aspirated. The catheter is then inserted using the Seldinger technique: a blunt guidewire is passed through the needle (a), then the needle is removed. A dilating device may be passed over the guide wire to slightly enlarge the vessel. Finally, the central line itself is then passed over the guidewire, which is then removed. All the lumens of the line are aspirated and flushed. The catheter is finally secured with sutures to the skin (b).

Intraosseous catheterization is very difficult to impossible in most chelonians due to the density of their bones and the small intramedullary spaces. In giant tortoises, however, the best site for placement of an intraosseous catheter appears to be the gular scutes at the front of the plastron (Heard, pers. comm.). This area was originally identified using a CAT scan. A small hole sufficient to accommodate a 2–3-inch (5–8-cm), 22-gauge spinal needle is first drilled through outer gular scute. The needle is then placed and secured to the shell with glue or putty (e.g., Loctite All Purpose Repair Putty). Once it hardens the latter provides excellent adhesion to the shell.

Fluid Therapy

When a fluid deficit is clearly identified or the hydration status of the patient is unknown, perianesthetic fluid therapy is indicated to replace the deficit in active circulating volume and restore tissue perfusion and homeostasis. Hypotonic fluids such as 5% dextrose in water (D5W) generally diffuse primarily in the intracellular space whereas isotonic crystalloids contain a sodium concentration similar to that of the extracellular space, making them the ideal solution for replacing extracellular volume deficits.

There is still debate on the best type of fluids to administer to reptiles given their blood is hypotonic compared to birds and mammals. There are several guidelines for fluid replacement in reptiles, but most of the standard crystalloids, such as lactated or acetated Ringer's, and normal saline solutions can safely be used. Two recipes of isotonic solution are diluted saline (9 parts 0.9% NaCl and 1 part sterile water) and Reptile Ringer's (2 parts 2.5% dextrose/0.45% saline with 1 part lactated Ringer's). It is generally accepted a rate of 25 mL/kg every 24 hours is appropriate as a rehydrating rate. In chelonians, total fluids given at one time should not exceed 2–3% of total body weight (Norton 2005). Constant rate infusion is preferable over intermittent boluses. Fluids can be administered orally, intravenously, or intracoelomically. Oral rehydration is recommended for clinically stable, mildly to moderately dehydrated patients, whereas the IV route is preferred in severely dehydrated patients. Intracoelomic fluids should be avoided in patients with present or suspected respiratory disease, intracoelomic space-occupying lesion, obstipation, and egg retention (McArthur 2004).

Traumatized patients that have suffered severe hemorrhage should be promptly fluid resuscitated. In these cases the IV route is considered ideal for fluid administration. In these patients, however, the low intravascular volume and vasoconstriction often limit IV access.

In the presence of life-threatening hypovolemia, the IV administration of hypertonic solutions (i.e., 7.5% NaCl) and colloids (hydroxyethyl starches and dextrans) is indicated to provide selective intravascular volume expansion. The recommended doses of hypertonic solutions and colloids in mammals are 2–4 and 5–10 mL/kg, respectively. The safety of such indications has not been proved in chelonians. Thus, the author (A. Vigani) recommends starting with lower initial volumes (1–2 mL/kg) and then reassessing the response of the patient.

Analgesia

Sladky (2023) provides an excellent review of the current literature on pain assessment and analgesia in reptiles.

A survey of the use of analgesics by reptile veterinarians almost 20 years ago indicated analgesia is withheld in more than 50% of the patients by more that 60% of the responders (Read 2004). This finding may be partially explained by our inability to detect pain in reptiles due to the lack of definitive information on behaviors proven to be pathognomonic of pain. Ultimately, pain assessment is made even more difficult by the evidence reptiles seem to voluntarily suppress pain-related behaviors when they are observed (Fleming & Robertson 2006; Sladky 2023). Sadly, for all these reasons, pain control in reptiles has been largely overlooked. The current knowledge and better understanding of pain perception in reptiles support the importance of providing appropriate analgesia whenever an invasive procedure is performed. Sladky (2023) provides an excellent review of the current literature on pain assessment and analgesia in reptiles.

Opioids

Among opioid analgesics, morphine has been shown to provide analgesia in chelonians whereas butorphanol, even at dosages largely exceeding the mammalian therapeutic doses, did not have any effect on thermal threshold (Sladky et al. 2007). The analgesic action of morphine (1.5 mg/kg) in chelonians appears to have a time of onset of 2–8 hours post administration and duration of more than 24 hours. Unfortunately, this analgesic effect is coupled with a significant, long-lasting respiratory depression (Sladky et al. 2007). Meperidine, a synthetic μ pure agonist, induced significant decrease in the duration of limb retraction after formalin injection in Speke's hinged tortoise (*Kinixy's spekii*) at a dose of 20 mg/kg. This drug appears to provide a degree of analgesia equivalent to morphine (Wambugu et al. 2010). Pharmacokinetic data of buprenorphine in red-eared sliders (*Trachemys scripta elegans*) established the subcutaneous administration of 0.075–0.1 mg/kg every 24 hours is sufficient to maintain plasma drug concentrations considered analgesic for humans (Kummrow et al. 2008). The analgesic effect of buprenorphine in chelonians has not been evaluated. Tramadol, an atypical synthetic opioid, has been recently shown to provide long-lasting analgesia in chelonians with minimal respiratory depression. In red-eared sliders (*Trachemys scripta elegans*), the oral administration of 10–25 mg/kg increased thermal threshold for up to 96 hours (Baker et al. 2011). These dosages are much higher than those generally used in clinical practice (0.5–4 mg/kg). Preservative-free morphine can also be administered intrathecally for prolonged analgesia of 24–48 hours' duration (Mans 2014).

Nonsteroidal Anti-inflammatory Agents

Nonsteroidal anti-inflammatory agents (NSAIDs) are widely used in reptiles based on their proven potent analgesic activity in mammals. Interestingly, there is no proven scientific evidence of the analgesic activity of NSAIDs in chelonians. This could be due to our incapacity to effectively assess pain. To the authors' knowledge a limited number of studies evaluated pharmacokinetics and pharmacodynamics of NSAIDs in chelonians. In green iguanas (*Iguana iguana*) the oral administration of meloxicam at 0.2 mg/kg resulted in plasma concentrations considered analgesic for mammals (Divers et al. 2010). In loggerhead sea turtles (*Careta careta*), it was shown that the clearance of meloxicam was significantly higher than reported for the iguana, suggesting the need for more frequent dose intervals to maintain effective plasma concentrations (Soloperto et al. 2012). This may not, however, correlate with analgesia because the plasma concentration of NSAIDs does not directly correlate with clinical effect.

The safety of the use of NSAIDs in reptiles has been evaluated in studies involving repeated daily administrations. No significant biochemical abnormalities or histopathological lesions were seen with meloxicam (Hernandez-Divers et al. 2004). Despite this, it is still possible NSAIDs can cause severe side effects, as reported in mammals. Normal hydration status and renal function should always be ensured prior to NSAID administration. Although the clinical use of NSAIDs in reptiles does not appear to delay wound healing, it has been shown that the administration of selective NSAIDs cyclooxygenase-2 inhibitors to geckos after tail amputation significantly retards the regenerative process (Sharma & Suresh 2008).

Local and Regional Anesthesia

Local anesthesia represents an irreplaceable component of a multimodal anesthetic approach. Local anesthetics prevent the transmission of nerve impulses by interrupting the sodium influx into the neurons. In sensory nerve fibers, the signal from a noxious stimulus is then stopped at its origin and is prevented from reaching the central nervous system. Local anesthetic agents vary in potency and duration of action. Lidocaine and bupivacaine represent the most commonly used agents in veterinary practice. Bupivacaine is more potent and longer acting compared to lidocaine, but the actual duration of action in reptiles is undetermined. In chelonians, the local injection of local anesthetics is useful for facilitating minor surgical interventions, but local anesthesia alone is not sufficient to provide analgesia for more invasive procedures. The infiltraton around the surgical site (local block) represents the most

diffuse use of local anesthetics in chelonians, but more advanced techniques have also been described (Hernandez-Divers et al. 2009).

Brachial nerve blockade for forelimb surgery has been evaluated (Mones et al. 2021, 2023) in eastern box turtles (*Terrepene carolina carolina*). Unfortunately, the technique was unreliable in producing brachial plexus motor and sensory blockade, and further research is required to identify an effective and consistent technique (Mones et al. 2023).

Mans (2014) summarizes intrathecal administration of preservative-free local anesthetics and opioids for surgical anesthesia of the hind end and for prolonged analgesia, respectively. Lidocaine (2%) injected intrathecally at an approximate dose of 1 mL per 25 kg in hybrid Galapagos tortoises (*Geochelone nigra*) was sufficient to perform phallectomy (Rivera et al. 2011). The technique provided adequate analgesia, without the need for supplemental systemic analgesics. The ambulatory function returned to normal within 60 minutes after administration in all the animals in the study.

The short analgesic effect limits the single administration use of local anesthetics to the perioperative period. To provide prolonged analgesia using local anesthetics, repeated administrations are required. For this purpose, the placement of long-term intrathecal catheters is possible in chelonians (Fig. 10.9).

Spinal anesthesia was used for surgical removal of cutaneous fibropapillomas in green sea turtles (*Chelonia mydas*) (Futema et al. 2020). Animals were administered 2% lidocaine (0.2 mL/10 cm of carapace) in the epidural/subarachnoid space of the tail. The technique was effective for all animals, with fast onset of motor and sensory blockade (3 ± 1.76 minutes) and relatively fast recovery time (83.9 ± 16.2 minutes). Fibropapillomas were removed from all animals with no signs of pain (i.e., no behavioral response during surgical procedure, such as head and forelimb movement, showing discomfort).

Although the authors are unaware of any toxicity studies in chelonians, the safe dosages for local anesthetics (lidocaine <10 mg/kg and bupivacaine <2 mg/kg) appear similar to those of mammals. The analgesic agents for which pharmacokinetic and pharmacodynamic data are currently available in chelonians are listed in Table 10.1 and summarized by Sladky (2023).

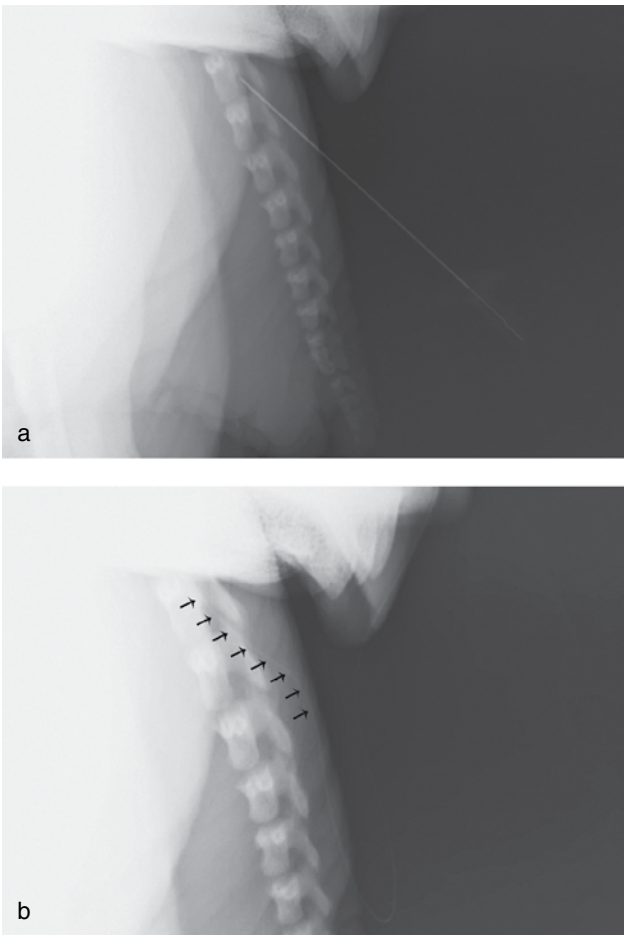


Figure 10.9 Lateral radiographic views of the placement of an inthathecal catheter in a Galapagos tortoise (*Chelonoidis nigra*). A Tuohy needle is slowly advanced between the spinous processes of two consecutive coccygeal vertebrae and placed in the vertebral canal (a) into the intrathecal space (space between dura mater and leptomeninx). The catheter is threaded through the needle and advanced a few centimeters into the vertebral canal (b). The needle is then withdrawn over the catheter. The catheter is secured to the skin with sutures to prevent it becoming dislodged. The catheter can be used for repeated administrations of analgesics and local anesthetics. The small black arrows indicate the catheter placed into the intrathecal space. Courtesy of the University of Florida.

Anesthetic Induction and Maintenance

Generally, induction and maintenance of anesthesia are relatively simple, but at times they can be particularly challenging and frustrating to the anesthetist.

Mask induction with inhaled anesthetics can be used, but is associated with pronged induction times and is not recommended for use alone. Aquatic species are well adapted to the episodic breathing pattern and able to stay apneic for very extensive periods of time, preventing the adequate delivery of inhaled anesthetic (Bienzle & Boyd 1992). Inducing respiration by gently moving the forelimbs forwards and backwards may reduce induction times.

Awake intubation and induction is more effective, but stressful to the animal. The mouth is forcibly opened and

Table 10.1 Analgesic agents used in chelonian species.

Drug	Dose (mg/kg)	Route	Analgesic Activity	Comments	Source
Buprenophine	0.075–0.1	IV, IM	Not established	Elevated drug plasma concentrations up to 24 hours	Kummrow et al. (2008)
Butorphanol	2.8–28	IM, IV	None	No analgesic effect even at high doses; at high doses prolonged respiratory depression	Sladky et al. (2007)
Lidocaine	0.8	Intrathecal	Good	Duration of analgesia up to 60 minutes; temporary paraparesis can occur	Rivera et al. (2011)
Lidocaine	1	SQ (local infiltration)	Moderate	Used alone not sufficient analgesia for celioscopy	Hernandez-Divers et al. (2009)
Meloxicam	0.2	SQ	Not established	Anecdotal evidence of clinical efficacy	McArthur (2004)
Meperidine	20	IV, IM	Good	Analgesic efficacy similar to morphine	Wambugu et al. (2010)
Morphine	1.5	IV, IM	Good	Dose-dependent respiratory depression	Sladky et al. (2007)
Tramadol	5–10	PO	Good	Long-lasting analgesic effect up to 96 hours	Baker et al. (2011)
Tramadol	10–25	SQ	Good	Slower onset and shorter duration of analgesia compared to PO administration	Baker et al. (2011)

IM, intramuscular; IV, intravenous; PO, per os; SC, subcutaneous.
Where possible recommended dosages are based on published pharmacokinetic and pharmacodynamic data. Sladky (2023) gives a comprehensive review of reptile analgesia.

the endotracheal tube inserted through the glottis. This allows controlled ventilation to deliver the inhaled anesthetic. Large tortoises, however, are unbelievably powerful animals and are impossible to forcibly intubate without sedation. Furthermore, strong laryngeal sphincter muscles seal the glottis of aquatic species, making awake intubation difficult. Repeated attempts to force open the closed glottis are not recommended due to risk of causing severe tissue damage. Instead, gentle manipulation and patience in waiting for the animal to voluntarily open the glottis often facilitate the intubation. A short piece of PVC pipe used as mouth gag facilitates intubation and protects the endotracheal tube (Fig. 10.10).

Injectable sedative and anesthetic agents are commonly administered intramuscularly due to the difficulty of gaining IV access without previous sedation. Intramuscular (IM) administration of ketamine combined with benzodiazepines or alpha-2 adrenergic agonists often produce adequate sedation and muscle relaxation. The pectoral muscles are a preferred site for IM injections. Alternatively, the triceps muscle may be used when accessible in larger animals. Reported parenteral drug combinations and dosages are given in Table 10.2, and recommended induction and anesthesia protocols are discussed at the end of the chapter.



Figure 10.10 A piece of PVC pipe used as an oral speculum facilitates intubation and protects the endotracheal tube. Both the mouth-gag and the endotracheal tube are secured with tape to the head of the animal to prevent dislodgment.

In some species the presence of easily accessible veins and venous sinuses facilitates direct IV administration of anesthetics. In sea turtles, the cervical venous sinus is an easily accessible site for injection (Moon & Hernandez

Table 10.2 Selected sedative and anesthetic protocols used in chelonian species.

Species	Protocol (Drug)	Dose (mg/kg)	Route	Onset (Minutes)	Reversal (Drug and Route)	Recovery (Minutes)	References
Aldabra tortoises *Aldabrachelys gigantea*	Medetomidine + ketamine + morphine	0.03 3 0.4	IM	30–45	Atipamezole IM Naloxone IM	Up to 45	Vigani (2010)
Aldabra tortoises *Aldabrachelys gigantea*	Medetomidine + ketamine	0.025–0.08 3–8	IV	45	Atipamezole IV	Up to 15	Lock et al. (1998)
Chinese box turtles *Cuora flavomarginata*	Medetomidine + ketamine + morphine	0.1 10 1.5	IM	30	Atipamezole IM Naloxone IM	Up to 21	Hernandez-Divers et al. (2009)
Desert tortoises *Gopherus agassizii*	Medetomidine	0.15	IM	20	Atipamezole IM	30–60	Sleeman & Gaynor (2000)
Desert tortoises *Gopherus agassizii*	Sevoflurane	5% in O_2	Inhaled	5	Not administered	Up to 35	Rooney et al. (1999)
Florida soft-shell turtles *Apalone ferox*	Tricaine (MS-222)	1 g/L	Immersion	Not specified	Not administered	Not specified	Bagatto et al. (1997)
Galapagos tortoises *Chelonoidis nigra*	Medetomidine + ketamine	0.1 10	IV	11	Not administered	Up to 70	Knafo et al. (2011)
Galapagos tortoises *Chelonoidis nigra*	Medetomidine + ketamine + morphine	0.02 2 0.4	IM	30	Atipamezole IM Naloxone IM	Up to 60	Vigani (2010)
Gopher tortoises *Gopherus polyphemus*	Medetomidine + ketamine	0.1 5	IV	Not specified	Atipamezole	Not specified	Dennis & Heard (2002)
Greek tortoises *Testudo greca*	Alphaxalone/alphadolone	9–16	IM	25–40	Not administered	Up to 4 hours	Lawrence & Jackson (1983)
Kemp's ridley sea turtle *Lepidochelys kempi*	Medetomidine + ketamine	0.015–0.03 2.5–3	IV	15	Not administered	200	Smith et al. (2000)
Leatherback sea turtles *Dermochelys coriacea*	Medetomidine + ketamine	0.03–0.1 3–12	IV	20	Atipamezole IV	Up to 120	Harms et al. (2007)
Loggerhead sea turtles *Caretta caretta*	Alfaxalone	3–10	IV	Rapid	None	Up to 90	Phillips et al. (2017)
Leopard tortoises *Geochelone pardalis*	Medetomidine + ketamine	0.1 5	IV	16	Atipamezole IV	Up to 30	Lock et al. (1998)

(*Continued*)

Table 10.2 (Continued)

Species	Protocol (Drug)	Dose (mg/kg)	Route	Onset (Minutes)	Reversal (Drug and Route)	Recovery (Minutes)	References
Loggerhead sea turtle *Caretta caretta*	Propofol	5	IV	2	Not administered	Up to 170	MacLean et al. (2008)
Loggerhead sea turtle *Caretta caretta*	Medetomidine + ketamine	0.05 5	IV	9	Atipamezole IV	Up to 84	Chittick et al. (2002)
Red-eared sliders *Trachemys scripta elegans*	Propofol	10–20	IV	2–4	Not administered	90–120	Ziolo & Bertelsen (2009)
Red-eared sliders *Trachemys scripta elegans*	Medetomidine + ketamine	0.1–0.2 5–10	IM	Not specified	Atipamezole IM	60	Greer et al. (2001 a&b)
Red-eared sliders *Trachemys scripta elegans*	Midazolam	1.5	IM	6	Not administered	40	Oppenheim & Moon (1995)
Side-neck turtle *Podocnemis expansa*	Xylazine + propofol	1.5 5–10	IM IV	1–2	Not administered	156–198	Santos et al. (2008)
Snapping turtle *Chelydra serpentine*	Ketamine + midazolam	20–40 2	IM	15	Not administered	210	Bienzle & Boyd (1992)
Soft-shell turtle *Pelodiscus sinensis*)	Lidocaine	700 mg/L	Immersion	6	Not administered	5	Park et al. (2006)
Yellow-footed tortoises *Geochelone denticulata*	Medetomidine + ketamine	0.1 5	IV	16	Atipamezole IV	Up to 30	Lock et al. (1998)

IM, intramuscular; IV, intravenous.

Foester 2001). It is often used for induction, but limited information is available on the rate of distribution of anesthetics using this route. If the desired effect is not achieved at the recommended dosage of a drug, it is recommended not to repeat the administration to avoid over-dosage (Wood et al. 1982).

The dorsal coccygeal vein is in the present authors' experience a safe and reliable site for IV injection in unsedated snapping turtles (*Chelydra* spp. and *Macrochelys temminckii*). The subcarapacial venous sinus is easily accessible for injections in small chelonians, however extravasation of drug is likely when this access is used. The subcarapacial sinus runs close to the subdural space where the cervical vertebrae join the carapace. As described above, deaths in gopher tortoises (*Gopherus polyphemus*) have been associated with the inadvertent injection of propofol into this space while attempting subcarapacial injection (Quesada et al. 2010).

When the IV route is utilized, propofol titrated to effect is a good choice for induction of anesthesia. Di Giuseppe et al. (2018) showed major differences in induction times and effects between occipital sinus, subcarapacial sinus, and dorsal coccygeal vein injection (5 mg/kg). Although occipital and subcarapacial injections provided the fastest inductions, we do not recommend these routes for injection other than for euthanasia. Di Giuseppe et al. (2018) also found limited to no effect from the coccygeal vessel injection. In the present authors' experience the induction times for this site can be prolonged and the authors may not have waited long enough for peak effect (sometimes 30 minutes or more). Used as a single agent, propofol requires doses between 4 and 8 mg/kg to produce anesthesia.

Alternatively, the combination of ketamine (5 mg/kg) and medetomidine (0.05 mg/kg) given intravenously appears to be safe in many aquatic and terrestrial species. Although no longer available, alfaxalone/alfadolone at 24 mg/kg given intracoelomically was shown to produce surgical anesthesia in red-eared sliders (Lawrence & Jackson 1983). A new formulation of alfaxalone (Alfaxan®) is now available, but it does not produce analgesia. It can be administered intravenously or intramuscularly for short surgical procedures, at the same dosages described for the previous mixture. The low concentration (10 mg/mL), however, precludes IM, as well as subcutaneous, injection in large tortoises. It can be used at a low dosage (and volume) as part of a multidrug anesthetic combination.

Soft-shell aquatic turtles appear to possess an amphibian-like modality of fluid absorption across nonenteral surfaces (e.g., skin and mucous membranes beside the enteral mucosa) (Bagatto et al. 1997). In spiny and Florida soft-shell turtles (*Apalone apinifera* and *Apalone ferox*, respectively), tricainemethane sulfonate (MS-222) has been tested as an immersion anesthetic. A concentration of 1 g/L provided a quick onset of surgical anesthesia. All the animals in the study survived and the technique was considered safe by the authors (Bagatto et al. 1997). Lidocaine-hydrochloride diluted in bicarbonate-buffered water was also used as anesthetic in soft-shelled turtles (*Pelodiscus sinensis*). Immersion at 700 mg/L produced anesthesia within 6 minutes after exposure. Recovery time was short after removal of the animal from the anesthetic solution (Park et al. 2006).

Succinylcholine and other neuromuscular blocking agents alone have been used in the past for immobilization of chelonians. This class of drugs does not have any anesthetic or analgesic properties and the patient is completely conscious while paralyzed. The depolarization before muscle relaxation associated with succinylcholine also causes pain, lactic academia, and hyperkalemia. For these reasons, the use of neuromuscular blocking agents alone for immobilization is considered unacceptable.

Endotracheal intubation is facilitated by the use of a tongue depressor to better expose the glottis. In aquatic turtles there is abundant soft tissue at the base of tongue, which can make visualization of the glottis difficult (Fig. 10.11).

Gentle upwards pressure on the skin surface between the mandibular branches helps to expose the glottis. The size of endotracheal tube can be estimated either by external palpation of the trachea or by visualizing the glottal diameter during inspiration. The glottal opening is usually smaller than the tracheal diameter. Cuffed endotracheal tubes can be used, but overinflation of the cuff can potentially cause tracheal injury. The trachea is relatively short, particularly in sea turtles, and the selective intubation of a bronchus is possibly if a long endotracheal tube is inserted too far.

Immobility has a substantial negative impact on ventilation due to the important role of limb movement for lung expansion (Taylor et al. 2010; Gatten 1974a). The respiratory drive is also depressed by the direct effect of anesthetic agents on the respiratory centers. This predisposes the patient to hypoxemia and hypercapnia. Hypoventilation also prevents the constant delivery of anesthetic when inhalation anesthesia is used. Manual or mechanical intermittent positive pressure ventilation (IPPV) is therefore recommended for general anesthesia. Tidal volumes are highly variable and influenced by species and body position. Sea turtles have much higher tidal volumes compared to terrestrial tortoises (Lutcavage & Lutz 1996). The lung compliance is also much lower in dorsal recumbency compared to ventral recumbency (Lutcavage et al. 1989). Concerns exist to the possible



Figure 10.11 Glottal apparatus of an alligator snapping turtle (*Macrochelys temminckii*) during breath-holding (a) and inspiration (b). Note the perfect seal of the closed glottis. Waiting for the animal to voluntarily open the glottis facilitates the endotracheal intubation.

detrimental effect of positive pressure ventilation on the cardiovascular system. However, examination of the effect of artificially manipulating lung volume on blood flows and heart rate in the freshwater turtle (*Trachemys scripta elegans*) showed increases in lung volume have no effect on pulmonary blood flow (Herman et al. 1997).

It is difficult to assess effective artificial ventilation in the clinical setting. Current recommendations for IPPV are 2 to 6 breaths per minute using tidal volumes ranging from 15 to 20 mL/kg, with peak airway pressures less than 10 cmH_2O. In intubated chelonians Heard used a capnograph to monitor adequacy of ventilation, as well as spontaneous ventilation. End-tidal CO_2 usually starts around 20 mmHg. Values below 10 or above 30 mmHg appear to be indicative of either hypocapnia (excessive ventilation) or hypercapnia (too little ventilation). Return to spontaneous ventilation is very difficult to visually assess in chelonians. Hence, capnography can be a sensitive monitor to determine normal respiration, especially in the recovery period.

For pronged procedures, anesthesia can be maintained by use of supplemental doses of the drug combination used for induction or more commonly by use of inhaled anesthetics. Gaining familiarity with multiple anesthetic agents and protocols in different species allows prediction of the patient response and the duration of effect of each specific anesthetic agent or combination.

Important aspects of patient care during anesthesia include continuous patient monitoring, appropriate fluid therapy, maintenance of the specie's preferred body temperature, appropriate analgesia, and lubrication of the eyes. In giant tortoises the protection of the limbs and the phallus (frequently prolapsed in males during anesthesia) is also critical for avoiding severe crushing injuries caused by the weight of the anesthetized animal.

Monitoring

The extreme physiologic resilience of reptiles should never be considered an excuse to overlook constant assessment of an anesthetized patient. Information is now available on the application of several types of monitoring equipment in chelonian anesthesia (Bailey & Pablo 1998; Mosley et al. 2004; Hernandez-Divers 2004). The accuracy and reliability of much of this equipment, however, is only beginning to be determined and for the most part has not been validated. This underlines the importance of the role of the anesthesiologist in the constant direct assessment of anesthetic depth, cardiopulmonary function, body temperature, and other physiologic parameters.

Anesthetic Depth

The accurate assessment of anesthetic depth is challenging. Several authors have previously proposed guidelines for the assessment of the stage of anesthesia in chelonians (McArthur 2004). Stages 1 and 2 are associated with minimal muscle relaxation, persistence of head withdrawal reflex, and voluntary response to painful stimuli. These anesthetic stages are indicated for noninvasive or minimally invasive procedures.

Stage 3 (surgical anesthetic stage) is characterized by immobility, absence of head withdrawal reflex, marked muscle relaxation occurring cranio-caudally as anesthetic depth increases, and no voluntary muscle response to noxious stimulation. This is considered a suitable stage for performing invasive surgical or diagnostic procedures.

The deepest anesthetic stage (stage 4) represents severe medullary depression due to anesthetic overdose. This stage is associated with life-threatening, severe cardiovascular

depression and is clinically detected by the loss of all reflexes, including the vent and corneal reflexes.

In chelonians, hypoventilation and apnea are common during anesthesia, even at lighter stages. Therefore, the visual assessment of external signs of respiration does not represent a good indicator of anesthetic depth and ventilatory support should be provided to all anesthetized chelonians. Alternatively, intubated chelonians should be monitored with a capnograph. Heart rate is influenced by multiple factors, including temperature and oxygenation, making this an unreliable parameter for the assessment of anesthetic depth (McArthur et al. 2004; Krosniunas & Hicks 2003).

Cardiovascular Function

The main aim of cardiovascular monitoring is to ensure adequate blood flow to the tissue. Monitored variables include heart rate and rhythm, pulse, and changes in intravascular volume caused by blood loss. It has been reported that baseline heart rate in reptiles, maintained within its preferred optimal temperature zone, can be estimated using the formula $33.4 \times (Wt_{kg}^{-25})$ based on allometric scaling (Sedgwick 1991). However, insufficient data is available on the reliability of this calculation in chelonians. Furthermore, given heart rate is highly affected by variations in body temperature, any kind of approximation is of limited significance and potentially misleading during anesthesia.

Direct auscultation of cardiac sounds is a simple method of basic assessment of heart rate and rhythm. In anesthetized patients, an esophageal stethoscope can be placed into the thoracic esophagus to the level of the heart for direct auscultation. Since it may cause reflux of gastric contents, the trachea should be intubated prior to its placement. The stethoscope tubing has to be slowly advanced until the maximal sound intensity is reached. It can be connected to a standard stethoscope headpiece for intermittent monitoring or to a portable amplified speaker for continuous assessment.

The electrocardiogram (ECG) detects the electrical activity of the heart. It should be noted the presence of normal electrical activity does not indicate normal cardiac function. Myocardial conduction can continue despite absence of myocardial contraction, which is referred to as pulseless electrical activity, therefore the monitoring of cardiovascular function should not rely solely on an ECG. The ECG can be used as a standard three limb lead configuration, but the thick scaly skin limits its sensitivity in this configuration and requires the use of a hypodermic needle for effective lead attachment (Bailey & Pablo 1998). A base-apex ECG configuration represents a good alternative during anesthesia. Esophageal base-apex ECG lead configurations are commercially available in different sizes and are often combined on the same tubing with an esophageal stethoscope. For anesthetic monitoring, the ECG is usually viewed in lead II. The reptilian ECG tracing comprises three primary complexes: P wave, QRS complex, and T wave. An SV wave may precede the P wave and represents the depolarization of the sinus venosus (Fig. 10.12). As in mammalian species, the P wave and the QRS complex represent atrial depolarization and ventricular depolarization, respectively. The T wave indicates ventricular repolarization. In chelonians, this repolarization phase is physiologically prolonged (Holz & Holz 1995). Due to the paucity of research, there is still limited understanding regarding ECG interpretation in chelonians and reptiles in general (Kik & Mitchell 2005).

The use of an 8-Hz Doppler ultrasonic flow probe is a good alternative to direct auscultation to detect blood flow. It also allows the detection of pulse in major vessels. For these reasons many authors promote the Doppler as the most useful and reliable cardiovascular monitoring device in reptiles (McArthur 2004; Schumacher 2007). Several types of probes are available: adult and pediatric flat probes and pencil probes. In chelonians the pencil probe is most useful for the detection of cardiac blood flow. It is placed on either side of the neck on the ventral aspect of the thoracic inlet (Fig. 10.13). Flat probes can also be taped over the carotid arteries (ventro-lateral aspect of the neck), the coccygeal artery (base of the tail), and femoral arteries for continuous assessment of pulse rate and quality. Pediatric probes are preferred over adult probes due to the higher sensitivity in detecting flow in small vessels.

Determination of peripheral pulse rate and rhythm can also be obtained with the use of a pulse oximeter. As discussed in the next section, pulse oximetry is more often used as a respiratory monitor. Unfortunately, the use of pulse oximetry in chelonians for detecting pulse is limited by placement sites for the probe. Reflectance probes placed

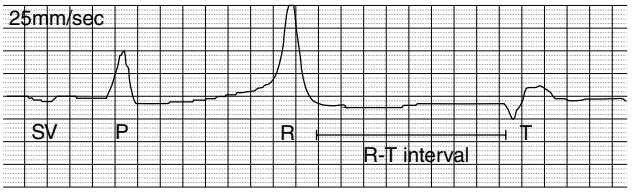


Figure 10.12 Electrocardiographic tracing of an anesthetized Galapagos tortoise (*Chelonoidis nigra*). On the tracing the following waves are identified: sinus venosus depolarization (SV), atrial depolarization (P), ventricular depolarization (R), ventricular repolarization (T). Note that systolic phase of the cardiac cycle is physiologically prolonged (the R-T interval is approximately 1.6 seconds).



Figure 10.13 Cardiovascular monitoring of a juvenile alligator snapping turtle (*Macrochelys temminckii*) during anesthesia. An 8-Hz Doppler pencil probe is placed on the side of the neck with the detecting crystal directed towards the thoracic inlet. The ECG is used in a standard three-limb lead configuration.

in the oral cavity or the cloaca may be a better choice. Some pulse oximetry units are extremely sensitive, and the presence of a strong pulsatile signal does not necessarily correlate with adequate blood flow to the tissues. When the probe is correctly applied, less than 10% of normal blood flow is required for pulse oximeters to detect a pulse (Bailey & Pablo 1998).

During surgery hemorrhage is common and monitoring blood loss is always indicated to determine the need for intervention. In small patients (<1 kg) any detectable blood loss can produce a significant decrease in circulating blood volume and consequent deterioration of patient homeostasis.

Respiratory Function

As discussed above, the direct visualization of respiratory movements such as thoracic excursions can be difficult. The presence of respiratory movements does not indicate adequate ventilation. The use of respiratory monitoring, therefore, is essential.

Arterial blood gas analysis is the ideal method for assessment of respiratory gas exchange, directly measuring the degree of oxygenation (arterial oxygen concentration, PaO_2) and ventilation (arterial carbon dioxide concentration, $PaCO_2$). Unfortunately, the clinical applicability of blood gas analysis in chelonians is limited. Arterial blood sampling in chelonians is difficult and impractical. Additionally, multiple blood draws can represent a significant blood loss in very small patients. Reptiles tend to tolerate alterations in $PaCO_2$ and PaO_2 much more than mammals and thus normal values for mammals may not be applicable (Hernandez-Divers 2004). In mammalian species, venous blood gas analysis can be used for assessing ventilation (venous CO_2 concentration approximates arterial concentration) but not oxygenation. However, the reliability of venous blood gas analysis in chelonians has not been demonstrated. For all of these reasons, the value of routine blood gas analysis in chelonians remains questionable. Other monitoring devices of respiratory function are capnometry and pulse oximetry.

Capnometry measures carbon dioxide concentration in expired gases ($PetCO_2$). In mammalian species capnometry is a noninvasive monitoring tool for assessing ventilation due to the good correlation between the end-tidal concentration of CO_2 and arterial CO_2 concentration. In chelonians this correlation is not consistent due to cardiac shunting. The absolute values of $PetCO_2$ therefore may not be a reliable indicator of arterial CO_2 due to the unpredictable gradient between end-tidal and arterial carbon dioxide (Hernandez-Divers 2004). Capnometry is best used over time to assess trends and to identify potential anesthetic complications. For this purpose, devices with graphing capability (capnograph) that display a continuous waveform (capnogram) are more useful than standard capnometers. Any large, sudden decrease in $PetCO_2$ requires further investigation. These drops are commonly associated with obstruction or kinking of the endotracheal tube, but can also be indicative of an abrupt decrease in cardiac output.

Mainstream and sidestream capnometry devices are commercially available. Mainstream analyzers use a detecting window inserted into the anesthetic circuit. A sensor mounted on the detecting window measures $PetCO_2$. Sidestream analyzers continuously aspirate gas from the anesthetic circuit, and the sensor for the analysis is located away from the ventilator circuit. There are some concerns when capnometry is used in small species. A large detecting window (mainstream) or sampling chamber (sidestream) attached to the endotracheal tube adds significant mechanical dead space. Pediatric connectors can reduce this added dead space. The sensor of mainstream devices may add an excessive amount of weight on the endotracheal tube, causing possible kinking. Sidestream devices require the continuous removal of gas from the circuit (100–200 mL/min) and in very small animals this sampling rate can be similar to or higher than the tidal volume of the patient. Veterinary designed sidestream capnometers such as the Capnovet-10 (Vetronic Services, Devon, UK) use smaller sampling volumes and are suitable for use in patients weighing less than 100 g (Stanford 2004).

Pulse oximetry is used to noninvasively measure the oxygen saturation of arterial hemoglobin (SpO_2). A plethysmograph (to detect pulsatile blood flow) and a combined

spectrophotometer (to measure changes in light absorbance) constitute the functional components of a pulse oximeter. Although pulse oximetry is one of the most commonly used anesthetic monitoring devices in reptiles, its technical limitations and high susceptibility to measurement errors and artifacts should be considered. Pulse oximetry has been designed for use in mammals, meaning it detects typical mammalian pulse and is calibrated using the mammalian oxygen hemoglobin dissociation curve. In reptiles, the characteristics of these variables are markedly different when compared with mammals (Frische et al. 2001). In green iguanas it was shown the absorbencies for oxyhemoglobin (660 nm) and deoxyhemoglobin (990 nm) were in agreement with mammalian references, indicating that pulse oximetry could be reliable in certain reptile species (Diethelm et al. 1998). Unfortunately, the transmittance probes used in mammals do not provide consistent readings when applied to the skin of reptiles. Reflectance probes are more easily placed inside the esophagus or the cloaca to maximize the chance of reading. In the green iguana a reflectance pulse oximeter probe placed in the esophagus and was inaccurate (Mosley et al. 2004). Reptile blood generally contains higher physiologic concentrations of methemoglobin than mammals, which can cause artifacts in SpO_2 readings. Therefore, as for capnography, pulse oximetry is best used to look at the trends in measurements, rather than at the absolute saturation values.

Body Temperature

As in all ectothermic animals, normal thermoregulation in chelonians results from the direct interaction between the animal and the external environment. A series of behavioral patterns and modulations of the cardiovascular system tightly regulate the amount of heat derived from the environment (Galli et al. 2004). During anesthesia, all of these mechanisms are blunted or even abolished and hypothermia is a common occurrence. The direct effect on the cardiovascular system is a progressive decrease in cardiac output and an increase in intracardiac shunting (Krosniunas & Hicks 2003). The anesthetist, therefore, is responsible for appropriately monitoring and modulating body temperature in anesthetized chelonians. The aim is to minimize variations from the species' preferred body temperature range allowing better patient homeostasis (Gatten 1974b). Intraoperatively, this goal is accomplished by appropriately insulating and actively warming the patient (Fig. 10.14).

Patient temperature can be continuously monitored using cloacal or esophageal probes. The patient should not be in direct contact with cold surfaces and should be covered with plastic drapes during prolonged surgical procedures to decrease the dispersion of internal heat. Warm water bottles, circulating warm water blankets, and forced warm air blowers, in ascending order of efficiency, also represent suitable tools for actively increasing and maintaining normothermia. When active warming is provided, attention should be paid to not overheating the patient. Increasing the temperature above the ATR increases oxygen consumption and the animal breathing room air (e.g., during the recovery period) may be unable to meet the increased oxygen demand. It should be noted that body temperatures above 38°C are lethal for most chelonian species.



Figure 10.14 Active warming the patient with a forced warm air blower (Bair Hugger®, Arizant Healthcare Inc., Eden Prairie, MN, USA). The maintenance of the patient's temperature within the preferred body temperature range is an important aspect of patient care in chelonians. Unpredictable disarrangement of the chelonian's homeostasis can occur in response to sudden changes in body temperature.

As mentioned in a previous section, the preferred body temperature or ATR in chelonians is species-dependent. For example, many freshwater turtles will tolerate temperatures between 20 and 25°C whereas sea turtles and land tortoises are better adapted to temperatures between 25 and 30°C (George 1996; McArthur et al. 2004).

Suboptimal temperatures are associated with decreased metabolic rate and consequent unpredictably prolonged clearance of anesthetic agents. When body temperature declines, recovery times are commonly prolonged while inhaled anesthetic requirements are reduced.

Blood Glucose

Monitoring blood glucose in juvenile patients and debilitated patients or during prolonged anesthesia is recommended to detect hypoglycemic episodes. However, the

occurrence of hypoglycemia in anesthetized chelonians has not been documented and the need for repeated glucose checks is debatable.

Recommended Sedatives and Anesthetic Agents

Injectable Drugs

Combinations of parenteral drugs belonging to different classes permit a reduction in the required dosages of each agent, therefore reducing their potential side effects. It has been shown multiple drug combinations provide better sedation, muscle relaxation, and shorter induction and recovery times compared to the use of single agents. The administration of specific antagonists for some classes of sedatives makes it possible to modulate the duration of their effect.

Alpha-2 Adrenergic Agonists

Alpha-2 adrenergic agonists are extensively used sedatives in chelonian anesthesia (Lock et al. 1998; Sleeman & Gaynor 2000; Holz & Holz 1994). The rapid onset of action, the potent sedation, and the possibility to reverse their sedative effect with specific antagonists are the major advantages of alpha-2 agonists compared to other sedatives. They are also characterized by a mild analgesic activity (Greer et al. 2001a). Alpha-2 adrenergic agonists are part of many anesthetic protocols owing to their synergistic effect with other agents, such as ketamine (Greer et al. 2001a; Chittick et al. 2002). Xylazine when combined with ketamine produced moderate sedation in freshwater turtles (*Trachemys*) (Holz & Holz 1994). Xylazine (1.5 mg/kg), administered intramuscularly, followed by IV induction with propofol (5 mg/kg), also produced moderate sedation for 2.5 hours in Amazonian turtles (*Podocnemis expansa*) (Santos et al. 2008). In loggerhead sea turtles (*Caretta caretta*), medetomidine (0.05 mg/kg) combined with ketamine (5 mg/kg) was shown to produce rapid induction (Chittick et al. 2002). Wild leatherback sea turtles (*Dermochelys coriacea*) were effectively immobilized for measurement of physiologic variables with a combination of medetomidine (0.03–0.08 mg/kg) and ketamine (3–8 mg/kg) (Harms et al. 2007). In Galapagos tortoises (*Geochelone nigra*) medetomidine (0.1 mg/kg) and ketamine (10 mg/kg) given intravenously as a combination produced a surgical plane of anesthesia sufficient to perform celioscopy for about 45 minutes (Knafo et al. 2011). In adult Aldabra tortoises (*Aldabrachelys gigantea*), IM medetomidine (0.02–0.03 mg/kg), ketamine (2–3 mg/kg), and midazolam (0.1 mg/kg), have been used by the author as an induction and maintenance anesthetic protocol for both diagnostic and minor surgical procedures.

Pronounced cardiopulmonary side effects, however, are common after administration of alpha-2 adrenergic agonists in chelonians and appear to be similar to those seen in mammals (Dennis & Heard 2002). The effect of alpha-2 adrenergic agonists on the cardiovascular system appears to be dose-unrelated. Bradycardia and hypoxemia were described in desert tortoises (*Gopherus agassizii*) sedated with medetomidine (0.15 mg/kg) (Sleeman & Gaynor 2000). Medetomidine (0.1 mg/kg) produced good sedation, but also moderate bradycardia in leopard tortoises (*Geochelone pardalis*) and yellow-foot tortoises (*Geochelone denticulata*) (Lock et al. 1998). Similar effects were seen in Aldabra tortoises (*Aldabrachelys gigantea*) at a dose of 0.025–0.08 mg/kg (Lock et al. 1998). In gopher tortoises, the combination of medetomidine (0.1 mg/kg) and ketamine (5 mg/kg) produced moderate hypertension, hypercapnia, and hypoxemia (Dennis & Heard 2002). For these reasons, the use of supplemental oxygen is highly recommended when alpha-2 adrenergic agonists are used.

Severe cardiovascular changes can be also caused by the IV administration of reversal agents. The antagonist atipamezole (0.5 mg/kg) given IV was demonstrated to produce severe hypotension and even undetectable carotid pulse in gopher tortoises (*Gopherus polyphemus*) (Dennis & Heard 2002). Based on these findings, it is recommended to utilize the IM route for injection of the reversal agent of alpha-2 agonists.

The stereoisomer dexmedetomidine is now commonly used in veterinary anesthesia. Its potency in mammals appears to be twice as high as that of medetomidine (Kuusela et al. 2001). There are no published studies on the sedative effect of dexmedetomidine in chelonians. Medetomidine is still commercially available as a compounded preparation at high concentrations (10, 20, and 40 mg/mL). In large chelonians (>100 kg), these concentrated solutions are a good choice for IM administration to significantly reduce the volume of injection.

Ketamine

Ketamine is a dissociative anesthetic commonly utilized in many reported anesthetic protocols for chelonians. Ketamine has a large margin of safety due to its supportive cardiovascular effects and its lower respiratory depression when compared to other induction agents, such as barbiturates and propofol. Used alone, ketamine requires very high dosages to produce general anesthesia in chelonians (30–50 mg/kg), does not produce adequate muscle relaxation, and is associated with prolonged induction and recovery times of up to 24 hours (Holz & Holz 1994). The combination of ketamine with other sedatives produces a

synergistic effect at reducing the doses of the single agents. Benzodiazepines, alpha-2 adrenergic agonists, opioids, and potentially alfaxalone improve the anesthetic profile of ketamine, producing better muscle relaxation and making it possible to obtain a plane of anesthesia more suitable for surgical interventions (Chittick et al. 2002). Benzodiazepines are primarily added to produce muscle relaxation (Bienzle & Boyd 1992). Alpha-2 adrenergic agonists are often used to significantly decrease the ketamine dose and to achieve deeper anesthetic planes (Greer et al. 2001b; Lock et al. 1998; Harms et al. 2007). Medetomidine and xylazine added to ketamine is a very common induction protocol for both aquatic and terrestrial species. Several dosing regimens have been reported in different chelonians, showing significant interspecies variability in dose and sedative effect (see Table 10.2). Ketamine also has intrinsic analgesic properties due to its antagonist effect on N-methyl-D-aspartate receptors. The presence of this type of receptor has been demonstrated in chelonians (Bickler et al. 2000). The analgesic effect of ketamine is mild and short-lived for treatment of surgical pain and superior analgesia is provided by the use of a multimodal approach. The addition of more potent systemic analgesics, such as opioids, and the use of local anesthetics are recommended for management of acute surgical pain.

Tiletamine/Zolazepam

The moderately potent and long-acting dissociative anesthetic tiletamine is usually combined with the long-acting benzodiazepine zolazepam. It has usually been avoided for use in chelonians because of the potential for prolonged recoveries. In Heard's experience, however, chelonians are surprisingly resistant to the effects of this combination, requiring relatively high dosages and only showing a relative short period of immobilization. For example, immobilization of the African spurred tortoise requires up to 30 mg/kg IM.

Propofol

Propofol is a fast-acting hypnotic agent formulated for IV injection only. Several reports describe the safety of propofol as an induction agent in several chelonian species (McArthur 2007; Ziolo & Bertelsen 2009; Smith et al. 2000) (see Table 10.2). Propofol produces induction of general anesthesia within 1–2 minutes after injection (Santos et al. 2008). The duration of effect is usually 30–45 minutes at the typical dosages of 2–10 mg/kg. Large species appear to require lower doses compared to small chelonians (McArthur 2004). In a study in loggerhead sea turtles (*Caretta caretta*), propofol (5 mg/kg) produced an adequate plane of anesthesia for laparoscopic sex determination. The duration of effect lasted 30 minutes (MacLean et al. 2008). Prolonged apnea following induction with propofol is a common complication in chelonians and prompt intubation and manual ventilation are therefore required. Dose-dependent hypotension can be severe following rapid administration. Slow injection over 1 minute allows the anesthetist to titrate the administration to the desired effect, minimizing the cardiovascular depression. Propofol does not have any analgesic activity and it should always be combined with analgesics when performing surgical procedures. Propofol given as a constant rate infusion (0.2–0.4 mg/kg/min) or as incremental boluses (0.5–1 mg/kg) is suitable for maintenance of anesthesia in mammals, but the safety and the appropriate rates of infusion in reptiles have not been determined. The fast induction and recovery time and the possibility of modulating the effect by adjusting the dose make propofol the author's (A. Vigani) anesthetic of choice whenever the IV route is accessible.

Midazolam

Midazolam is a benzodiazepine with similar potency to diazepam. Compared to diazepam, the more hydrosoluble molecule of midazolam produces more constant absorption and better bioavailability after IM injection. Midazolam used alone, even at dosages 10 times higher than the therapeutic doses for mammals, was repeatedly shown not to produce significant sedation in some chelonian species (Harvey-Clark 1993). In sliders (1.5 mg/kg IM) provided moderate sedation with minimal cardiovascular and respiratory changes (Oppenheim & Moon 1995). In snapping turtles (*Chelydra serpentina*), the combination of midazolam and ketamine appeared to produce better sedation and muscle relaxation compared to use of single agents (Bienzle & Boyd 1992). General anesthesia, however, could not be achieved even at high dosages. The recommended dosages for chelonians range between 0.1 and 1 mg/kg. When midazolam is used in chelonian anesthesia, it is suggested to combine it with other agents, such as ketamine or propofol, to produce adequate anesthetic depth (Holz & Holz 1994; Wood et al. 1982). The sedative effect of midazolam can be reversed by the specific antagonist flumazenil (0.01–0.04 mg/kg).

Alfaxalone

Alfaxalone is a neuro-steroid that exerts its anesthetic effect by binding to GABA receptors. It was originally introduced in the 1970s as a mixture with alfadolone for induction of anesthesia. The trade name of the compound in the veterinary market was Saffan®. This formulation was later withdrawn from the market because of the occurrence of lethal anaphylactoid reactions in small animals.

These adverse effects were induced by the presence in the compound of Cremophor EL® as a solubilizing agent.

Recently alfaxalone, as a new water-soluble formulation, has been reintroduced to the veterinary market under the brand name of Alfaxan®. The water solubility of this preparation is due to the binding of the alfaxalone molecule to a cyclodextrine molecule. This mixture does not cause histamine release, unlike the old formulation. The physiological effects of alfaxalone are identical to those of propofol and include dose- and rate-dependent cardiopulmonary depression and hypotension.

Unlike propofol, alfaxalone can also be administered via the IM route, providing a possible alternative of anesthetic induction when vascular access is not available. It should be noted, however, that the use of the IM route requires higher dosages compared to the IV route. In chelonians alfaxalone given IM produced anesthesia at a dosage of 10–20 mg/kg (Lawrence & Jackson 1983). Alfaxan® is available at a concentration of 10 mg/mL and its use in large chelonians (>10 kg) therefore may be limited by the very large volume of drug which then must be injected intramuscularly. It can, however, be used at a low dosage and relatively low volume (0.5–1 mg/kg) for its sedative effects as part of a multidrug induction combination.

Alfaxalone (3–10 mg/kg) IV in yearling loggerhead sea turtles (*Caretta caretta*) produced rapid induction (Phillips et al. 2017). The recoveries, as would be expected, were dose-dependent (up to 90 minutes). Similarly, the severity of cardiopulmonary effects increased with dosage. Hypoxemia and hypercapnia, associated with apnea in many animals, were most severe at the recommended induction dosage of 10 mg/kg. In red-eared sliders (*Trachemys scripta scripta*) alfaxalone IV had similar physiological effects as in loggerhead sea turtles, but the recommended dosages for good immobilization/relaxation were higher (10–20 mg/kg) (Shepard et al. 2013). Not surprisingly, the cooler (18–20°C) temperature turtles required a lower dosage to achieve the same effect as in warmer animals (22–25°C).

Neuromuscular Blocking Agents

The use of nondepolarizing neuromuscular blocking agents (NNMBAs) has been recently described to facilitate endotracheal intubation in chelonians (Kaufman et al. 2003). Nondepolarizing neuromuscular blockers have a much safer toxicological profile compared to depolarizing agents such as succinylcholine. NNMBAs do not have any anesthetic or analgesic activity, therefore they should never be utilized alone for immobilization. They must be considered only as complementary to a balanced anesthetic technique. Rocuronium is a NNMBA with rapid onset and intermediate duration of action. Rocuronium (0.2 mg/kg IM) has been shown to permit endotracheal intubation in Gulf Coast box turtles (*Terrapene carolina major*) and in Amazon turtles (*Podocnemis expansa*) within 15 minutes after administration (Kaufman et al. 2003; Scarpa Bosso et al. 2009). The effects of NNMBAs can be antagonized with neostigmine. In the studies mentioned above, recovery time (time to walking) from rocuronium occurred within 30 minutes after administration of neostigmine (0.04–0.07 mg/kg IM). Glycopyrrolate (0.01 mg/kg) can be coadministered with neostigmine to prevent its potential parasympathetic effects.

Inhaled Anesthetics

Currently, the inhalants isoflurane and sevoflurane are favored for maintenance of anesthesia in reptiles (Shaw et al. 1992). High concentrations of inhaled anesthetics and awake endotracheal intubation are required when these agents are used for induction. The potency of inhaled anesthetics is conventionally expressed as the minimal alveolar concentration (MAC). The values of MAC for isoflurane and sevoflurane in green iguanas (*Iguana iguana*) were 1.8% and 3.1%, respectively (Barter et al. 2006). Specific values of MAC for chelonian species have not been determined yet, but clinical evidence suggests the inspired concentrations required for surgical anesthesia are similar to the ones reported for other reptiles. Sevoflurane, by virtue of its low solubility in blood, is associated with faster anesthetic induction and recovery times when compared to isoflurane in mammals. Similar findings were shown in reptiles. In green iguanas (*Iguana iguana*), recovery time was significantly longer in animals anesthetized with isoflurane (35 ± 27 minutes) when compared to sevoflurane (7 ± 4 minutes) (Hernandez-Divers et al. 2005). Recovery times after 2 hours of anesthesia with 2% isoflurane averaged 4 hours in Kemp's ridley sea turtles, whereas prolonged anesthesia in desert tortoises, induced and maintained with sevoflurane, was associated with recovery times averaging 30 minutes (Moon & Stabenau 1996; Rooney et al. 1999). However, the high intracardiac shunting typical of aquatic chelonians may have contributed to these significant differences.

Interestingly, it has been shown in green iguanas that the MAC of inhalants tends to decrease over time, most likely reflecting limitations to anesthetic uptake and distribution. The progressive decrease in anesthetic requirements could also suggest that for any given end-tidal anesthetic concentration, the plane of anesthesia may deepen over time during prolonged procedures (Brosnan et al. 2006). For this reason, it is important to constantly monitor the depth of anesthesia and to titrate the concentration of inhalant to decrease the risk of overdose.

Chelonians can voluntarily breath-hold and successful use of inhaled anesthetics requires controlled ventilation for adequate drug uptake and elimination. Pure oxygen is the carrier gas usually utilized with inhalants. However, experimental evidence suggests hyperoxia depresses ventilation in both terrestrial and aquatic chelonians (Glass et al. 1978). Hypoxia, however, appears to be a common anesthetic complication in chelonians, supporting the use of high inspired oxygen concentrations. Consequently, the ideal carrier gas mixture that would provide adequate oxygenation and maintain appropriate ventilation is still undetermined.

Inhalants do not provide any analgesia and therefore appropriate addition of analgesics is required for any surgical procedure. Intraoperative pain management and use of balanced anesthetic techniques will also decrease the requirements of inhalant and hence side effects. For example, the cardiovascular depression associated with inhalant anesthesia in reptiles, as in mammals, has been shown to be dose-dependent (Mosley et al. 2004). For this reason, the multimodal approach to chelonian anesthesia using injectable and inhaled agents has gained the favor of many investigators (Shaw et al. 1992; Moon & Hernandez Foester 2001; McArthur 2004; Chittick et al. 2002) (see Table 10.2).

Recovery

Recovery time from anesthesia appears to be prolonged in chelonians when compared to mammals exposed to the same anesthetic agent. This difference may be due to the lower efficiency of the metabolic pathways of reptiles (McArthur et al. 2004). Additionally, temperature significantly affects the metabolic rate and the cardiovascular physiology of chelonians (Krosniunas & Hicks 2003). Both represent critical factors affecting a timely and successful recovery from anesthesia. For instance, hypothermia is associated with a decrease in metabolic function, which could delay the clearance of many injectable agents. Additionally, the amplification of intracardiac shunting, occurring when body temperature is below the ATR, can decrease the elimination of inhaled anesthetics through the lungs. Warming the patient above the preferred temperature for the species is also discouraged owing to the risk of increased oxygen demand (Galli et al. 2004). Consequently, the maintenance of body temperature within the ATR is recommended. Respiratory depression also persists during the recovery period. Noticeably, chelonians can occasionally take spontaneous breaths in the early postoperative period, but these should not be misinterpreted as signs of complete recovery from anesthesia. It is recommended to maintain the patient intubated until consistent spontaneous ventilation and voluntary movements are present.

When using inhalation anesthesia it is important to adjust the vaporizer setting in relation to how soon a procedure will be ending, as well as the effects of the induction drugs. In some cases there will be little to no need to supplement anesthesia with an inhalant, but the chelonian should be intubated, monitored with a capnograph and ventilation adjusted based on end-tidal CO_2. The animals are recovered in either an incubator or warmed environment and extubation can occur when there is evidence of apparently adequate spontaneous respiration and/or the animal is ambulating.

There is evidence that catecholamines modulate cardiac shunting in chelonians (Overgaard et al. 2002). Particularly in *Trachemys*, epinephrine was shown to increase pulmonary blood flow by directly reversing the presence of right-to-left shunting. Several studies in alligators (Gatson et al. 2017) and chelonians (Balko et al. 2018; Goe et al. 2016; Greunz et al. 2018) have now shown epinephrine administered intramuscularly hastens recovery after inhalation anesthesia. Interestingly, this also seems to be true after total parenteral anesthesia (Heard, pers. obs.). This may be secondary to increased cardiac output, alterations of shunting, and better delivery to the routes of elimination/excretion. Goe et al. (2016) also showed electrical stimulation of the acupuncture site GV-26 hastened recovery in common snapping turtles (*Chelydra serpentina*). In addition to reversal of alpha-2 adrenergic agonists and midazolam with atipamezole and flumazenil, Heard also routinely uses epinephrine during recovery from anesthesia in chelonians and other reptiles without any observed adverse effects.

Recommended Anesthetic Protocols

Chelonians can be crudely divided into groups based on their response to anesthetic drugs, as well as their size. See Table 10.2 for published and recommended anesthetic regimens. Based on known effective drug dosages, the giant tortoises (Galapagos and Aldabra) and sea turtles appear very to moderately sensitive (Turner et al. 2001). As discussed below, the exception is the African spurred tortoise (Turner et al. 2001). Other dry-land tortoises (e.g., *Gopherus* spp.) seem similar and require the lower end of the drug dosages (McGuire et al. 2014). The freshwater aquatic turtles appear to require the highest drug dosages for a similar predictable immobilization. Box turtles appear to fall between the dry-land tortoises and freshwater turtles.

There is no single best drug for parenteral induction and maintenance in chelonians, rather a combination of drugs and techniques is used to promote a more rapid recovery and less adverse physiological effects (Table 10.2). Analgesia (Table 10.1) is also an essential component of any protocol for painful procedures and can be attained with a multimodal approach proportionate to the procedure and need (i.e., opioids, NSAIDs, and local/regional anesthesia).

The African spurred tortoise is the largest land tortoise from Africa. It has become a common chelonian in captivity because of its size and fecundity; hatchlings are also readily available for sale and they are easy to care for. Despite this, they pose a major challenge for veterinarians. In awake animals it is virtually impossible to access vessels for either collection of blood or for IV injection. Consequently, to work with this species in a clinical setting it is usually necessary to anesthetize them. Unfortunately, they are unusually resistant to the effects of anesthetic drugs and it is very difficult to even administer an IM, let alone an IV, injection. Surprisingly the best and most consistent anesthetic combination is tiletamine/zolazepam (10–30 mg/kg). Alternatively, an intramuscularly administered combination of medetomidine (dexmedetomidine) (50 μg/kg), ketamine (5–8 mg/kg), and midazolam (0.2 mg/kg) ± hydromorphone (0.2 mg/kg) can be used. When using either drug protocol it may take up to 30–45 minutes for peak effect after IM injection. Even then, there may be a narrow window of 10–15 minutes of relaxation sufficient to allow intubation.

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11

Snakes and Lizards (Squamates)

Catherine J.A. Williams, Tobias Wang, and Mads F. Bertelsen

Introduction

Sedation and anesthesia are essential to the veterinary care of lizards and snakes. They are required for surgery and other painful or invasive procedures, to facilitate handling, and to enhance the quality or safety of diagnostic procedures while minimizing stress and discomfort. The field of reptile anesthesia has undergone a gradual and continuing evolution from hypothermia and manual restraint to contemporary balanced and well-controlled anesthesia. However, there is still much to be learned and there continues to be value in defining, exploring, and improving protocols. Several excellent reviews on reptile anesthesia are available (Bertelsen 2019; Mans et al. 2019a,b; Perpiñán 2018; Schnellbacher et al. 2019; Schnellbacher & Shepard 2019; Sladky & Mans 2012a), but controlled clinical studies remain relatively scarce. In general, squamates are rather resilient or "tough" and life-threatening anesthetic complications are rare, but should obviously be avoided or at least minimized.

Taxonomy and Biology

The nomenclature and taxonomy of the class Reptilia remains controversial and continues to be revised (Burbrink et al. 2019; Pyron et al. 2013). The order Squamata is by far the most speciose group within Reptilia and contains more than 50 families and approximately 10,600 species of amphisbaenians (worm lizards), lizards, and snakes. While squamates thrive in very different habitats, range across a broad geographical distribution from the tropics to the near-Arctic, and vary tremendously in size from a few centimeters to 8 m, most anatomical and physiological features as well as reactions to anesthetic drugs are surprisingly uniform.

Anatomy and Physiology

Reptiles are ectothermic vertebrates with relatively low metabolic rates, usually some five to 10 times lower than that of a mammal at the same temperature (Nagy 2005). The low rates of oxygen consumption are reflected in the anatomy and physiology of their cardiorespiratory systems. Lizards, snakes, and other reptiles generally have low blood pressures as well as low heart and ventilation rates compared to mammals. Despite the anatomical differences, there are striking similarities in the regulation of pulmonary ventilation and cardiovascular functions that reflect the common evolutionary roots of reptiles and mammals (Taylor et al. 2010, 2014; West 2011).

Cardiovascular System

All reptiles possess two atria divided by a complete atrial septum (Jensen et al. 2019). Each atrium opens into the ventricle through a separate atrio-ventricular ostium guarded by valves, such that oxygen-poor blood enters the ventricle from the right atrium separately from the oxygen-rich blood that enters the ventricle from the left atrium. The ventricular wall of lizards and snakes has a thin compact layer and most of the myocardium is trabeculated, giving it a spongy appearance. The spongy myocardium accounts for most of the mass and allows a high ejection fraction (Jensen et al. 2014; Williams et al. 2019a). The ventricular anatomy is complicated and the lumen is divided into three major compartments by septa, primarily the vertical septum and muscular ridge. The three compartments are called the cavum arteriosum (contains the blood which is ejected into the systemic arteries), cavum pulmonale (which holds the blood destined for the pulmonary circulation), and the smaller cavum venosum. The atrioventricular valves play an important role in directing blood flows

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when these cava are filled during diastole (Jensen et al. 2014). Thus, the oxygen-rich blood that enters from the left atrium is primarily directed into the cavum arteriosum on the left side of the heart, whereas the oxygen-poor blood runs through the cavum venosum into the cavum pulmonale. During cardiac contraction (systole), the oxygen-rich blood enters the two aortic arches through the cavum venosum, whilst the oxygen-poor blood enters the pulmonary artery directly from the cavum pulmonale.

Since the three chambers remain in contact with each other during cardiac contraction, there are equal systolic blood pressures in the systemic and pulmonary arteries. Two exceptions, the python and varanid lizards, are discussed below. The normal arterial pressures of lizards and snakes are considerably lower than those of mammals, but may increase drastically during stress or restraint (Stinner & Ely 1993; Wang et al. 2001a) while large intraspecies pressure differences may correlate with the species' general activity level.

While the admixture of oxygen-rich and oxygen-poor blood flows entering the ventricle can be greatly reduced by the ventricular septa, the squamate heart has a large potential for intracardiac mixing and shunting of blood (Hicks 1998). This may occur as an overall left-to-right (L-R) shunt or a right-to-left (R-L) shunt; during normal conditions, shunting actually happens in both directions (Ishimatsu et al. 1996, 1988). An L-R shunt represents oxygenated pulmonary venous blood re-entering the pulmonary circulation, while an R-L shunt is deoxygenated systemic venous blood that bypasses the lungs and returns into systemic circulation. R-L shunting results in large reductions in the partial pressure of oxygen in the arterial blood (PaO_2) and hence results in very large alveolar-arterial PO_2 differences (Hlastala et al. 1985; Wang et al. 1998a). The effects of R-L shunts on arterial PCO_2 are much smaller (Malte et al. 2017).

The resistances in the systemic and pulmonary circulations largely determine the magnitude and direction of cardiac shunts. Thus, increased pulmonary vascular resistance diverts blood flows into the systemic circulation (R-L shunts) and vice versa (Galli et al. 2007). Any anesthetic that alters vascular resistances in the systemic or the pulmonary circulation is therefore likely to affect the cardiac shunt pattern. Systemic vasodilatation will tend to produce R-L shunts (Greunz et al. 2018), whilst systemic constriction, for example following alpha-adrenergic stimulation, will result in L-R shunts (Goe et al. 2016).

The cardiac shunt pattern of reptiles is highly regulated, where vagal innervation of smooth muscle in the pulmonary artery allows pulmonary vasoconstriction and promotes large R-L shunts (Filogonio et al. 2020; Taylor et al. 2009). Therefore, when vagal tone is high during breath holding, a low heart rate, low pulmonary perfusion, and large R-L intracardiac shunts result (Wang et al. 2001b). In contrast, periods of pulmonary ventilation are characterized by decreased pulmonary resistance, increased pulmonary blood flow, small R-L shunt, and tachycardia (Filogonio et al. 2016; Krosniunas & Hicks 2003). The functional significance of cardiac shunts remains unresolved, despite many proposed hypotheses (Burggren et al. 2020; Hicks 2002).

In contrast to most lizards and snakes, where large cardiac shunts are common, the vertical septum and muscular ridge (the two major septa that divide the squamate ventricle) are so well-developed in varanid lizards and pythons that the level of cardiac shunting is very small (Jensen et al. 2014). Contrary to all other squamates, these two separate groups also have high systemic arterial blood pressures and low pulmonary arterial pressures, i.e., ventricular pressure separation (Burggren & Johansen 1982; Jensen et al. 2010; Joyce et al. 2016; Wang 2003).

Respiratory System

The squamate glottis is located at the base of the tongue, quite rostrally in the oral cavity. The glottis is closed during most of the respiratory cycle, opening only during inspiration and expiration. This closed glottis breath-hold allows reptiles to have a super-atmospheric pressure in the lung, which combined with the high lung compliance leads to a relatively large volume of air available for gas exchange in these periods. This volume will be lost on intubation, as the glottis is held open. The trachea of squamates has incomplete cartilaginous rings, while those of chelonians and crocodilians have complete tracheal rings (Kardong 1972a,b; Perry 1998). Most squamates have paired unicameral lungs where the gas exchange surface is enlarged by deep, narrow faveoli. Lizards and more basal snakes have two roughly symmetrical lungs, while the left lung is reduced in size or absent in more derived snakes and in amphisbaenians the right lung is reduced. The gas exchange surface of some snake lungs lie along the trachea (van Soldt et al. 2015) and gas exchange occurs in the cranial portion of the snake lung, while the caudal portion is typically reduced to an air sac-like structure. In iguanas and monitor lizards, the airflow has been found to be unidirectional during normal breathing, potentially allowing greater efficiency of gas exchange (Cieri & Farmer 2016).

Both the relative lung volume and the compliance of the reptilian lung far exceeds that of mammals, but the surface available for gas exchange is considerably smaller due to the structure of faveoli in comparison with the alveoli of mammals. The barrier between the air and blood is also

thicker than in the mammalian lung, so the pulmonary diffusion capacity for both O_2 and CO_2 is considerably smaller than in mammals (Glass 1991; Perry 1983; Starck et al. 2015).

The basic breathing pattern of most species of lizards and snakes consists of single breaths, each starting by opening of the glottis and an exhalation driven by elastic recoil that, in some species, may be assisted by active contraction of the hypaxial musculature. Inhalation is always active, and is typically followed by a period of breath-holding that may last a few seconds to many minutes or even hours depending on metabolism (Milsom 1991). The breathing pattern varies enormously amongst squamates. In many species, the breathing pattern consists of single individual breaths, whereas other species cluster their breaths into ventilatory episodes of numerous (typically three to 15) breaths and longer nonventilatory periods (Milsom 1991; Wang et al. 1998b). A given species may change between these breathing patterns when metabolism changes in response to altered body temperature, digestion, physical activity, or disturbance.

Reptiles, most notably freshwater turtles, are remarkably resistant to ambient hypoxia. While green iguanas can breath-hold dive *in extremis* up to 4.5 hours (Moberly 1968), chelonians may survive complete environmental anoxia for hours or days at their normal body temperatures and weeks to months at the low temperatures of winter hibernation (Belkin 1963; Ultsch 1985). An increase in body temperature leads to increased metabolic oxygen consumption, and consequently to requirement for increased ventilation.

Implications for Inhalational Anesthesia

The large R-L shunts of most squamates mean that systemic arterial PO_2 (PaO_2) is much lower than that of the lungs. In rattlesnakes, for example, Wang et al. (1998a) documented a PO_2 difference of almost 100 mmHg at 15°C that could be attributed to R-L shunt. There is probably also a contribution from V/Q inhomogeneity and pulmonary shunts (Powell & Hopkins 2004). In comparison, the pulmonary to arterial difference created by a small physiological shunt in mammals and birds is minor. The consequence of R-L shunting may be that induction and recovery from inhalational anesthesia is slower and less predictable than in mammals and birds. These effects are most pronounced in chelonians, where flow patterns may be altered by drugs reducing the resistance of pulmonary arteries, therefore reducing R-L shunt (e.g., atropine) (Filogonio et al. 2014, 2016; Greunz et al. 2018), or those increasing systemic resistance and cardiac output (e.g., adrenaline) (Goe et al. 2016).

Vascular Access Sites

The most reliable vascular access site is the ventral tail vessels, located immediately ventral to the coccygeal vertebrae. In snakes, these vessels are mostly approached from the ventral midline, but in many lizards a lateral approach is often more convenient. The palatine veins may be accessed in larger anesthetized snakes (Fig. 11.1). Indwelling catheters may be placed in the cephalic, femoral, abdominal, or ventral cervical vessels using cut-down techniques. Fluids and certain drugs may be administered by the intraosseus route. In lizards, intraosseus catheterization may be performed in the humerus, femur, or tibia following local analgesia of the cannulation site. Cardiac puncture for drug administration as well as for obtaining mixed arterial/venous blood samples is an option in snakes, but minor damage to the myocardium following cardiac puncture has been documented in ball pythons (Isaza et al. 2004; McFadden et al. 2011) the procedure is likely stressful and these authors see the approach as a last resort.

Preanesthetic Considerations

Body weights vary markedly, and an accurate weight should be obtained prior to administering drugs to the reptilian patient. The hydration status of the subject should be assessed and abnormalities corrected. Animals should be subjected to a physical examination prior to anesthesia and if time, budget, and facilities allow, a blood sample for packed cell volume, complete blood count, and plasma biochemistry profiles, as well as ultrasonographic or radiographic imaging may aid in preanesthetic evaluation.



Figure 11.1 Placement of an over-the-needle catheter in the palatine vein of an anesthetized Burmese python (*Python bivittatus*). Care must be taken to avoid the palatine teeth. It is recommended the catheter be removed prior to recovery.

Withholding food prior to surgery is not generally indicated, but large quantities of feed in the stomach may theoretically impair pulmonary function. In infrequently feeding snakes, massive increases in oxygen consumption and cardiac output follow feeding (Enok et al. 2016; Overgaard et al. 1999; Secor et al. 2000), as do increases in organ weights (Andersen et al. 2005; Secor & Diamond 1997). As these factors are all likely to increase the risk of anesthetic complications, elective procedures should be avoided in recently fed snakes. That said, no effect on recovery times was found in garter snakes anesthetized 1, 2, 3 and 10 days post feeding (Preston et al. 2010).

Maintaining Body Temperature

Induction time, anesthetic dose, and recovery time (Arena et al. 1988; Dohm & Brunson 1998; Green et al. 1981; Preston et al. 2010) as well as general metabolism are all temperature dependent and maintaining the animal's body temperature within the preferred optimum zone (POZ) is highly beneficial. This can be achieved by placing the animal on heating pads, circulating water blankets, water bottles, beanbags etc. For most temperate and tropical species, a body temperature of 25–35°C during induction, anesthesia, and recovery will be appropriate. In garter snakes anesthetized with methohexital, recovery time at 21°C was twice as long as at 31°C (Preston et al. 2010), and warming animals toward the high end of the POZ once the procedure is over may be attempted to hasten recovery. This approach, however, requires that the increased oxygen consumption be met by providing appropriate ventilation and potentially by oxygen supplementation to the inspired air.

Monitoring Physiological Function

Most monitoring modalities for domestic species can be applied to reptiles. Body temperature should be monitored with a cloacal or esophageal thermometer or temperature probe able to measure low temperatures. Heart rate and rhythm may be monitored using ECG or Doppler flow detection units. The latter offers simple audible monitoring. In most snakes, heart rate can usually be determined by visual inspection of the ventral scales approximately 25% of the snake's length from the head, and the heart rate may be visually observed in the jugular groove of many lizards. Blood pressure may be measured invasively only following cut-down procedures, limiting usefulness to research settings. Commercially available oscillometric devices applied to the tail of snakes or the femoral region of lizards unfortunately seem to have limited value, but may perhaps provide trend information (Chinnadurai et al. 2009, 2010). Respiration may be assessed visually and in intubated animals main stream or side stream capnography provides useful information, although incomplete gas mixing, cardiac shunting, and dilution as a consequence of excessive sampling rates of the devices used may give rise to erroneous or systematically low end-tidal carbon dioxide readings (Hernandez-Divers et al. 2005).

The use of pulse oximetry in reptiles remains controversial and problematic (Diethelm & Mader 1999; Hernandez-Divers et al. 2005; Mosley et al. 2004) as values obtained may not correlate with measured arterial oxygenation. However, continuous monitoring with pulse oximetry may provide information on trends that reflect changes in oxygenation over time. Regional tissue oxygenation evaluation may be a useful additional technique (Cushing et al. 2020).

Arterial blood gas analysis provides valuable information on oxygenation and acid-base status, especially in relation to whether the lungs are properly ventilated. Cost-effective portable equipment is increasingly available with internal temperature correction and options for species correction. In some cases, automated blood gas analyzers have been calibrated for specific species of reptiles (Malte et al. 2014). However, arterial samples are normally not easy to obtain and most vascular sampling sites yield venous blood. Cardiac puncture likely results in an unknown mixture of arterial and venous blood. Venous blood samples are readily available (Ratliff et al. 2019), but their relationship to arterial values varies wildly and oxygen levels are exquisitely sensitive to tissue extraction. In anesthetized iguanas, for example, arterial and venous oxygen pressures were very close and carbon dioxide pressures only slightly different. This may suggest very low tissue metabolism and oxygen consumption during anesthesia (Mosley et al. 2004). However, venous O_2 was similar in bearded dragons anesthetized with either 21% or 100% inspired oxygen. This indicates venous oxygen levels do not reflect arterial oxygen partial pressure in the arteries or the lungs (Ratliff et al. 2019). The use of venous blood gas samples in conscious animals will reflect not only tissue metabolism and respiratory status, but also will be influenced by shunt and therefore are expected to vary widely and may not be suitable for diagnostic value.

Depth of Anesthesia

The clinical signs associated with induction of general anesthesia in reptiles are fairly consistent. Generally, muscle relaxation in lizards and snakes starts at mid-body and moves forward, then backwards so that tail tone is lost last

(Bonath 1977; James et al. 2018). In varanids induced with inhalation anesthetics, the front limbs lose tone first, followed by the hind limbs and the neck approximately simultaneously. Then righting reflex is lost, and finally the tail tone (Bertelsen et al. 2005a). The tongue retraction "reflex" in snakes and varanids persists beyond the loss of tail tone and righting reflex (Schumacher et al. 1997) and often is present at the surgical plane, as is the corneal reflex (lizards) (Arena et al. 1988; Bertelsen & Sauer 2011). Loss of these reflexes may indicate excessive anesthetic depth. Animals retain the ability to react to painful stimuli even after the loss of righting reflex and tail tone. The response to toe or tail pinching or surgical incision should therefore be evaluated before deciding surgical anesthesia has been achieved.

Endotracheal Intubation

Due to the large oral cavities and rostral position of the glottis, lizards and snakes are easily intubated. The glottis is visualized at the bottom of the mouth, immediately caudal to the tongue (Fig. 11.2a). A noncuffed endotracheal tube of appropriate size is inserted and taped in place, allowing positive pressure ventilation either manually or using mechanical ventilators (Fig. 11.2b). Snakes and some lizards may be intubated awake following the application of topical analgesics to the glottis, however premedication, for example with midazolam, may aid intubation and lower the minimum anaesthetic concentration of inhaled anaesthetics required (Larouche et al. 2019). It is common practice to induce with a swiftly acting injectable, for example alfaxalone or propofol, and maintain on inhalation anaesthesia (Hansen & Bertelsen 2013; Knotek 2017; Morici et al. 2018; Perrin & Bertelsen 2017; Rasys et al. 2019). Endotracheal tubes are commercially available down to 1 mm internal diameter (ID), but for the smallest subjects over-the-needle intravenous (IV) catheters (12–25 gauge) may be used. The adapter from a commercially available 3-mm ID endotracheal tube will usually fit the connector for an over-the-needle catheter (Heard, pers. comm.). When using very small tubes care should be taken to ensure the end does not become obstructed by mucous, and air can move freely back and forth into the trachea.

A piece of rubber tubing, a folded gauze pad, or a wooden mouth gag, depending on the size of the subject, may be used to prevent the animal from biting on the tube. In small reptiles, taping the animal, the endotracheal tube, and the breathing system to the table, a board, or a tongue depressor may prevent tube displacement and injury.

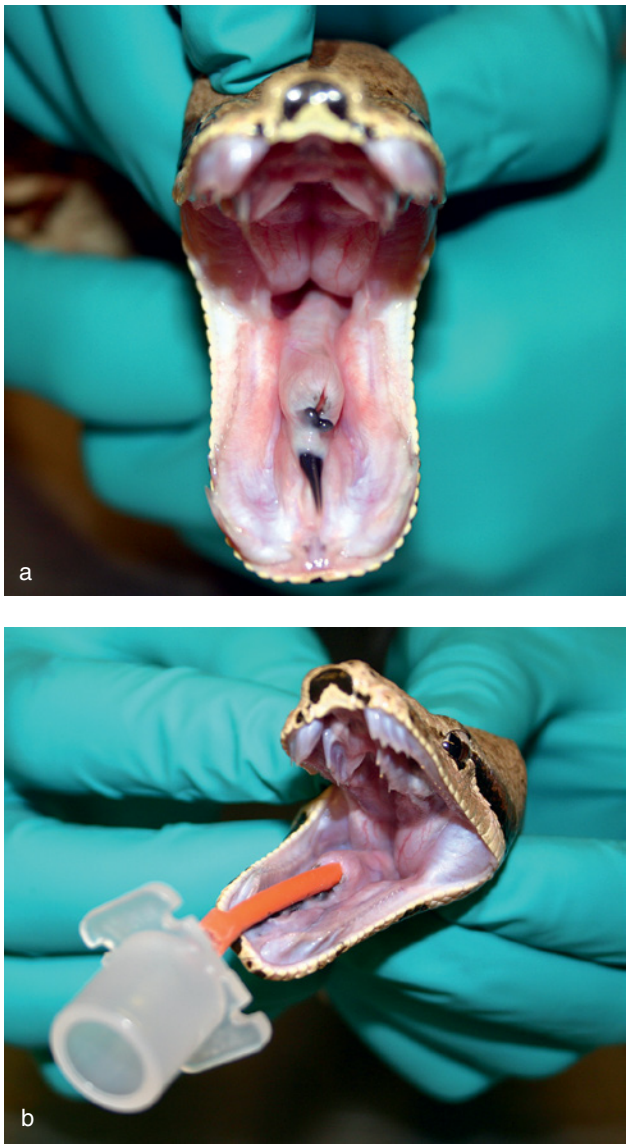


Figure 11.2 (a) The oral cavity of a boa constrictor (*Boa constrictor*). Note the rostral location of the partly open glottis. (b) The oral cavity of a boa constrictor showing the endotracheal tube within the glottis after intubation.

Ventilation

The combination of very low metabolic rates and extreme resilience to hypoxemia allows anesthetized reptiles to experience long periods of apnea without overtly deleterious effects. Although the consequences of apnea during anesthesia are largely unknown, supplementary external ventilation is recommended during deep or prolonged anesthesia, that is, conditions when spontaneous ventilation is usually lost in reptiles. Apart from preventing hypoxemia and hypercapnia, external ventilation ensures delivery and removal of inhalational anesthetics anesthetic

agents, thus providing anesthetic stability and reducing recovery times (Bertelsen et al. 2015; Jakobsen et al. 2017).

Following endotracheal intubation, external ventilation may be achieved by manually "bagging" the animal or by means of a mechanical ventilator of appropriate size. For many species, specialized laboratory animal or very small animal equipment is necessary to avoid over-ventilation, and even with this equipment it may be hard to achieve sufficiently low respiratory rates. When artificially ventilating lizards and snakes, the larger tidal volume and lower minute ventilation compared to mammals should be taken into consideration and, if available, capnography should be used to monitor the level of ventilation. A minute ventilation of 50–75 mL/kg and a frequency of 0.5–2 breaths per minute will be adequate in most species, with end tidal pressures of 10–12 cmH_2O (Bertelsen et al. 2015; Jakobsen et al. 2017; Sladky & Mans 2012b).

Inhalation Anesthesia

Inhalational anesthesia is commonly used for induction and maintenance of reptile anesthesia. As in other species, the advantages of inhalational anesthetics include superior control of anesthetic depth, wide safety margins, excellent muscle relaxation, faster recovery, and "built-in" oxygen supplementation. As mentioned above, induction and recovery times in reptiles tend to be longer and more variable than in mammals and birds due to breath-holding, intracardiac shunting, and slow circulatory time.

Anesthetic Potency

Minimum alveolar concentration or minimum anesthetic concentration (MAC) is the standard measure of potency of inhalational anesthetic agents (Quasha et al. 1980) MAC is defined as the anesthetic concentration that prevents gross purposeful movement in 50% of an anesthetized population subjected to a supramaximal noxious stimulus, traditionally a surgical incision. Apart from permitting comparison of anesthetic agent potency, the value allows standardization and comparison of various depths of anesthesia as multiples of MAC. Using MAC values also provides a way of assessing the synergism between two anesthetics. Other terms essentially equivalent to MAC are sometimes reported in birds and reptiles (e.g., minimum anesthetic dose, effective dose 50, minimum infundibular concentration). Generally, MAC for a given agent varies little across mammalian species (Quasha et al. 1980) and the limited number of reports available indicate that the same applies to reptiles, although evolutionary differences in cardiopulmonary performance may give raise to greater variability among reptiles (Bertelsen et al. 2005b; Larouche 2019; Larouche et al. 2019).

As MAC only "accounts for" 50% of the population, vaporizer settings of 1.3 MAC are recommended to achieve surgical anesthesia. As a likely consequence of R-L intracardiac shunting and low minute ventilation, the equilibrium between inhaled substances and body occurs more slowly in reptiles. Consequently, effective MAC decreases over time in iguanas (and probably other reptiles), indicating that inhaled gas levels should be decreased toward the end of lengthy procedures (Barter et al. 2006; Brosnan et al. 2006; Williams et al. 2019a).

Equipment

Inhalant anesthetics are delivered either by agent-specific vaporizers using oxygen or a mix of oxygen and nitrous oxide as the carrier gas. Standard anesthetic machines fitted with non-rebreathing (Bain's) or circle systems are used, and for smaller specimens laboratory animal equipment has great potential. Commercially available small animal face masks, as well as masks home-made from plastic bottles or syringe cases work well.

Due to low metabolic rates, oxygen consumption is low (<1 mL/kg/min; Perry 1989) and flowrates may be reduced considerably compared to mammalian settings. In practice, the flow rate is often determined by the performance of flow meters and vaporizers, and rates of 250–1000 mL/min will be appropriate for most reptiles.

Induction

Unlike in chelonians, where inductions may be prohibitively prolonged, mask induction is generally feasible in lizards and snakes (Fig. 11.3). Animals may also be induced in chambers or plastic bags filled from a vaporizer at maximal setting, or simply by adding a small volume of the concentrated agent on a piece of cotton wool (e.g., ~1 mL isoflurane per liter of chamber volume). With the latter approach, close attention should be paid as inductions may be quite rapid and toxic levels could be reached if animals are left too long. Care should be taken to ensure that the anesthetic does not come into direct contact with the animal.

Early Inhalants

One of the first reports of anesthesia in reptiles is that of John Tait describing the surgical removal of venom glands from rattlesnakes under chloroform anesthesia, which was also used for immobilization of snakes for artistic purposes 100 years earlier (Bause 2016; Tait 1938). Later, prolonged



Figure 11.3 Mask induction of a monitor lizard with isoflurane. Note the use of a standard small animal face mask.

induction and recovery periods were described in several snake species anesthetized with methoxyflurane (Burke & Wall 1970; Gandal 1968). There are no recent reports on the use of either agent, and other drugs have long superseded them.

Ether anesthesia is associated with very long induction (40–60 minutes) and recovery periods in lizards and snakes (Bonath & Zschege 1979; Brazenor & Kaye 1953). While still occasionally used in physiological research and venom production, the agent must be considered obsolete in a clinical setting. It is also flammable and potentially explosive, therefore it is a hazardous chemical to store and use.

Halothane

Halothane delivered at 3–6% results in moderate sedation to profound anesthesia in lizards and snakes. At halothane concentrations of 5.8% the mean induction time at 22–25°C has been reported to be 24 minutes in lizards ($n = 38$) and 35.3 minutes in snakes ($n = 12$) (Bonath 1977, 1979; Bonath & Zschege 1979). Shorter induction times (5–19 minutes) were reported using 5% halothane in a 3:1 nitrous oxide/oxygen mixture (Custer & Bush 1980) A transient initial excitement stage has been described in rattlesnakes at very high concentrations (Hackenbrock & Finster 1963).

In snakes, halothane significantly decreases respiration rate and tidal volume, leading to respiratory acidemia, while heart rate decreases mildly or remains unchanged (Bonath 1977, 1979; Bonath & Zschege 1979; Custer & Bush 1980). Recovery times following brief anesthetic events are relatively short (24–35 minutes), while recovery times from deeper anesthesia are reported to be much longer (Bonath 1977, 1979; Bonath & Zschege 1979). No information exists on the potency of halothane in reptiles, and data on cardiopulmonary function during halothane anesthesia are limited to that described above. In the clinical setting, halothane has been replaced by isoflurane and sevoflurane.

Isoflurane

Isoflurane is used extensively in reptiles. In lizards, the time to initial relaxation and loss of righting reflex breathing 5% is typically 4–9 minutes (Hernandez-Divers et al. 2005; Mauthe von Degerfeld 2004; Schildger et al. 1993; Spelman et al. 1996) while the time to complete relaxation is 13–20 minutes depending on the species (Bertelsen et al. 2005a; Mosley 2000). In snakes, induction times with mask induction tend to be slightly longer (Schildger et al. 1993), but direct intubation of the awake snake followed by mechanical ventilation with the drug leads to rapid induction. As mentioned, faster inductions may be achieved using higher inspired concentrations by adding isoflurane directly to the induction chamber or by use of an injectable agent prior to intubation.

Isoflurane causes a moderate (~25%) reduction in heart rate (Hernandez-Divers et al. 2005; Maas & Brunson 2002) and a severe reduction in respiratory rate (Maas & Brunson 2002) when compared to values in manually restrained animals. It should be considered, however, that values in manually restrained subjects are significantly higher than in undisturbed animals (Bertelsen et al. 2005a). During anesthesia, a dose-dependent reduction in systemic blood pressure is observed (Chinnadurai et al. 2010; Mosley et al. 2004). At low concentrations animals continue breathing (Spelman et al. 1996), but at levels adequate for surgical anesthesia mechanical ventilation is usually necessary.

The minimum alveolar concentration at 30–35°C has been reported to be 1.11% (95% confidence interval 0.94–1.28%) in ball pythons (Larouche et al. 2019), $1.9 \pm 0.59\%$ in rat snakes (Maas & Brunson 2002), $1.8 \pm 0.3\%$ to $2.1 \pm 0.6\%$ in iguanas (Barter et al. 2006; Mosley et al. 2003a) and $1.54 \pm 0.17\%$ in monitors (Bertelsen et al. 2005b). These values indicate vaporizer settings of 2–2.5% will be appropriate to maintain surgical anesthesia in most subjects. As a likely consequence of R-L intracardiac shunting at the beginning of anesthesia, MAC decreases over time in iguanas (Barter et al. 2006), indicating inhaled gas levels should be decreased toward the end of lengthy procedures. The MAC decreases with decreasing body temperature (Dohm & Brunson 1998). In an attempt to determine the cardiac anesthetic index, seven iguanas were subjected to up to 9.2% isoflurane without any apparent signs of cardiac arrest, suggesting a very wide margin of safety (Mosley et al. 2003b).

Recovery time depends on the depth and duration of anesthesia, and is relatively short (2–12 minutes) following brief, shallow anesthetic events (Schildger et al. 1993; Spelman et al. 1996), intermediate (30–40 minutes) following light surgical anesthesia, and more prolonged (50–70 minutes) following deep anesthesia (Bertelsen et al. 2005a; Mosley 2000). In general, recovery times appear longer and more variable in snakes than in lizards.

Sevoflurane

Induction times using sevoflurane are slightly shorter than with isoflurane (Bertelsen et al. 2005a; Hernandez-Divers et al. 2005). In lizards induced with 8%, the time to initial relaxation and loss of righting reflex is around 6 minutes (Hernandez-Divers et al. 2005) while the time to complete relaxation is approximately 11 minutes (Bertelsen et al. 2005a). As for isoflurane, direct intubation of the awake animal followed by mechanical ventilation with the drug leads to rapid induction. The addition of 66% nitrous oxide will speed up inductions slightly (Bertelsen et al. 2005a).

Sevoflurane induction has been subjectively judged as smoother and associated with less breath-holding than with isoflurane (Hernandez-Divers et al. 2005), but the respiratory rate during induction appears to be similar or even marginally lower with sevoflurane (Bertelsen et al. 2005a). Sevoflurane causes a moderate reduction in heart rate and a severe reduction in respiratory rate compared to values in manually restrained animals (Hernandez-Divers et al. 2005; Maas & Brunson 2002). The hemodynamic effects of sevoflurane in iguanas are similar to those with isoflurane (Barter et al. 2006).

The minimum alveolar concentration at 30–35°C has been reported to be 2.42 ± 0.57% in rat snakes (Maas & Brunson 2002), 2.51 ± 0.46% in monitor lizards (Bertelsen et al. 2005c), and 3.1 ± 1.0% in iguanas (Barter et al. 2006), indicating vaporizer settings of 3–3.5% will be appropriate to maintain surgical anesthesia in most subjects. In a study of monitor lizards, the coadministration of 66% nitrous oxide resulted in a 25% reduction in sevoflurane MAC (Bertelsen et al. 2005c) and similar reductions are likely to occur in other species and with other inhalants, as shown with isoflurane in ball pythons (Larouche et al. 2019).

With modern inhalant anesthetics, the length of the recovery period appears to be influenced more by the duration and depth of anesthesia (and the extent of intracardiac shunting) than by the agent used (Brosnan et al. 2006). After a short time, relatively superficial anesthesia sevoflurane will result in faster recoveries than for isoflurane (Hernandez-Divers et al. 2005), but following prolonged, deep anesthesia that difference is marginal (Bertelsen et al. 2005a).

Desflurane

Desflurane is the least soluble of the volatile anesthetics, and thus theoretically has the fastest inductions and recoveries. However, it may cause airway irritability, requires specialized heated vaporizers, and is rarely used in veterinary practice. The minimum alveolar concentration at 34–35°C has been reported to be 8.9 ± 2.1% in iguanas, with hemodynamic effects being similar to those of isoflurane and sevoflurane (Barter et al. 2006).

Nitrous Oxide

Nitrous oxide (N_2O) may be used as a supplemental anesthetic (at 50–66% with oxygen) during induction with inhalational agents (Bennett 1998; Custer & Bush 1980; Larouche et al. 2019), resulting in marginally shorter induction times (Bertelsen et al. 2005a). Sixty-six per cent N_2O delivered with sevoflurane reduced the latter's MAC 25% in monitor lizards (Bertelsen et al. 2005c) and that of isoflurane by 17% in ball pythons (Larouche et al. 2019). Assuming that a relationship of simple linear additivity between sevoflurane and nitrous oxide exists, the MAC for N_2O in varanids can be estimated to be 244%. Apart from reducing the concentration of the primary agent, which may improve cardiopulmonary function, the use of N_2O likely provides improved analgesia over delivery in 100% oxygen.

Carbon Dioxide

Inhalation of carbon dioxide (CO_2) is occasionally used as a cheap and easy way to immobilize venomous snakes during venom extraction (Wang et al. 1993). Unconsciousness is thought to be mediated through central nervous system acidosis and is accompanied by temporarily very low oxygen levels in the arterial blood (Wang et al. 1993). This procedure is not recommended in clinical practice.

Small amounts of CO_2 can be added to the inhaled gases to avoid the respiratory alkalemia that often develop when the minute volume of mechanical ventilation exceeds the reptile's normal and low rate. As an example, it can be suitable to add 1–3% of CO_2, which then allows for high rates of mechanical ventilation that ensures high oxygenation of the lungs (Crossley et al. 1998; Overgaard et al. 2002). Also, use of a 10% CO_2 mixture has been suggested to stimulate respiration during recovery (Malley 1997), but the ventilatory response to hypercapnia is complex in squamates as intrapulmonary chemoreceptors may inhibit ventilation (Milsom 1991).

Parenteral Anesthesia

Numerous injectable anesthetics have been used in snakes and lizards with varying success. These include etorphine hydrochloride (Hinsch & Gandal 1969; Wallach & Hoessle 1970), pentobarbital sodium (Arena et al. 1988; Betz 1962; Karlstrom & Cook 1955), thiopental sodium (Karlstrom & Cook 1955), methohexital (Preston et al. 2010; Wang et al. 1977), MS-222 (Green & Precious 1978; Karlstrom & Cook 1955), urethane (Calderwood 1971), nicotine (Calderwood 1971), decamethonium iodide (Brazenor & Kaye 1953), 2,2,2-tribromoethanol (Rasys et al. 2019), procaine hydrochloride (Livezey 1958), and the muscle relaxant tubocuraine chloride (Brazenor & Kaye 1953). While still occasionally used in experimental settings, these agents must be considered obsolete in clinical practice.

Propofol

Provided vascular access is available, propofol is these authors' agent of choice for anesthetic induction. Administered intravenously or intraosseously at dosages of 5–10 mg/kg, propofol will cause induction in 1–5 minutes (Anderson et al. 1999; Bennett et al. 1998; Bertelsen et al. 2015; McFadden et al. 2011). Propofol administered perivascularly is ineffective, but unlike barbiturates does not cause tissue damage. Administration via the ventral tail vessels is generally feasible in patients larger than 250 g, although there are significant species differences.

In lizards and snakes, propofol causes a slight decrease in heart rate from handled levels and a marked respiratory depression (Anderson et al. 1999; Bennett et al. 1998). The respiratory depression is dose dependent and appears to be affected by the duration of administration: low doses given slowly cause less apnea than high doses administered as a bolus.

The duration of anesthesia depends on dosage: 5 mg/kg results in 20–30 minutes of anesthesia, while anesthesia and recovery times are longer following 10 mg/kg dosage. Anesthesia may be maintained by inhalation or by continuous propofol infusion. An infusion rate of 0.5 mg/kg/min proved excessive in green iguanas (Bennett et al. 1998) and rates of 0.2–0.4 mg/kg/min are likely more appropriate. For most species, a dose of 5–10 mg/kg given slowly is appropriate for short procedures or as induction for inhalational anesthesia.

Alfaxalone

The steroid anesthetic alfaxalone is highly insoluble in water and was originally formulated in combination with alphadalone and a cremaphor solubilising agent. Alfaxalone soon found some use in reptiles (Calderwood & Jacobson 1979; Lawrence & Jackson 1983), but its use was discontinued as cremaphor was associated with allergic reactions in domestic animals. More recently, alfaxalone has been solubilized with 2-hydroxypropylbeta-cyclodextrin (Estes et al. 1990). When given intravenously, this formulation has much the same effects as propofol. In veiled chameleons and leopard geckos, a surgical plane of anesthesia lasting for 5–10 minutes was achieved 2 minutes following 5 mg/kg IV (Knotek et al. 2011; Morici et al. 2018) and enabled tracheal intubation in agamid lizards 1 minute after administration (Knotek 2017). In green iguanas, 5 mg/kg IV resulted in about 15 minutes of anesthesia with minimal effect on heart rate and respiratory rate (Knotek et al. 2013), while in bearded dragons 12 mg/kg IV provided "surgical anesthesia" in five out of eight animals, lasting approximately 15 minutes (Perrin & Bertelsen 2017). Interestingly, unlike propofol, alfaxalone is effective when administered intramuscularly or subcutaneously at higher dosages. In iguanas, 10 mg/kg provides light sedation, 20 mg/kg provides a level suitable for minor procedures or for endotracheal intubation and supplementation with inhalational anesthesia, and 30 mg/kg provides an anesthetic plane suitable for surgical procedures of limited duration (up to 40 minutes) (Bertelsen & Sauer 2011). In iguanas there is an initial dose-dependent depression of respiration followed by a significant increase in frequency over time (Bertelsen & Sauer 2011). In accordance with principles of metabolic scaling, smaller individuals require higher dosages. A dosage of 5 mg/kg IV via the jugular vein was sufficient for tracheal intubation in leopard geckos, while 15 mg/kg intramuscular (IM) in combination with midazolam provided sufficient sedation for venipuncture (Doss et al. 2017; Morici et al. 2018). In contrast, 20 mg/kg IM alfaxalone after 10 mg/kg butorphanol premedication did not result in surgical level anesthesia in bullsnakes (Sadar & Ambros 2019).

In pythons, both IM and subcutaneous administration cranial to the heart resulted in faster inductions and a deeper plane of anesthesia than alfaxalone administered more caudally, probably due to the hepatic metabolism of caudally administered drug (James et al. 2018; Yaw et al. 2018). Alfaxalone in combination with dexmedetomidine was found to be sufficient for celiotomy in brown anoles (Rasys et al. 2019), and as a sole agent was preferable to ketamine in galliwasps (Kleinschmidt et al. 2018). In both ball python and bearded dragons, alfaxalone-induced animals have been reported to have increased reaction to external stimuli, so reducing external stimulation may aid smooth recoveries (James et al. 2018; Perrin & Bertelsen 2017).

Ketamine

Ketamine hydrochloride has been used extensively in reptiles, primarily snakes, since its introduction in the late 1960s (Glenn et al. 1972; Schumacher et al. 1997).

The effective dosage depends on body temperature (Arena et al. 1988): at lower body temperatures lower doses are required, but both induction and recovery are prolonged (Arena et al. 1988; Green et al. 1981). Effects are highly species dependent (Arena et al. 1988; Cooper 1974; Hill & Mackessy 1997; Ogunranti 1987; Schildger et al. 1993), but large individual variation is also observed (Cooper 1974; Hill & Mackessy 1997).

Reported dosages range from 12–44 mg/kg for sedation (Bennett 1998; Glenn et al. 1972; Schildger et al. 1993; Spelman et al. 1996) to 55–88 mg/kg for surgical anesthesia (Bennett 1998; Glenn et al. 1972; Schildger et al. 1993), while yet higher doses (100–220 mg/mL) are occasionally reported (Arena et al. 1988; Harding 1977). The time to peak effect following IM injection is approximately 30 minutes (Cooper 1974; Custer & Bush 1980; Glenn et al. 1972; Green et al. 1981).

In snakes and lizards, moderate ketamine dosages are associated with increased heart rates (Arena et al. 1988; Schumacher et al. 1997), hypertension (Schumacher et al. 1997), and respiratory depression, peaking at 30–60 minutes (Arena et al. 1988; Ogunranti 1987; Schumacher et al. 1997). At increasing dosages, ketamine will induce apnea, bradycardia, and eventually death (Cooper 1974; Custer & Bush 1980; Glenn et al. 1972; Green et al. 1981).

The very extended recovery periods represent the main problem with ketamine anesthesia in reptiles. Reported recovery times range from 6–24 hours at 15 mg/kg (Hill & Mackessy 1997) to 2–3 days at 40–80 mg/kg and 6–7 days at 100–130 mg/kg (Custer & Bush 1980; Glenn et al. 1972; Green et al. 1981).

Ketamine may be combined with sedatives, such as benzodiazepines and alpha-2 agonists, for better muscle relaxation, a reduction in required dose, and shorter recovery times (Bennett 1998; Budden et al. 2018; Fink et al. 2018; Heard 2001; Malley 1997), and may provide long-term anaesthesia for extended procedures (Barrillot et al. 2018a). Due to the variable effects, long recovery periods, and the availability of alternative protocols, the authors rarely use dissociative agents.

Zolazepam-Tiletamine

The potent cyclohexamine tiletamine combined with the benzodiazepine zolazepam has found some use in reptile anesthesia (Boever & Caputo 1982; Gray et al. 1974; Read 2004), but very little published information exists. The onset of effects is faster than with ketamine (Mauthe von Degerfeld 2004), while cardiopulmonary effects are likely similar to those produced by ketamine. In early studies, dosages of 30–40 mg/kg administered to iguanas resulted in surgical anesthesia lasting 8–16 hours, while variable effects were seen with doses of up to 88 mg/kg in snakes (Boever & Caputo 1982). In Komodo dragons, dosages of 5.5 mg/kg caused repetitive head and neck movements 10–25 minutes before resulting in sedation (Spelman et al. 1996). In iguanas 10 mg/kg resulted in a brief period of excitement followed by good relaxation (Mauthe von Degerfeld 2004). Despite its long duration of action and variable effects, low doses (2–5 mg/kg) may be useful for sedation prior to handling or intubation, particularly of larger animals.

Sedatives

Sedative and tranquilizing drugs such as benzodiazepines and alpha-2 agonists may be used in squamates, and can reduce MAC and provide additional anesthetic depth (Bisetto et al. 2018; Doss et al. 2017; Larouche et al. 2019; Rasys et al. 2019). Reversal with atipamezole can make alpha-2 agonists attractive sedative agents for fast recoveries, and their administration in combination with ketamine or midazolam is gaining use (Barrillot et al. 2018b; Cushing et al. 2020; Rasys et al. 2019; Sadar & Ambros 2019; Yaw et al. 2020). Due to the difficulty in accessing the vascular system and airways, sedatives have gained popularity in turtles and tortoises, and as information gained in chelonians can probably be extrapolated to snakes and lizards, readers are also referred to Chapter 10.

Other Techniques

Hypothermia, once used as a means of immobilizing reptiles (Broeckhoven et al. 2017; Calderwood 1971; Kaplan 1969; Keifer & Zheng 2017) is considered an unacceptable clinical practice, as is electro-immobilization.

Recovery

As mentioned above, recovery times in reptiles are prolonged compared to birds and mammals. Body temperature critically affects speed and quality of recovery so animals should be kept within their preferred temperature zone. If mechanical ventilation is used, animals should gradually be weaned off ventilation. The easiest way to do so is by manual ventilation every 1–5 minutes using an Ambu-bag or similar to allow carbon dioxide to build up. A capnograph is useful in detecting spontaneous respirations during recovery. Breath holds of 5–10 minutes with inflated lungs will not cause deleterious effects.

Despite previous clinical concern over the effect of hyperoxia on respiration in reptiles based on past physiological data (Glass & Johansen 1976) there appears to be little effect of recovery in room air (21% oxygen) as opposed to 100% oxygen. While faster recoveries were experienced when ventilating iguanas with 21% oxygen following short-term isoflurane anesthesia (Diethelm & Mader 1999), no difference could be demonstrated following longer anesthetic events (Bertelsen et al. 2005a). Reversal of any alpha-2 agonists allows faster recovery from combination injectable anaesthesia, but will also remove any analgesic effect, while flumazenil may be used to reverse benzodiazepines (Doss et al. 2017; Yaw et al. 2020). IM administration of epinephrine may reduce recovery times without apparent adverse effects (Heard, pers. comm.).

Complications

Complications are relatively rare using the protocols suggested above, but respiratory depression or apnea and prolonged recoveries are commonly encountered (Read 2004). These problems may be reduced by providing adequate mechanical ventilation and by maintaining body temperature within physiological limits.

Analgesia

Since the first edition of this book, pain perception and modulation have received an increasing amount of attention in reptiles (d'Ovidio & Adami 2019; Mans et al. 2019b; Mosley 2011; Perry & Nevarez 2018; Sladky & Mans 2012a, 2019; Williams et al. 2019b). A slower return to normal feeding in ball pythons experiencing a surgical incision under isoflurane than in those anesthetized without incision underlines the need for perioperative analgesia in reptiles (James et al. 2017). However, there is a continuing need for well-controlled analgesic studies. While thermal and chemical nociceptive models have provided well-tested methodologies and are the basis for many of the following recommendations, they may not replicate the effect of treatment in spontaneously painful conditions, where published trials are still lacking.

In anoles, the administration of the μ-receptor opioid morphine (5 mg/kg IM) caused an increased latency of the tail-flick response (Mauk et al. 1981). Similarly, morphine (10–20 mg/kg) increased thermal withdrawal latency in red-eared sliders (Sladky & Miletic 2007) and bearded dragons (Sladky et al. 2008), but appears to be ineffective in corn snakes at dosages up to 40 mg/kg (Sladky et al. 2008) and at 10 mg/kg in ball pythons (Williams et al. 2016). Morphine causes severe respiratory depression, but another μ-receptor opioid, tramadol, appears to have similar effects on thermal withdrawal latency (10–15 mg/kg PO, SC) in turtles with much less respiratory depression (Baker et al. 2011). Similarly, another μ-receptor opioid, hydromorphone (0.5 mg/kg IM), increased thermal withdrawal time in sliders (Mans et al. 2012). Fentanyl patches have been seen to provide plasma levels that would be expected to be effective in skinks and snakes (Darrow et al. 2017; Gamble 2008; Kharbush et al. 2017), but despite clinical experience of analgesia in patients with chronically painful conditions (snakes with arthritis), fentanyl patches were not effective in a thermal nocioceptive test and significantly depressed respiration (Kharbush et al. 2017).

The predominant κ-receptor opioid butorphanol (20 mg/kg SC) was ineffective in bearded dragons and sliders, and only effectively increased thermal withdrawal latency in corn snakes at exceptionally high doses, which have extreme sedative effects and are unsuitable in clinical patients (Sladky & Miletic 2007; Sladky et al. 2008). In iguanas, butorphanol (1 mg/kg IM) failed to decrease the minimum anesthetic dose of isoflurane and did not provide demonstrable analgesia in a heat pad test (Fleming & Robertson 2012; Mosley et al. 2003a).

Nonsteroidal anti-inflammatory drugs (NSAIDs) have, perhaps mistakenly, been expected to behave much the same across species, although tissue concentrations of COX-1 and -2 in inflamed tissue varies among reptiles (Royal et al. 2012; Sadler et al. 2016). Nevertheless, clinical evidence supports the efficacy of NSAIDs in reptiles and they appear widely used (Hernandez-Divers 2006; Read 2004). A pharmacokinetic trial of meloxicam in iguanas showed excellent bioavailability following PO administration, and suggested that administration of meloxicam at a dose of 0.2 mg/kg IV or PO results in plasma concentrations of >0.1 μg/mL for approximately 24 hours (Divers et al. 2010). Furthermore, daily administration of high doses (1 or 5 mg/kg) for 12 days did not induce any histologic changes in gastric, hepatic, or renal tissues (Divers et al. 2010). Similarly, daily administration of meloxicam (0.2 mg/kg IM for 10 days) in iguanas failed to demonstrate any significant clinical, biochemical, or hematological abnormalities (Trnkova et al. 2007). In an attempt to evaluate the effect of meloxicam (0.3 mg/kg IM) and butorphanol (5 mg/kg IM), the postoperative physiological stress response in ball pythons was evaluated and failed to demonstrate an effect of either drug (Olesen et al. 2008). However, even in the saline-treated control group there was only minimal measurable physiological response to surgery, questioning the validity of the model. COX-2 expression in inflamed skin did not change in experimental lesions in pythons (Sadler et al. 2016), so further study

is required to investigate whether a less selective NSAID would be more effective in snakes.

Despite the lack of current comprehensive documentation, analgesics should be part of any anesthetic regimen that involves potentially painful procedures. μ-receptor opioids and NSAIDs are the most relevant candidates for successful treatment, and suggested dosages of selected drugs are given in Table 11.1. Future directions include preliminary work suggesting that alpha-2 agonists may provide thermal antinociception in pythons (Bunke et al. 2018).

As in any species, preemptive analgesia offers intraoperative as well as postoperative analgesia, and likely will reduce the amount of anesthetic needed (Ong et al. 2005; Page et al. 1998). Local analgesics (e.g., lidocaine, bupivicaine) are commonly used in reptiles, using doses extrapolated from the mammalian literatures (Chatigny et al. 2017; James et al. 2017; Sladky & Mans 2012b). Given their action on sodium channels, central to nociception in reptiles, they are expected to be effective given both locally as infiltrations and as nerve blocks and regional protocols (Mans et al. 2019b; Wellehan et al. 2006). In small subjects, diluting the drugs (e.g., 1:10 in sterile saline) prior to administration will help to allow sufficient volume to provide analgesia to the surgical area while avoiding overdosing. Intrathecal lidocaine administered under alfaxalone has been shown to provide antinociception, but requires skills in administration (Ferreira & Mans 2018). Systematic research into the duration of action and the effects of dilution and mixing (e.g., bupivacaine and lidocaine coadministration) on the efficacy of local anaesthetics is currently still lacking in reptiles for local administration, but its use is recommended by these authors on clinical grounds.

Selected Protocols

For most snakes and lizards the authors recommend one of three approaches (Table 11.2): induction with propofol (5–10 mg/kg IV) or alfaxalone (5 mg/kg IV, 20–30 mg/kg

Table 11.1 Selected anesthetic, sedative and analgesic drugs used in snakes and lizards.

Generic Name	Dosage (mg/kg)	Reversal Agent	Reference
Propofol	5–10 IV/IO	None	Bennett et al. (1998); Anderson et al. (1999); McFadden et al. (2011)
Alfaxalone	5–10 IV 10–40 IM (cranial administration preferred) 5–30 SC (cranial administration preferred)	None	Knotek et al. (2011); Bertelsen and Sauer (2011); James et al. (2018); Rasys et al. (2019); Yaw et al. (2018)
Midazolam	0.5–2	Flumazenil	Larouche et al. (2019); Sadar and Ambros (2019)
Medetomidine	0.05–0.2	Atipamezole	Barrillot et al. (2018); Wightman et al. (2015)
Dexmedetomidine	0.025–0.2	Atipamezole	Bisetto et al. (2018); Cushing et al. (2020); Fink et al. (2018); Rasys et al. (2019); Sadar and Ambros (2019); Yaw et al. (2020); Budden et al. (2018); Bunke et al. (2018); Doss et al. (2017)
Ketamine	10–40[a]	None	Glenn et al. (1972); Custer and Bush (1980); Schumacher et al. (1997); Barrillot et al. (2018b); Cushing et al. (2020); Fink et al. (2018); Rasys et al. (2019); Sadar and Ambros (2019)
Zolazepam-tiletamine	2–10	Flumazenil for zolazepam	Mauthe von Degerfeld (2004)
Meloxicam	0.1–0.3	None	Divers et al. (2010); Hernandez-Divers (2006)
Morphine	5–15	Naltrexone, naloxone	Sladky et al. (2008); Williams et al. (2016)
Tramadol	10–15	Naltrexone, naloxone	Baker et al. (2011)
Lidocaine	1–5		Chatigny et al. (2017)
Bupivicaine	1–2		Chatigny et al. (2017)

IM, intramuscular; IO, intraosseous; IV, intravenous; SC, subcutaneous.
[a] Dosages up to 220 mg/kg have been reported (Arena et al. 1988).

Table 11.2 Recommended anesthetic protocols for snakes and lizards (refer to text for details).

Type	Premedication	Induction	Maintenance
Small snake	None	Propofol 5–10 mg/kg IV Chamber induction with isoflurane or sevoflurane	Isoflurane or sevoflurane by endotracheal tube
Large snake	None or Alfaxalone 10 mg/kg, cranial administration IM/SC or Telazol 5–10 mg/kg IM	Propofol 2–7 mg/kg IV Direct intubation[a] followed by ventilation with isoflurane or sevoflurane Chamber induction with isoflurane or sevoflurane	Isoflurane or sevoflurane by endotracheal tube
Venomous snake	None	Propofol 5–10 mg/kg IV[b] Chamber induction with isoflurane or sevoflurane	Isoflurane or sevoflurane by endotracheal tube
Small lizard	None	Propofol 5–10 mg/kg IV Alfaxalone 20–40 mg/kg IM/SC administered cranial to liver Chamber induction with isoflurane or sevoflurane	Isoflurane or sevoflurane by endotracheal tube
Large lizard	None or Telazol 5–10 mg/kg	Propofol 3–10 mg/kg IV Mask with isoflurane or sevoflurane	Isoflurane or sevoflurane by endotracheal tube

IM, intramuscular; IV, intravenous; SC, subcutaneous.
[a] Desentization of the glottis with a drop or spray of local analgesic recommended.
[b] If properly restrained.

IM, cranial half of animal) followed by isoflurane or sevoflurane anesthesia for longer duration, or mask or chamber induction with isoflurane or sevoflurane. For large and aggressive specimens, injection with low doses of ketamine (e.g., 5 mg/kg IM) or tiletamine/zolazepam (e.g., 3 mg/kg IM), with or without (dex-) medetomidine (e.g., 50–100 μg/kg IM) or midazolam (e.g., 1 mg/kg IM), may be used to allow safe handling. Dosages of commonly used drugs are presented in Table 11.1. These anesthetic regimes are supplemented by the use of local anesthesia, NSAIDs, and opiate administration where nociception is expected.

Field Techniques

For fieldwork, when equipment must be kept to a minimum, the protocols using parenteral drugs are recommended. Depending on the size of the animal and the invasiveness of the procedure, IM alfaxalone (10–40 mg/kg, cranial half of animal) or IV propofol (5–10 mg/kg) may be employed. Liquid isoflurane or sevoflurane administered directly into a small airtight container or plastic bag containing the animal is another straightforward means of induction even in the field and remains popular in telemetry studies, but care should be taken to ensure effective breathing of the animals once removed from the container.

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12

Venomous Reptile Restraint and Handling

Frederick B. Antonio

Introduction

This chapter presents information and recommendations for the restraint of venomous reptiles in either a clinical environment or field conditions. For simplicity, a venomous reptile refers to venomous snakes. A section at the end of the chapter will review the management of venomous lizards of the family Helodermatidae (Gila monsters and beaded lizards). Envenomation will be referred to as snakebite, although it is recognized that helodermids can also inflict a serious bite.

It is intended that the use of the techniques described in this chapter will greatly reduce the probability of snakebite. There is always some inherent risk, however, when handling and restraining venomous reptiles. The combination of planning, training, and gaining experience for the skills necessary for proper handling will significantly reduce the probability for error.

In recent years captive venomous reptiles have increased in popularity in the private sector. They are the topics of numerous television series, and are portrayed as both exciting and dangerous, often by actors and commentators that inspire young viewers to engage in interactions with venomous species. Many private collectors, researchers, and zoo professionals have only a vague notion of the potential lethality of their charges. Their ignorance includes both the potential physiological effects of venoms and the behaviors that make venomous snakes difficult to restrain (Altimari 1998). Some states within the United States prohibit personal possession of venomous reptiles while others lack any regulation. Florida annually issues over 500 venomous reptile permits for personal possession. Many private collections are "underground" and reptile clinicians should expect to examine virtually any species of native or exotic venomous reptile. Safe handling of these animals requires veterinarians, researchers, and support staff to be familiar with and use proper methods. The following presents current procedures and techniques designed to limit unrestrained contact with venomous reptiles and thereby promote safety during examinations, clinical procedures, and fieldwork.

General Characteristics

Snake venoms evolved primarily to aid in prey acquisition and secondarily for defense. More than 2700 snake species are currently recognized within about 18 families and 420 genera (Greene 1997). Of these, 250–500 species may induce serious physiologic effects in humans. These belong primarily to the families Elapidae (cobras, kraits, mambas, coral snakes, and seasnakes) and Viperidae (true vipers and pitvipers).

Almost every colubrid snake family has at least one species whose venom has the potential to produce either morbidity or mortality in humans. These include Colubridae (*Dispholidus*, *Thelatornis*), Dipsadidae (*Hydrodynastes*, *Xenodon*, *Waglerophis*), Atractaspididae (A*tractapis*, *Homoroselaps*), Homalopsidae (*Cerberus*, *Enydris*, *Homalopsis*), Natricidae (*Macropisthodon*, *Rhabdophis*), Psammophiidae (*Malpolon*, *Psammophis*, *Rhamphiophis*), and Pseudoxyrhophiidae (*Leioheterodon*, *Madagascarophis*) (Fry 2006). Of these, the most commonly imported are the boomslang, *Dispholidus typus*; African twigsnake, *Thelotornis capensis*; Blanding's treesnake, *Boiga blandingi*; road guarder, *Conophis lineatus*; Japanese water snake, *Rhabdophis tigrinus*; and false pitvipers, *Xenodon* spp.

The evolution of reptilian venom systems (Fry et al. 2006) demonstrates some extant "nonvenomous" snake taxa and certain lizards of Varanidae (monitor lizards) and Iguania to have toxin-secreting oral glands. A thorough review of nonfront-fanged colubroid snakes (Weinstein et al. 2011)

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analyzes documented case reports of bites inflicted by approximately 100 species and discusses clinical management of medically significant species, most commonly referred to as "rear-fanged" snakes. Studies of this kind confirm toxic salivary secretions in extant reptiles, usually products of the Duvernoy's gland, that present a continuum of toxicity from mild to severe. Their presence and effects in human victims require further study to build clinical evidence as to their potential severity. Thus, it is prudent for the clinician to treat suspect or unusual species, especially opisthoglyphs, with the same precautions as they do recognized venomous species.

Venom delivery systems originate from modified salivary glands. These vary from mucous-producing oral glands to well-developed encapsulated glands with separate compressor musculature to express venom through a duct to individual hollow fangs. There are four dental patterns in snakes (Greene 1997): aglyphous, undifferentiated maxillary teeth (present in primitive snakes and some colubrids), opisthoglyphous (enlarged teeth, which may be grooved to facilitate induction of salivary secretions) located on the posterior ends of the maxillary bones (present in rear-fanged snakes), proteroglyphous, enlarged true hollow fangs located on the anterior end of the maxillary bones that have restricted movement (present in elapids), and solenoglyphous, elongated hollow fangs located on highly movable maxillary bones, and folded back along the roof of the mouth when not in use (present in vipers and pitvipers). These four basic dental morphologies represent a progression in efficiency for venom induction when biting.

One impressive variation in fang structure with management implications is found in the elapid species referred to as spitting cobras. Eye injuries by spitting snakes (Chippaux 2006) include African species (*Naja nigricollis, N. katiensis, N. mossambica, N. pallida, N. crawshayi* and *Hemachatus hemachatus*) and some populations of Asian cobras (*Naja sputatrix*). These species have a fang structure and discharge orifice to defensively eject venom aimed at the eyes of an intruder. Target accuracy and the distance of ejection are from 1 to 5 m (Russell 1980). Full-face shields (Fig. 12.1) are recommended at all times when working these species. If venom comes in contact with an eye, wipe remaining venom away from the eyes and begin immediate copious irrigation with sterile saline solution (Boyer & Murphy 1999). A long-sleeved lab coat or protective garment is recommended to shield skin. Venom may also be expressed on the inside of a restraint tube. Expelled venom must be treated with extreme caution during both the procedure and the clean-up process. Dried venom on glass can be aerosolized during cleaning and cause injury to eyes and mucous membranes.



Figure 12.1 Full-face shields and protective garments are recommended when working with all species of spitting cobras. Red spitting cobra, *Naja pallida*, Central Florida Zoo and Botanical Gardens.

Snake Behavior

Handling and restraint should be approached every time as a novel experience that may be significantly different from previous procedures. Planning the procedure with the total focus of all persons involved is required. Complacency or a casual approach, no matter how experienced the handler, can result in an unexpected and disastrous outcome.

Every species exhibits different behaviors when manipulated. Defensive behaviors vary with the individual temperament of each snake, and the handler must observe and read these behaviors to adjust their response and modify techniques if needed. Altimari (1998) describes the temperaments of many captive venomous snake species. Viperids tend to defensively coil and may strike out in any direction. Elapids are more dangerous to manipulate and may initially attempt to flee. However, they can turn and strike at any time, or strike first then look for an escape route. Striking distances are approximately two-thirds of the total body length. For some species, however, when traveling and lunging while striking it is difficult to determine a safe working distance in an open environment. Always overestimate the strike range.

Snakebite

In the United States prior to 1950, exotic venomous snakes were primarily found in zoos. Increased interest in reptiles during the latter part of the 20th century has resulted in the United States becoming the major importer of reptiles, representing 80% of the world trade or approximately 2,000,000

reptiles imported annually (Keyler 2006). The vast majority of snakebites occur in private collections comprising a large variety of genera and species (Seifert 2006a). Of these, nearly half are elapid bites. The incidence of non-native envenomations has increased significantly over the past decade. Statistics on snakebite in clinical situations are difficult to obtain, as many are not reported to data surveillance systems. Toxic Exposure Surveillance System (TESS) data for 2002 showed the number of exotic snakebites in the United States to be 125 (Keyler 2006), and around 100 exotic bites are reported to the American Association of Poison Control Centers annually (Lai et al. 2006).

In a survey of 40 academic institutions that used venomous reptiles in research projects (Ivanyi & Altimari 2004) 18 facilities reported 42 envenomations and six dry bites from 20 species. The majority of these bites (87.5%) were the result of inappropriate capture techniques and inadequate restraint methods, including free handling snakes, pinning, handling with gloves, and improper use of restraint tubes. Card and Roberts (1996) surveyed North American zoos to determine the incidence of venomous reptile bites received by staff. Out of 30 reptile collections that maintained venomous reptiles, 21 zoos reported a staff member bitten during a 25-year period with a total of 31 incidents. Of these, 15 envenomations occurred during routine handling, five during physical restraint, and one during a veterinary procedure. In a survey of 32 venom extraction facilities worldwide (Powell et al. 2006) envenomation averaged one per facility every 2 years. Although records of envenomation in veterinary medicine are lacking, the potential is ever present when a client presents a venomous reptile for examination and treatment. In many cases this is a novel experience for the practitioner, who lacks behavioral knowledge of the species, handling expertise, and proper equipment.

Antivenom

Antivenom is the only product recommended for treatment of snakebite. The goal of this immunotherapy is to neutralize venom components with antibodies and prevent them from reaching their sites of action. All snakebites are medical emergencies requiring effective response protocols and knowledgeable case approach by the treating physicians once the victim arrives in the emergency room. Treatment of snakebite is outside the scope of this chapter, but it remains the responsibility of the veterinary clinician or researcher to either possess the appropriate antivenin or know the nearest local source for the species to be restrained.

The appropriate foreign antivenom for exotic snake species should be present when working with these species as it is not stocked in hospital pharmacies. Ideally it should be provided by the client and accompany the snake during transport to the clinician. Antivenom for native species is usually stocked at local hospitals for venomous species found in that region. It is recommended to contact local hospital pharmacies to periodically check on current inventories as antivenom can be difficult to obtain and supplies may be limited.

Treatment of envenomations is a challenge to physicians as most have never treated a snakebite victim. Case approaches, the appropriate use of antivenom, and patient support have also been controversial. Locating and obtaining appropriate antivenom may be difficult, resulting in critical delays (Seifert 2006b). Species-specific antivenom should be sought unless there is evidence for cross-species efficacy. Most private collectors do not routinely maintain exotic antivenoms (Keyler 2006). Lack of sufficient appropriate antivenin can be a determining factor in choosing not to accept cases or engage in specific research projects that involves the handling of venomous snakes.

In the United States, foreign manufactured antivenin can be imported by facilities or individuals under an Investigational New Drug license issued by the Food and Drug Administration, Department of Health and Human Services. These products may be species-specific or polyvalent. Some antivenoms have shown cross-species neutralization (Minton 1999), but evidence must be available for efficacy before relying on this strategy. The appropriate antivenom should be provided by a responsible owner or researcher and travel with the snake to the clinic. If the owner does not have the appropriate antivenom, the nearest source should be located prior to arrival. For long-term studies, the acquisition and stocking of the appropriate antivenom is recommended.

An Online Antivenom Index (OAI), developed by the Association of Zoos and Aquariums (AZA) and the American Association of Poison Control Centers, lists specific antivenoms for the treatment of exotic snakebite and their locations across the country. This antivenom inventory can be accessed by calling Poison Control (US phone: 1-800-222-1222) to locate the nearest source for specific antivenom appropriate for the species. In most cases the source is an AZA facility that logs their institutional inventory on the OAI site. Poison control centers have access to this information and should be consulted when locating a potential source of antivenom for projects or procedures involving venomous snakes.

An additional source for foreign antivenoms is the Miami-Dade Fire Rescue Antivenin Bank (formerly the Florida Antivenin Bank, Inc.), which stocks a significant inventory of antivenoms. Information on their holdings and procedures for requesting antivenom can be found on their website (www.venomousreptiles.org). A phone call can arrange an emergency response (Emergency Envenomation, phone

786-336-6600 or nonemergency 786-331-4444) to arrange antivenom transport to the attending hospital. This service can be a critical element in the treatment of snakebite when quantities of appropriate antivenom are lacking.

Management Guidelines

Strict protocols for handling venomous reptiles, routine husbandry, and staff training promote safety for staff and animals. Written protocols for snakebite response must be in place prior to receiving venomous reptiles. Snakebite protocols and case approaches for attending physicians should be established with the local hospital and emergency room physicians to help ensure swift and consistent treatment. A list of consulting physicians who are experts in treating snakebite should be readily available as a resource for local treating physicians because few will be familiar with proper clinical management of snakebite.

The following venomous reptile handling protocols serve as a baseline for establishing best practices and may be expanded to incorporate unique aspects of facilities or research projects.

1) Venomous reptiles should not be handled by anyone except designated personnel.
2) Staff should be thoroughly trained, knowledgeable, and comfortable with handling procedures.
3) Always review techniques and procedures with staff. Set up the workspace in advance and clear the area of unnecessary objects or obstacles. Have all appropriate tools readily available.
4) Never work with venomous reptiles when in a hurry, mentally distracted, or on medication that may impair alertness, reflexes, or response time.
5) Two qualified personnel should always be present. Assistance is often needed and a second person is crucial should snakebite occur.
6) Cages should remain locked until they are ready to be opened. Always announce a cage is to be opened so the attention of support staff is immediately focused on the procedure.
7) All cages should be clearly marked "VENOMOUS". An additional label should state the name of the species (common and scientific name), the number of animals in the enclosure, the type of antivenom to be administered, and the typical number of vials recommended for a moderate envenomation.
8) Never handle a reptile that appears dead directly with your hands. Always use a tong or snake hook to test for movement. The mouth of a dead specimen should be carefully taped closed to avoid unintentional contact with the fangs.

Equipment and Methods

Venomous reptiles can be managed safely by using the proper tools and techniques. Training and experience play a significant role in developing expertise. A working knowledge of snake behavior and the reaction of snakes to stimuli will aid in strategizing the best methods to use for a particular procedure. An organized and methodical approach to handling and restraint increases control and is reassuring to support staff that may be unfamiliar with working venomous reptiles. The equipment and methods described here are proven techniques. Innovations can produce further modifications for specific procedures. Historic methods such as pinning a snake behind the head for manual restraint (Fig. 12.2) are dangerous manipulations and should be discouraged.

Snake Hooks

The manipulation of venomous snakes using snake hooks (Fig. 12.3), as opposed to tongs, lowers the potential of injury to the animal. Reptiles have a single occipital condyle supporting their skulls on the cervical spine. Rough handling or improper restraint can cause spinal injury (Frye 1991) when the snake twists or thrashes. Vertebral morphology and the limitations of movement by vertebrae and axial musculature have been reviewed by Gasc (1976). Using tongs for restraint may also induce the snake to bite itself. This can result in self-inflicted fang penetration and envenomation. Although the effects of self-envenomation are usually minimal due to immunity, mechanical damage due to fang penetration can have a serious outcome.



Figure 12.2 Pinning behind the head for manual restraint is not recommended. Snakes when struggling can move fangs independently while dislodging the mandible to succeed with envenomation. Eyelash viper, *Bothriechis schlegeli*, The Orianne Society.



Figure 12.3 Snake hooks (top to bottom): wide-blade python hook, extension hook, double-handled hook, various styles, L hook or pinning hook.

The choice of snake hook is dependent on the size and species. Hooks come in a variety of sizes and configurations, and can be homemade or purchased from specialty suppliers (e.g., Midwest Tongs and Animal Capture Equipment Inc.). Two main design aspects need to be considered when choosing the appropriate hook. First, the length of the hook handle must be longer than the striking distance to the hand. In most species this is usually two-thirds of the length of the snake or more. The second is that the terminal end of the hook, which supports the snake, should be of sufficient diameter to comfortably hold the weight of the snake. Large, heavy animals require the wider support surface found on larger diameter hooks. Python hooks have wide flattened surfaces of 3–6 cm for added comfort to the snake during lifting. This results in a more consistent manipulation of large vipers (genus *Agkistrodon, Bitis, Crotalus, Lachesis*, and *Vipera*). The main disadvantage of python hooks is they usually lack sufficient shaft length for large specimens. A hook with a terminal L-shaped end is not recommended. The snake will slide down the shaft if it is lifted higher than the handle of the hook. Hooks are relatively simple tools that can be made and tailored to problematic species or individuals.

Basic steps when using a hook:

1) Always set up all required equipment first (transfer or holding containers, and a clear work area) and review the procedure steps with personnel. It is desirable to have a second potential handler with a hook should assistance be required.
2) Always open bags, containers, and cages using proper safety methods.
3) The hook tip is initially inserted under the anterior portion of the snake and slid caudally to the midpoint or its approximate center of gravity, on the body side facing the handler.
4) Once the hook is at the desired location, lift the snake in one motion, just high enough for the head and tail to clear the surface. This will induce the snake to hold and balance. If it is still moving and not balanced, gently set the animal down and repeat the process.
5) Once balanced, lift and move the snake to the desired location. Prevent the head and tail from touching objects during transfer. This will often startle the snake and induce it to come off the hook.
6) Gently set the snake down and remove the hook. Be prepared to use the hook to keep the snake under control or to further manipulate it for the intended procedure.

Longer-handled hooks for larger and more agile snakes may have a second grip located above the base grip of the hook. Using two hands on the hook, with the second (anterior) grip as a pivot point, aids in lifting heavier specimens while increasing dexterity and control of the specimen. Care must always be taken that the position of the second grip (hand closest to the snake) is outside the striking range of the snake.

Some snakes require double-hooking to distribute their weight at two points. This includes very large specimens where support on a single surface will cause discomfort or injury. Snakes with medical problems (e.g., fused vertebrae or a recent surgery) are also supported this way. Active snakes and arboreal prehensile-tailed species are also handled with greater control when double-hooked.

The use of two snake hooks requires more finesse than the use of one.

1) Hold a hook in each hand and insert them under the middle portion of the snake, on the same side of the body that is facing the handler.
2) Move the hooks away from each other to points dividing the snake's length into thirds. While the hooks are being moved to these locations, each hook should be lifted slightly testing the snake's tendency to balance.
3) Once the hooks are appropriate for balance, lift the snake and determine if it is stable. If so, transfer the snake in a smooth, deliberate movement.
4) When lifting, the outward pressure (away from the snake's midpoint) of the hooks will help keep tension on the snake and not draw the hooks together if the snake tries to progress forward.

This technique requires practice, but is not difficult. Each snake reacts differently to the double-hooking process. For specimens that benefit from double hooking, this is an excellent technique and should be used routinely.

Tongs and Forceps

Various styles of snake tongs and forceps (Fig. 12.4) are available from reptile equipment dealers (e.g., Midwest Tongs and Animal Capture Equipment). They should not be used as a primary method of restraint due to their potential to injure. Many snakes will thrash or bite the tongs when held tight enough for restraint. If tongs are used directly for restraint, the contacting surface of the tongs should be padded to create a firm but soft restraint. This style of tong can be very useful when working in the field, primarily with small to medium-sized specimens. In captivity, tongs should only be used as a last resort or in an emergency. Their use is not an acceptable substitute for lack of training or skill with a snake hook (Altimari 1998).

Long-handled tongs are ideal when used for feeding, removing cage items, manipulating container lids, holding restraint tubes, and lifting holding bags. Tong length must always be longer than the maximum striking distance of the snake.

Elongated forceps (Fig. 12.4) are used for feeding small snakes, removing retained shed or ectoparasites, and assessing the depth of anesthetized animals. Forceps length may range from 30 to 45 cm. They must be used cautiously when working in close proximity to the head, allowing for potential movement and strike ability.

Protective Gloves

Wearing protective gloves for handling venomous snakes (Fig. 12.5) has been used by a limited number of researchers. While this method does have its advocates, extreme caution must be used as it places the handler in close proximity to the snake. Defensive strikes may not only target the gloves, but also the handler's arms and body that are not protected. Some snakes appear not to recognize gloves as strike targets as they do bare fingers and hands. This gives the impression that the snake is tame and not prone to biting. That condition can change quickly and the snake should always be handled so that its strike range is limited to the padded/protective areas of the gloves. A popular manufacturer, HexArmor, produces the Hercules™ R6E glove made with SuperFabric® that may offer sufficient protection for most small to medium-sized species. The company does not offer any guarantees in regard to protection from snakebite. The condition of the gloves with prolonged use needs to be monitored as the integrity of the material may break down over time (R. Keszey, pers. comm.).

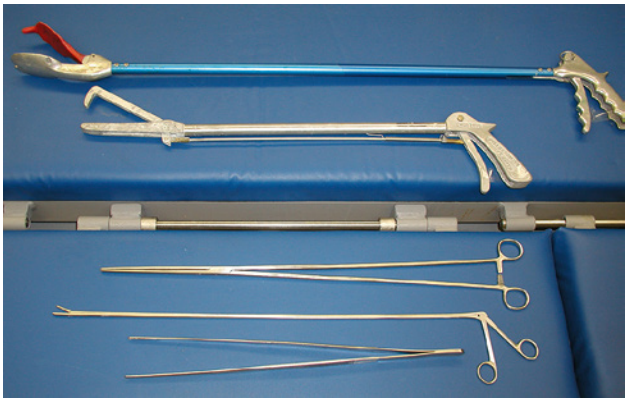


Figure 12.4 Tongs and forceps (top to bottom): Midwest Tong®, Pilstrom Tong®, hemostatic forceps, endoscopic forceps, and tissue forceps.



Figure 12.5 Puncture-resistant gloves can offer protection from snakebites of small to medium-sized species, but all handling precautions must be met as this method requires the handler to work in very close proximity to the snake. Tiger rattlesnake, *Crotalus tigris*, Glades Herp Farm.

Shift Boxes

Most snakes will enter boxes, where they can seek visual and tactile security. Shift boxes are placed either inside the enclosure or attached to the outside. Box size need only be large enough for the snake to lie comfortably in a resting coil. Many snakes prefer to wedge into a tight-fitting space for physical and tactile security. Normally, the snake's head when residing in a shift box is pointed toward the opening (entrance hole) awaiting the passing of potential prey. They will commonly strike out at any movement in front of the opening. Training some elapids to enter shift boxes (Kipp et al. 2006) is achieved with classical conditioning techniques. This is a very useful management tool for long-term captive animals requiring routine handling.

Shift boxes are most appropriate for large, swift elapids. They can be designed to attach directly to the cage (Fig. 12.6). In snake collections requiring multiple



Figure 12.6 Shift box and interfacing cage for an arboreal snake. Not shown are the transparent top and side panels of shift box. Used for Gold's tree cobra, *Pseudohaje goldii*, Central Florida Zoo and Botanical Gardens.



Figure 12.7 Shift box in cage. The shift box door can be slid close with a snake hook and locked. Black mamba, *Dendroaspis polylepis*. Courtesy of Medtoxin Venom Laboratories.

enclosures, the openings in cages, shift boxes, and the points of attachment are standardized so boxes can be interchanged. Cages are also designed with a center divider that allows the handler to shift the snake from one side to the other to facilitate safe servicing. The divider slide space should be sufficiently narrow to prevent escape when the divider is removed.

Shift boxes within a cage (Fig. 12.7) should be solid, with a bottom and locking door (Rossi 1995). They are easily fabricated from plywood and sealed with polyurethane to facilitate cleaning. A horizontal sliding door is designed to be closed with a hook once the animal is enclosed. A locking pin or mechanism for the shift box door is secured prior to removing from the cage and when transporting the snake.

Many styles and designs for shift boxes that attach to the outside of enclosures have been used to facilitate safe cage servicing or to aid with restraint and immobilization for veterinary procedures. Historically in zoos and research facilities, boxes have been designed and fabricated "in house" to fit a specific enclosure for a designated species or individual. Shift boxes have primarily been used for shifting large elapids that are dangerous to work in an open environment using a hook. However, any venomous species is a candidate for shifting to ensure a safe and controlled procedure.

Shift boxes attached to enclosures need to incorporate the following design elements:

1) Appropriate comfortable size for the snake.
2) Sturdy construction, able to endure dropping and long-term use.
3) Secure method of attachment to the enclosure.
4) Locking sliding door that corresponds to the door on the cage.
5) Large top-opening access door (lockable).
6) Clear top and/or side section to view the snake.
7) Adequate ventilation holes.
8) Sealed surfaces to promote easy cleaning.

Variants on the above design combine a squeeze for restraint. An interior sliding wall (Fig. 12.8) is used to push the snake toward the opening and into the restraint tube. Care is taken to ensure the restraint tube diameter matches the box opening so no gaps exist. Additionally, the tube and the box must be securely attached (usually manually braced) to prevent changes in restraint tube position. Once the snake enters the tube a safe distance it is grabbed and restrained using a normal tube restraint grasp.



Figure 12.8 Shift box/squeeze box. The inner panel manually slides towards the entrance hole in the box for tube restraint or against the transparent slotted end for injections. Dallas Zoo. Courtesy of Habitat Systems Limited.



Figure 12.9 Shift box/squeeze box. Features include removable squeeze apparatus, slotted end for injections, two capped side ports for tube restraint, and top capped feeding chamber with sliding false floor for protected feeding. Not shown is the removable center divider to create a "U-maze" to facilitate total entry of long snakes. Jacksonville Zoo and Gardens, black mamba exhibit, *Dendroaspis polylepis*. Courtesy of Habitat Systems Limited.

More advanced designs (e.g., by Habitat Systems Limited) combine features to aid in the husbandry and management of venomous snakes (Fig. 12.9). Optional elements include removable squeeze apparatus with a slotted end panel for injections, capped side ports with interchangeable openings of various diameters for tube restraint, enclosed top-feeding chamber with sliding false floor (drops feed rodent into the shift box without directly opening the box), and removable center dividers to create a "U-maze" to facilitate total entry of long snakes. These features increase control while emphasizing safety.

Some boxes incorporate a built-in restraint shield or framed wire mesh panel that can be pushed down for temporary restraint. A common application of this design using a wire mesh top panel is for king cobras (*Ophiophagus hannah*) that frequently retain spectacles. This design is also helpful if treatment requires repeated intramuscular injections.

Shift box design is a function of the intended use (Fig. 12.10). Shift boxes can be used to accomplish tube restraint and anesthesia using the entrance hole of the box. Variations have been described (Bertram & Larsen 2004), but the basic design and function remain the same. When using shift boxes, users must know how all doors operate (especially when removing the box and a second snake is in the cage!) along with corresponding locking and safety features. Some boxes are overdesigned, increasing the opportunity for door to be left open or unsecured. Doors and locks must always be double-checked visually and for movement prior to assessing if a snake is safely secured.



Figure 12.10 Traditional shift box. This simple design enables the snake to shift out of the cage, eliminating direct contact. The snake can then be transferred for anesthesia or other procedures. ourtesy of Habitat Systems Limited.

Unattended boxes that have been removed from the enclosure are placed in larger, secured and labeled containers to alert staff to the presence of a venomous snake.

Restraint or "Squeeze" Box

These boxes are used to restrain the movement of a snake for examination, measurement, and radiography (Quinn & Jones 1974). They consist of a box and a clear shield to press the snake against the bottom of the box for temporary restraint (Fig. 12.11). Most are made of wood, but acrylic boxes have the advantage of allowing the snake to be viewed from all sides, including the ventrum (Krebs et al. 2006).



Figure 12.11 Traditional restraint box for clinical and field applications. Primarily used for injections and measuring. Western diamondback rattlesnake, *Crotalus atrox*.

The size of the snake determines the size of the box; it should enable the animal to lay coiled in a normal position. The open top of the box is fitted with 0.5-cm Plexiglas shield, with a center handle, that can be lowered to press the snake against a thick foam rubber or other soft material pad.

It is important that the shield closely fits the sides of the box to prevent the snake from wedging its head through a gap. The shield is initially lowered using tongs, then secured by hand once safely in place. Holes are drilled into the shield to facilitate injections. Multiple holes are drilled across the shield since the position of the snake is random. Shields made of diamond-mesh expanded sheet metal have also been used (M. Whitney, pers. comm.), but care must be taken to avoid the snake striking and injuring oral areas.

Measurement is accomplished using a dry-erase ink marker to draw a mid-dorsal line equaling the length of the snake. A thin wire is superimposed over the drawn line, then straightened and measured. Map measurers have also been used to trace line lengths.

If a restraint box is to be used for a period of time, holes are drilled through the sides to permit the passage of aluminum rods to hold down the shield (Fowler 1978). If a restraint box is used for radiology, it must have a locking mechanism for the top acrylic shield. Snakes secured in such a fashion should not be left unattended and must be placed in a secured, labeled container.

Restraint Tubes

Manual restraint and immobilization of venomous snakes has been described using a wide variety of techniques for a variety of applications. For many procedures, manipulation of venomous snakes without chemical immobilization is desirable for initial examination, medication, and simple procedures including removal of adhered shed, palpation, blood sampling, and sex determination.

Techniques that employ restraint tools as the primary method of restraint, such as nooses, tongs, strap sticks, bucket restraint (Gillingham et al. 1983), noose tube restraints (King & Duvall 1984), strap boards (Ward & Harrell 1983), and manual restraint following pinning with a snake hook, are to be avoided. While used with some success by professional snake handlers in the venom extraction industry, these methods increase the risk of snakebite for the occasional handler and can injure the snake. Safer methods using clear tubes and shift, restraint, and anesthesia boxes are preferred. These remote-handling methods require more time and equipment, but greatly reduce direct contact with the snake. All procedures should optimize protected contact and effective control, thereby ensuring handler safety.

The standard for safe handling of venomous snakes is the Plexiglas tube restraint (Murphy 1971). This method minimizes the risk to the handler and potential injury to the snake. Clear, hollow tubes are available in a variety of acrylic materials. They can be purchased as individual tubes, usually sold in 2-m lengths, of various diameters (McMaster-Carr). Sets of restraint tubes are also available from some reptile supply companies. Thin-wall, flexible tubes crack easily and therefore are less safe than thicker-walled tubes. Polycarbonate hollow rods and PETG (a copolyester material) with a minimum wall thickness of 0.25 cm are best. These products are more durable and do not break if dropped.

The basic steps for tube restraint are as follows:

1) Choose a tube with an inside diameter that will not allow the snake to turn around (inside diameter less than the length of the snake's head or slightly larger than the snake's girth at mid-body).
2) Using a hook, place the snake on a smooth surface. Small and medium-sized specimens are worked on within a container. This is usually a trashcan or other open-top container large enough to facilitate movement by the handler to manipulate the snake into the tube. Large and more sedentary snakes are worked on the floor or the ground in field conditions. There must be ample open space for handlers to maneuver safely around the snake. Containers are preferred since they limit the range of motion and position of the snake.
3) Use tongs that are longer than the snake's striking range to hold the tube. Grasp the tube in the middle with the tongs in one hand (usually the left hand for a right-handed person) and slowly lower the open end of the tube toward the snake in a manner that will not induce the snake to strike at the tube. Snakes that strike the open end of the tube may incur oral lesions, primarily associated with the mucous membranes that cover the fangs.
4) Using a hook that is longer than the snake's striking range and held above that point, gently touch or hook the animal to manipulate it into the tube (Fig. 12.12). This is a combined maneuver moving the tube and the snake in a fashion that will entice it to enter the tube.

This procedure requires patience! Never hurry and always stay in control of the process.

1) The first goal is to get the snake's head inside the opening of the tube. This should be done quickly to reduce the chance of the snake striking.
2) Sometimes moving the snake backward with the snake hook will encourage it to move forward, entering the tube.



Figure 12.12 Tube restraint. Position of primary handler and snake in tube just prior to restraint. Florida cottonmouth, *Agkistrodon piscivorus*, Central Florida Zoo and Botanical Gardens.

3) Once the snake starts to enter the tube, hold the tube motionless so as not to startle the snake.
4) More active snakes require the tube to be worked down the body following its undulating movements.
5) Once the snake has entered the tube and is at least half way in (the tong grasp point on the tube if the tube is grasped in the middle) and still moving forward, lay the hook down (or hand it to an assistant) and with that hand quickly grasp the snake and the end of the tube at which the snake entered (Fig. 12.13). This secures the snake in the tube and prevents it from backing out. The other hand is used to grasp and support the animal.



Figure 12.13 Tube restraint completed. With large specimens, the primary handler secures the snake and tube while the secondary handler supports and restrains the body. Florida cottonmouth, *Agkistrodon piscivorus conanti*, Central Florida Zoo and Botanical Gardens.

Never overcommit to the grab! If the snake begins to back out of the tube or quickly progresses to the end of the tube, abort the procedure and start over.

1) Once restrained, immediately visually check your grasp. Both the tube and the snake should be held firmly to keep the snake from progressing forward or backward.
2) Make sure there is not an opening between your fingers and the palm of the hand that could allow the snake to withdraw a body coil and withdraw from the tube.
3) With medium to large snakes, the assistant should immediately support and restrain the animal's body once it has been successfully restrained. This permits the primary handler to focus their attention on securing the snake while supporting the tube with their other hand.
4) If a snake has a large girth at mid-body and a relatively small head, a smaller-diameter tube is inserted inside the open end of the tube and over the snake's head to keep it from turning around.

Snakes that are anesthetized require a controlled release from the restraint tube in the following sequence:

1) The primary handler grasps the tube midway with the tongs while maintaining tube restraint with the other hand.
2) The snake and tube are placed in a container and angled vertically. The grip on the snake is released and the hand is withdrawn rapidly from the container (and the snake's striking range).
3) The primary handler and the assistant pick up hooks for further handling.
4) The container is secured and labeled appropriately.

The primary handler and the assistant always review the procedural steps before and during the process to ensure a thorough understanding of roles and expectations.

Many large-bodied pitvipers will attempt to progress up the tube when released. This should be avoided to prevent the snake becoming stuck in the tube. While still maintaining manual restraint, these snakes should be pulled down the tube to a safe point near the end prior to release. When released, many snakes will quickly withdraw from the tube and immediately strike back at the handler. Alternatively, some species (i.e., elapids) will attempt to flee. Handlers need to be prepared to use hooks to keep the snake under control.

Tube restraint can also be accomplished directly from a shift box, facilitated by a squeeze apparatus adapted to the box (Fig. 12.14). The diameter of the restraint tube must match the hole in the shift box.

Tube restraint provides handlers and clinicians with a high degree of control during the examination. The snake is advanced to the end of the tube for cranial and oral



Figure 12.14 Tube restraint directly from a shift box containing a squeeze apparatus. In addition to tube restraint, the body of this 14' king cobra (*Ophiophagus hannah*) is also manually held in the shift box during examination to maintain control of the body. Central Florida Zoo and Botanical Gardens, photo credit Sarah Burke.

examination. Various locations along the snake's body can also be examined. Care is taken to keep a significant portion of the anterior body in the tube. Restraint tubes are also used for administering oral medications and force-feeding (Radcliffe 1975). The major advantage of this technique is that the snake is restrained without grasping the head, and the animal is positioned in a relatively straight line to facilitate examination, medication, tube-feeding, and anesthesia.

A variation of acrylic tube restraint (Mauldin & Engeman 1999) employs wire mesh cable holders as the restraint "tube". While this method can be used with some snakes, it is not recommended for venomous species since they will bite through openings in the mesh, resulting in either envenomation of the handler or oral trauma to the snake.

Restraint Tube Modifications

Clear acrylic restraint tubes can be modified for the needs of the clinician. Tubes can be cut to various lengths to facilitate safe handling (i.e., longer tubes for longer snakes). Tubes can be drilled to create access holes and elongated cutouts made for increased access for minor procedures. Appropriately sized PVC caps, rubber stoppers, or wooden corks can be temporarily or permanently secured at one end to prevent the snake from progressing through the tube.

Care must be taken when any opening is made along the length of the tube to prevent hands and fingers from crossing these openings. Many species are capable of biting and protruding a fang through openings. Bite attempts on the inside of the tube will release venom that will run down the inside of the tube to the hand. Handlers should wear latex gloves to prevent venom contact with the skin, which may lead to envenomation through microcuts. All tubes must be thoroughly washed and disinfected immediately after use.

Anesthesia Boxes

Full clinical examination and surgical procedures require chemical immobilization and anesthesia (see Chapter 12). This is essential when evaluating cranial features such as the nostrils, infra-orbital pits, spectacle and eyes, oral cavity, glottis, and tongue. More general procedures such as blood sampling, examination of the integument, removing adhered shed skin, removal of ectoparasites, cloacal examination and sampling, and palpation may be accomplished by tube restraint. Radiology may be performed on snakes in shift boxes, squeeze boxes (through a fixed acrylic shield), or through bags if the specimen is inactive. If an intended procedure presents a safety concern for personnel, full chemical immobilization is strongly recommended. Some snakes can be induced in restraint tubes with propofol administered into the ventral coccygeal vessels (Chapter 12).

A variety of containers for venomous snakes can be used as inhalant anesthesia boxes. Large clear plastic Rubbermaid® or Sterilite® storage boxes (Fig. 12.15) are available from retail stores. Snakes are placed directly into these boxes only if the lids can be secured to prevent escape. Transparent containers allow observation of the snake during anesthetic induction. A snake contained in a cloth snake bag may be placed inside an anesthesia box. However,

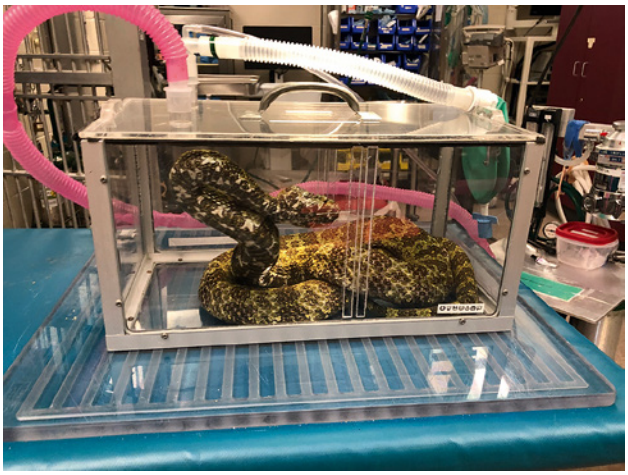


Figure 12.15 Anesthesia box. A clear plastic storage box fitted with an adaptor to receive the corrugated breathing tube from the anesthesia machine. The transparent container facilitates viewing to judge the level of induction. Mangshan pit viper, *Protobothrops mangshanensis*.

judging the anesthetic level will depend on evaluating declining movement in the bag. When testing the movement of a snake inside a bag, always use instruments (forceps, tongs) and never manually palpate the bag.

A snake contained in a shift box or ventilated restraint box can also be placed in an anesthesia box. The anesthesia box, fitted with an adaptor for the breathing system, allows for infusion of the inhalant anesthetic in oxygen from the machine. A shift box may also be enclosed in a plastic bag for administration of inhalation anesthetic through the opening. However, induction is very difficult to evaluate when the snake is enclosed in two containers.

Guidelines to assess whether a snake is safely anesthetized include lack of response to tactile stimulation, inhibition of tongue flicking, and lack of ability to right itself when turned over on its dorsum. Snakes can hold their breath for 15–20 minutes and anesthetic induction can be prolonged. Once anesthetized, a restraint tube is placed over the head and anterior portion of the body as a secondary safety precaution and the snake is then carefully removed from the box. For continued delivery of inhalant anesthetic can be maintained by a cover can be fitted over the open end of the restraint tube, a mask placed directly over the head if removed from a restraint tube, or direct endotracheal intubation whereby a tube is inserted through the snake's glottis and into the trachea (Chapter 12).

Transport

Safe transport and receiving of venomous reptiles require planning and setting up the appropriate equipment in advance. Securing the snake in a cloth bag and placing it in a ventilated locked box is recommended. The cloth bag should be of tight-woven, strong material that allows for good ventilation. Bags are examined for small holes that may be tested by the snake and enlarged, leading to escape. Bags are turned inside out so the seam is on the outside to avoid entanglement in loose threads. Only one animal should be contained in each bag to eliminate defensive striking and facilitate removal. Bags should be long (deep) enough to be easily knotted at the open end and additionally secured with strong tape or plastic cable ties.

To place a snake in a bag, the bag is hung inside an empty container and secured in an open position using clips (clothes pins work well). Tongs are used by an assistant to hold the sides of the bag open. They are then used to close the bag after the snake is guided in by a hook. Commercially available "snake baggers", long-handled rods with an attached and removable bag, increase safety in the bagging process (Bag-Em™, Animal Capture Equipment, Inc.; Snake Bagger®, Midwest Tongs). Never be too anxious to manually close the top of the bag. Most snakes tend to climb upward after being dropped into the bag. Always visually know where the snake is. Use tongs to close and secure the bag, or twist and pull the neck of the bag under the shaft of a secured snake hook prior to knotting.

When knotting, first transfer the bagged snake to a flat surface. Place the shaft of the snake hook across the twisted neck of the bag and pull to secure the snake in the far end of the bag. For additional security, the bag is secured with strong tape or cable ties on either side of the knot. This must be done away from the portion holding the snake. Bags are labeled to identify the snake species with a noticeable "VENOMOUS" notation made on the label. Red labels with the skull and crossbones motive symbolizing poison are most effective. Tongs are used to clamp the bag just under the knot for lifting. Bags should always be carried above the knot and away from the handler's body. Bagged snakes are placed in a suitable container or box while waiting for procedures or transport. Transport boxes containing more than one bagged snake have solid dividers to eliminate the potential for snakes biting each other.

Transport boxes are locked, well ventilated, and kept away from temperature extremes. Boxes are kept out of the sun and transported in air-conditioned vehicles to avoid hyperthermia. Boxes are clearly labeled "CAUTION – VENOMOUS SNAKES" and stored in locked rooms while awaiting transport.

The same level of caution used in bagging the snake must be used during removal from transport containers. Open the transport boxes using the level of caution as if the snake inside had escaped the containment bag. Keep fingers and hands away from openings (use tongs) and be prepared to hook a snake into a holding container. The bag is removed from the container using tongs. Snakes can bite through cloth bags induced by limited visual capability or when the bag is touched. Bites through either bags or screened surfaces can result in significant envenomation. Under these circumstances, a snake's fangs can become momentarily hung up in the bag material, resulting in the expression of large quantities of venom.

Prior to untying the snake bag, place the bag on a flat surface and position the shaft of the snake hook across the neck of the bag below the knot, securing the snake in the end of the bag. All extremities are held safely away from this portion of the bag. Once untied, tongs are used to secure the open bag end. It is then picked up and lowered into a container. The snake is released by picking up the bottom end of the bag with the tongs. Bags with a hemline sewn across the bottom corners of the bag provide an area of material to grab without pinching the snake.

A field transport box (Birkhead et al. 2004) for carrying large numbers of venomous snakes combines both tube restraint and a modified transport container. In this design,

10 polyethylene restraint tubes, capped at both ends, are secured by spacers in a transport container. The advantage of this design is that it allows individual containment of each snake that is positioned for immediate manipulation or restraint.

The International Air Transport Association (IATA) publishes Live Animal Regulations that are adopted by most airline carriers. When shipping airfreight, it is prudent to review these regulations in case airline employees question the design and features of the shipping crate and the methods by which the snakes are contained. IATA requirements (for snakes see Part 8, Container Requirement #44) are presented as examples to be adopted depending on the species and size of the snake. Specific suggestions in the IATA regulations include container rigidity, packing material, size and type of container, specification for snake bags, double-bagging snakes with a transparent mesh inner bag for inspection, wire-covered containers, and an abbreviated listing of venomous snakes and some colubrids that are considered venomous. It is the responsibility of the shipper to ensure materials and methods are appropriate for safe transport. It is rare that an airline employee will ask the shipper to open a container of venomous snakes for inspection. This is not the case for international shipments, which are routinely inspected by wildlife customs agents charged with monitoring species covered under the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).

Venomous Lizard Management

Gila Monsters and Beaded Lizards (Helodermatidae)

Venomous lizards known to produce significant envenomation in humans are restricted to two species, the Gila monster (*Helododerma suspectum*) and the Mexican beaded lizard (*Heloderma horridum*). As studies continue on the evolution of reptilian venom systems (Fry et al. 2006) additional "nonvenomous" lizard taxa will be recognized as having toxin-secreting oral glands. Currently this is restricted to some species of monitor lizards (family Varanidae), especially the desert monitor (Ballard & Antonio 2001).

Helodermatids are large, stout-bodied lizards with large heads, powerful jaws, and short legs adapted to digging. They are easily recognized by their colorful, intricate skin patterns and rounded tuberculate scales, which give them a beaded appearance. Gila monsters average 36 cm as adults while beaded lizards can reach 1 m in total length.

Helodermatids have evolved defensive venom tailored to create significant pain to ward off predators. Bites are extremely painful and can have systemic effects, including a rapid drop in blood pressure that may result in hypotensive shock (Preston 1988). Unlike snakes, the venom glands of helodermids are mandibular and appear as a rounded swelling located midway along the lower jaw. The large triangular-shaped head is the result of well-developed musculature associated with biting and maintaining a vice-like grip. When biting, helodermatids exhibit a pumping action of the jaw musculature while embedding the enlarged, grooved, venom-conducting teeth, located above the venom glands. There are accounts of severe gripping bites resulting in the use of pliers, crow bars, severing of jaw musculature, and decapitation to disengage the lizard from the bitten extremity. Severity of envenomation is a function of the amount of time the lizard is allowed to bite. Envenomation is treated symptomatically as there is no antivenom for helodermatids.

Helodermatids are deceptive, normally exhibiting slow movements and sluggish behavior, but are capable of swift lateral and upward movements of the head and upper body when attempting to bite. Of 21 venomous bites received by zoo workers over a 25-year period (Card & Roberts 1996), four were inflicted by helodermatids. The authors concluded that because helodermatids are generally considered relatively benign captives, this assumption misleads individuals into handling them carelessly. No matter how much their owner professes its tameness, all helodermatids should be handled with the same caution as for venomous snakes.

Manual restraint of helodermatids requires first pinning the head down on a flat surface with a snake hook or pinning bar (Fig. 12.16). Once secured, they are picked up



Figure 12.16 Pre-restraint position for helodermatids. The head should be immobilized prior to manual restraint. Gila monster, *Heloderma suspectum*, Central Florida Zoo and Botanical Gardens.



Figure 12.17 Helodermatids can be manually restrained by securing a firm grip at the base of the head with a forelimb held between the fingers to maintain control of the upper body. Once elevated, the second hand is used to support and hold the body. Gila monster, *Heloderma suspectum*, Central Florida Zoo and Botanical Gardens.

with a firm grip at the base of the head and a forelimb held between the fingers to maintain control of the upper body. Once elevated, the second hand is used to support and hold the body (Fig. 12.17). Locking hemostats (40–60 cm) have also been used to successfully pin helodermatids (Poulin & Ivanyi 2003) by using the interlocking base portion (area between the finger eyelets) as the pinning bar.

Helodermatids can be closely examined using manual restraint. Examination of the oral cavity using a hard rubber speculum has limited use since they will vigorously bite down on any object placed in the mouth.

Helodermatids can be anesthetized by administering an inhalant anesthetic into an induction chamber. Anesthetized helodermatids should again be pinned as described above before removal from the anesthetic chamber. One of the last reflexes to be lost is the defensive bite.

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Products Mentioned in the Text

Animal Capture Equipment, Inc.
1102 Baker Avenue
Bacliff, TX 77518
Phone: 866.339.9960
Web address: www.ace-cap.com

Habitat Systems Limited
4489 N.W. Second Avenue, Suite 3B
Des Moines, IA 50313
Phone: 888.909.5795
Web address: www.habitatsystemsltd.com

HexArmor
2000 Oak Industrial Drive NE
Grand Rapids, MI 49505
Phone: 877.692.7667
Web address: www.hexarmor.com

McMaster-Carr
6100 Fulton Industrial Blvd.
Atlanta, GA 30336-2852
Phone: 404.346.7000
Web address: www.mcmaster.com

Midwest Tongs
14505 S. Harris Road
Greenwood, MO 64034
Phone: 877.878.6647
Web address: www.tongs.com

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13

Crocodilians (Crocodiles, Alligators, Caiman, and Gharial)

Darryl Heard

This chapter is dedicated to Dr Gregory Fleming (deceased), a friend, colleague, and the original author of this chapter.

Introduction

Crocodilians are a very old order of reptiles with a great variety of extinct lineages. The living species represent only a small part of this evolutionary diversity, which included aquatic, semi-aquatic, and terrestrial species. The recently recognized 23 living species have increased to 27, and possibly 30, species based on molecular taxonomy (Grigg & Kirschner 2015). These species are distributed over four super families (gharials and gavials, crocodiles, alligators, and caiman).

Crocodilians are popular exhibit animals because of their size and appearance. Furthermore, many species are endangered and conservation programs, in both zoos and in situ, are making increased demands for safe and effective chemical immobilization and anesthesia.

Physiology and Anatomy

The physiology and anatomy of crocodilians is well described by Grigg and Kirschner (2015), and relevant areas for anesthesia are summarized in the following paragraphs.

Crocodilians spend much of their time either basking or with their bodies entirely submerged except for their eyes and nares. Each nostril acts as a waterproof valve that is closed with a muscular flap during submersion and between breaths. Immobilizing drugs can obtund this reflex, allowing water into the respiratory tract (Fleming 1996). The soft palate and gular fold form another respiratory valve. The elongated soft palate presses down against the gular fold, which protrudes from the floor of the pharynx. This seal allows the crocodilian to open its mouth underwater without water entering the internal nares and the glottis. The gular fold may need to be displaced to visualize the glottis for intubation (Fig. 13.1).

Crocodilians possess a pair of well-developed lungs. The primary respiratory muscle groups are the intercostal muscles and two transverse membranes, the postpulmonary and posthepatic membranes, both comprising primary fiberous tissue with a muscular component (Van der Merwe & Kotze 1993). The postpulmonary membrane separates the lungs from the liver. The posthepatic membrane is attached to a sheet of muscle attached at the os pubis. These two membranes act as a "diaphragm". Ventilation is achieved by expanding the intercostal muscles and then membranes pull the liver in a caudal direction to create a negative pressure in the lungs that draws air inward. The glottis is then closed, holding the air in the lungs. When the glottis relaxes air is passively expelled via the elastic recoil of the intercostal muscles and the postpulmonary/posthepatic membranes and lung tissue.

Recent studies have shown alligators, and possibly all crocodilians, have unidirectional airflow through the lungs (Farmer & Sanders 2010; Schachner et al. 2013). The significance of this for respiration and anesthesia is unknown.

Cardiovascular System

Crocodiles are the only reptiles that possess a four-chambered heart. The heart functions like a mammal's, with the exception of anatomical adaptations for an aquatic lifestyle. These include the foramen of Panizza, an opening between the left and right ventricle, the subpulmonary conus in the pulmonary outflow tract of the right ventricle, and the aortic anastomosis, which connects the two aortic arches just posterior to the heart (Axelsson 2001). In addition, crocodilians have a left aorta arising from the right ventricle that allows blood to bypass the lungs.

The foramen of Panizza is a small window located between the intraventricular septum at the confluence of the left and right aortic arches. This opening acts as a pressure valve,

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Figure 13.1 View of the gular fold of a Chinese alligator (*Alligator sinensis*) being depressed with a tongue depressor to access the epiglottis. Note the oral speculum constructed of a piece of PVC pipe wrapped with tape.

allowing blood to flow between the venous and arterial systems, resulting in venous admixture. When the animal is breathing, left ventricular pressure is greater, allowing a small amount of oxygenated blood to flow through the foramen of Panizza into the venous blood supply. When the crocodilian submerges, air held in the lungs restricts blood flow through the pulmonary capillary beds, resulting in pulmonary hypertension, which increases right ventricular and pulmonary arterial pressures. As a result, blood flows from right to left through the foramen of Panizza. Deoxygenated blood is diverted away from the lungs through the left aortic arch to organs that are not sensitive to low levels of oxygen (e.g., the liver and stomach) (Grenard 1991). Oxygenated blood is diverted to oxygen-sensitive organs (i.e., the heart and brain). A combination of blood shunting and anaerobic metabolism may allow an inactive crocodilian to stay submerged for 5–6 hours (Lane 1996).

The right-to-left shunt through the foramen of Panizza has clinical implications during anesthesia when the crocodilian does not have ventilatory support or is apneic. Shunting of blood away from the lungs will delay inhalant anesthetic uptake and removal. This emphasizes the importantance of assisted ventilation and potentially the use of epinephrine in the recovery period (see discussion below).

Renal Portal System

Crocodilians possess a portal system composed of the renal vein arising from the epigastric and external iliac veins. These vessels drain blood from the dorsal body wall, the cloaca, sex organs, and the bladder. Drugs injected into the caudal half of the body, base of the tail, and hind legs may be cleared by the kidneys prior to reaching the systemic circulation. In other reptile species, such as the red-eared slider, studies have shown a significant hepatic first-pass effect following hindlimb drug administration (Holz 1997). A study comparing front leg vs. hind leg injections of buprenorphine in the same species resulted in a 70% decrease in the bioavailability of buprenorphine when injected in the hind end (Kummrow et al. 2008).

Care should also be taken when administering nephrotoxic drugs in the hind legs. When possible, inject anesthetic drugs in the front legs. In some circumstances this may be too dangerous and this author uses the hind legs or tail for intramuscular (IM) injection. Unfortunately, uptake and circulation to the sites of action may be delayed and induction times prolonged.

Physiologic Reference Ranges

Obtaining heart and respiratory rates is very difficult in awake crocodilians. In one study (Huggins et al. 1969), juvenile American alligators (*Alligator mississippiensis*) and smooth-sided caimans (*Caiman sclerops*) were implanted with monitoring equipment and isolated from human contact for 12–20 hours before measuring cardiac and respiratory rates. Normal respiratory and heart rates at 22°C were 0.6 and 11.6 breaths per minute, and 1.6 and 14.2 beats per minute, respectively. Following visual contact with humans, both heart and respiratory rates doubled to 30 beats per minute and 6 breaths per minute (Huggins et al. 1969). Consequently, most captured crocodilians are likely to be tachycardic and tachypneic.

In general, heart and respiratory rates vary inversely with the size of the animal, and not surprisingly are affected by environmental temperatures (Franklin & Seebacher 2003). Prolonged exposure to temperatures above 40°C will cause irreversible cardiac damage. Heart rates as high as 55 beats per minute at 29°C have been recorded in Nile crocodiles caught in traps (Klide & Klein 1973; Loveridge 1979).

Thermoregulation

Crocodilians are poikilothermic, regulating their body temperatures with external environmental heat. They also operate at a preferred optimum body temperature (POBT) similar to mammalian internal body temperatures. For captive crocodilians, a good range for environmental temperatures is 25–35°C (Grigg & Kirschner 2015). Given a selection of temperatures, they are able to select the POBT for their metabolic needs.

Temperatures below and above POBT interfere with digestion and immune function. American alligators take twice as long to digest food at 20°C than at 28°C, while smooth-sided caimans digest food three times faster at

30°C than at 15°C (Coulson & Hernandez 983; Diefenbach 1975). Infection of American alligators kept at 30°C demonstrated the greatest white blood cell response to infection and survival of the infection, while alligators held above the POBT at 35°C succumbed to infection in 3 weeks (Glassman et al. 1981).

Crocodilians under general anesthesia should be kept at temperatures near their POBT or around 29.5°C. Environmental temperatures below POBT decrease metabolism and prolong clearance of parenteral drugs, resulting in delayed recoveries. Induction may also be prolonged because of slowed absorption and circulation times. For example, large Nile crocodiles induced with the neuromuscular blocker gallamine took twice as long to become recumbent at 14°C (40 minutes) than at 26°C (20 minutes) (Fleming 1996). In juvenile saltwater crocodiles, medetomidine (2.5 mg/kg IM) had no effect at 17°C and induction times were inversely proportional to body temperatures above 22°C (Olsson & Phalen 2013b).

Physical Restraint

All crocodilians are capable of inflicting serious damage by ether biting or lashing out with their tails. Since most anesthetic events begin with physical capture and restraint, Chapter 14 is offered as an introduction to techniques that facilitate safe handling in the perianesthetic period. If your anesthetic/restraint team is not familiar with these techniques, they should reach out to other experienced personnel for training and assistance. This should preferably occur before the need for anesthesia.

Successful restraint must be safe for both the handlers and the crocodilian. Reported injuries associated with physical restraint include fractured bones, damaged eyes, and drowning (Walsh 1987). Prolonged struggling will result in marked lactic acidemia, with pH levels dropping to 6.6–6.8 (normal range 7.2 ± 0.2). Like other reptiles, crocodilians take a prolonged period of time to recover from elevations in lactic acid that have been implicated in fatalities post restraint (Olsson & Phalen 2013b). The observation that captured crocodilians may become unconscious and drown if not allowed to rest after prolonged physical restraint may be due to the previously mentioned lactic acidemia (Sedgwick 1986).

Drug Delivery

Since most anesthetic episodes in crocodilians begin with capture and restraint (Chapter 14), it is uncommon for remote injection systems to be used.

Darts

Darting can be used to deliver immobilizing agents. There are several disadvantages, however, to their use: (1) it is difficult to get an accurate shot while the animal is in water; (2) it is difficult to determine if the dart has fully discharged; (3) the osteoderms covering most of the dorsal surfaces of crocodilians may deflect the dart; and (4) once the animal is darted, if unrestrained, it may submerge, become immobilized, and drown. Consequently, darting is more likely to be used in captivity in controlled situations (i.e., a dry enclosure). It is rarely used in the field (Blake 1993; Flammard et al. 1992).

Hand Syringe

The hand syringe has the advantage that it can be accurately placed and the rate of injection can be controlled. The animal, however, must be secured for safe injection. This technique can be used for hand-restrained small animals and for administering reversal agents to larger animals. Both IM and intravenous (IV) routes can be used as described below.

Pole Syringe

The advantage of a pole syringe is that crocodilians can be injected while unrestrained in a shallow pool, net, or snare. The main disadvantage is that the injector must be within 2.5 m of the animal and injection volumes are limited to 10–15 mL. If the anesthetic agent is not administered fast enough the pole syringe and handler may be damaged by the animal.

Injection Sites

The base of the tail just caudal to the hind legs has been common site for IM injections (Jacobson 1984). This area is composed of many layers of muscle with the vertebrae located deep within the muscle, and there is no risk of injecting into any internal organs when using a pole syringe. The main disadvantage is that in obese animals there may be a layer of fat, which if injected could delay drug absorption. Another factor to consider is the possibility of a significant hepatic first-pass effect following hindlimb drug administration (Mosley 2011). When possible, IM injections into the front legs are more effective for drug administration.

IV injections are accomplished by accessing the ventral tail vein (Fig. 13.2) (Wellehan et al. 2004). This site can be used to obtain blood samples, inject IV drugs, or for IV catheter placement. The spinal vein (Myburgh et al. 2014) should not be used for administration of anesthetic drugs.

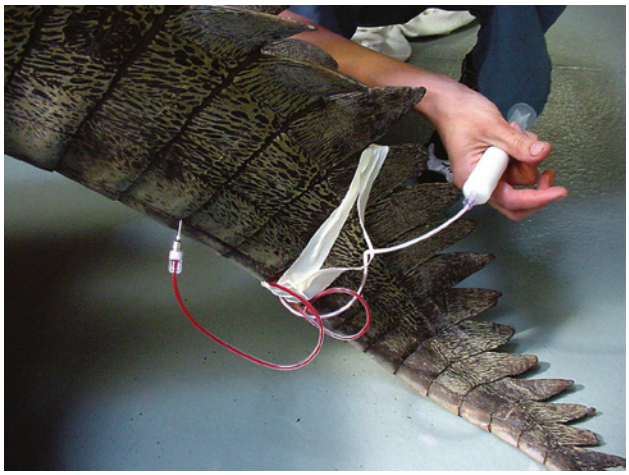


Figure 13.2 Intravenous blood draw via accessing the lateral coccygeal vein. The needle is inserted at a 90° angle at the lateral midline of the tail, just beneath the lateral spinus process of the vertebral body. This same approach may be used to complete intravenous injections of anesthetic drugs such as propofol.

Handling

Once the immobilizing drug has taken effect, it is prudent to use a pole or stick to stimulate the crocodilian a number of times to ensure there is no response. Once this is accomplished, the eyes should be covered with a damp towel and the jaw should be taped shut. Care must be taken to avoid taping the nostrils shut.

The crocodilian can then be rolled onto a stretcher or a large tarp. Care must be taken not to pull and tug on the legs of the animal. Large crocodilians may weigh up to 500 kg and pulling on their legs to move them or lift them may result in fractures or luxations (Blake 1993). To accommodate lifting a crocodilian out of shallow water, 1-m lengths of flat 2-inch commercial crane slinging can be placed under the chest and hind legs. By using the slings to lift, animals can be picked up and moved without pulling on the legs (Fleming 1996).

If the animal is to be intubated, a mouth gag, made of a steel ring, polyvinyl chloride (PVC) pipe, or wood block, should be used to prop open the mouth. Depending on the size of the animal, steel tubing (of varying diameters and widths) can be cut and wrapped with several layers of tape or leather so as not to damage the teeth. A hole in the middle of the gag allows for the passage of anesthetic tubes or endoscopic equipment.

Monitoring

Physiologic monitoring includes the use of a pulse oximeter, Doppler blood flow transducer, electrocardiography (ECG), ultrasound, capnography, and blood gas analysis. As in other reptiles, auscultation for monitoring heart and respiratory function is usually unrewarding. Anesthetic depth is evaluated using the withdrawal reflex of limbs, increasing or decreasing cardiac rates, righting response, and bite and corneal reflexes (Neill 1971; Heaton-Jones et al. 2002).

Electrocardiogram and reference values have been described for the American alligator (Heaton-Jones & King 1994). The ECG leads are attached to 2.5-cm needles passed through the skin. Although pulse oximetry may be used to assess heart rate it does not appear to accurately calculate oxygen saturation in reptiles (Mosley et al. 2004). Crocodilian skin thickness and pigmentation may further hamper measurement with the transmission probe, but a reflectance probe in the cloaca may improve the signal. Blood gases measurement is difficult to interpret because of variables such as temperature, feeding, and sample site (arterial, venous, or a combination of both) influencing the results. Blood lactate levels, however, are usually easy to obtain and measure with small portable monitors.

The Doppler blood flow monitor is a reliable method of obtaining heart rate (Bennett 1996; Neilson 1996). The probe is placed over the heart or a large blood vessel such as the ventral coccygeal, brachial, or femoral artery. Blood flow in the ophthalmic artery may be detected by placing the probe against the globe with the eyelid or third eye lid closed. Alternatively, a dorsally directed probe placed in the cloaca may also detect arterial blood flow. Unfortunately, this technique for prolonged monitoring stimulates evacuation in the cloaca.

Capnography is an important technique for the assessment of the adequacy of ventilation as well as for detection of spontaneous respiration (Fig. 13.3).

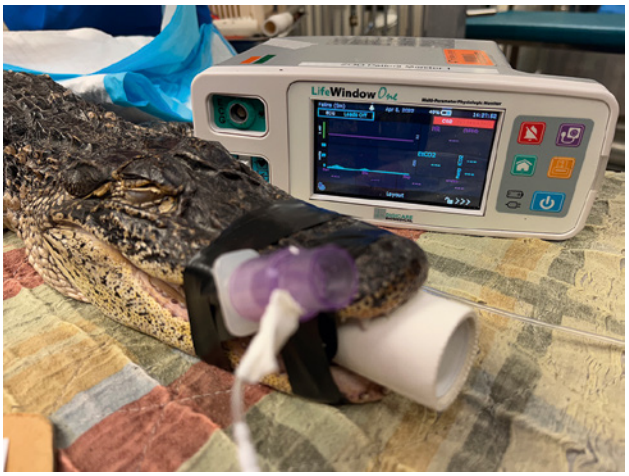


Figure 13.3 Anesthetized American alligator (*Alligator mississippiensis*) recovering from anesthesia. An endotracheal tube is still in place, with an attached in-stream capnograph sensor. Capnography is very useful for assessing the adequacy of ventilation and determining the presence of spontaneous ventilation before extubation. A PVC pipe is in place as a mouth gag.

Analgesia

For a comprehensive discussion of analgesia in animals please see Chapter 2.

As is common in exotic animal medicine, extrapolation of drug doses from similar species is needed to develop effective analgesia. The use of butorphanol as an analgesic in reptiles has been promoted for years based on research completed in birds (Paul–Murphy et al. 1999). Unfortunately, butorphanol in reptilian species (green iguanas and red-eared sliders) even at higher doses only resulted in sedation and no analgesia (Fleming & Robertson 2012; Sladky et al. 2007, 2008; Mosley et al. 2003, 2011). Consequently, this author does not recommend the use of butorphanol except perhaps as part of a multidrug immobilization regimen.

Morphine (0.8 mg/kg) and meperidine (pethidine) (2 mg/kg) in juvenile salt-water crocodiles showed analgesia as measured with thermal antinocioception (Kanui & Hole 1992). In red-eared sliders, morphine (1.5 and 6.5 mg/kg IM) resulted in analgesia, but caused long-lasting respiratory depression at higher doses (Sladky et al. 2007). Using the same methodology in bearded dragons, morphine (10 and 20 mg/kg IM) was analgesic, but the effect was delayed until 8 hours after administration (Sladky et al. 2008). In red-eared sliders, tramadol (5 mg/kg PO every 5 days) induced analgesia via both opioid and nonopioid pathways (Baker et al. 2011).

The use of meloxicam (0.2 mg/kg PO, IM, IV) has been reported in reptiles and IV or PO administration results in the same bio-availability (Hernandez-Divers et al. 2004; Whiteside & Black 2004). The present author has used meloxicam (0.05–0.1 mg/kg PO every 2 days) in medium to large alligators for up to a month.

Sedatives

The author has not used tranquilizers (i.e., phenothiazines) in crocodilians and is unaware of anyone presently using them.

Midazolam is the most commonly used benzodiazepine because it is water-soluble and is compatible when used in multidrug induction regimens. Midazolam (5 mg/kg IM) produced reliable relaxation and sedation for minor procedures in juvenile estuarine crocodiles while reducing indicators of stress (Olsson & Phalen 2013a). The combination of the long-acting zolazepam with tiletamine (Telazol) makes for an effective and safe drug combination for immobilization, although prolonged recoveries are possible.

Diazepam hydrochloride (0.22–0.62 mg/kg) administered 20 minutes prior to succinylcholine resulted in a smoother induction and lower doses of succinylcholine in American alligators (Loveridge & Blake 1972). Heart rates were decreased, respiration was maintained, and recovery for most was within 3 hours.

Reversal of benzodiazepines in mammals with flumazenil has been achieved in dogs at a ratio of 1:13 flumazenil to diazepam, and at 1:20 flumazenil to zolazepam (Lang 1987; Terpin et al. 1978). When using midazolam (5 mg/mL) the present author uses an equal volume of flumazenil (0.1 mg/mL) for convenience. If there are concerns the dose has not worked, an additional dose of the same volume is administered.

Local Analgesics

Due to the issues when using inhalation anesthesia described below, this author has changed to preferentially using parenteral anesthesia combined with either local or regional anesthesia (e.g., brachial, retrobulbar, and mandibular blockade) when applicable (e.g., limb amputation, enucleation). Toxic lidocaine doses have not been established for crocodilians, but extrapolating from mammals this author uses a maximum of 5–10 mg/kg for lidocaine and 1–2 mg/kg for bupivacaine.

A nerve locater can be used to assist in the accurate placement of local anesthetic around nerves (Wellehan 2006). Nerve locators use a pulsatile electric current passed through a needle in contact with the motor nerve (e.g., mandibular nerve) that innervates and thus stimulates an identifiable muscle (e.g., the digastricus muscle). Local anesthetic (e.g., 2% mepivacaine, 1 mg/kg) injected down the needle blocks nerve conduction. This technique has been used to provide analgesia in the mandible of American alligators, dwarf crocodiles (*Osteolaemus tetraspis*) and Yacare caiman (*Caiman yacare*) (Wellehan 2006). A more recent study (Bianchi et al. 2020) describes the use of a lateral approach through the mandibular fenestra (foramen) for nerve blockade in juvenile Nile crocodiles. The present author has used this approach successfully on several large crocodilians.

Muscle Relaxants

Although they have been utilized historically in Africa for the transportation and capture of wild crocodilians (Fleming 1996), the present author sees no need for the use of muscle relaxants given better capture and restraint techniques, and better alternative drugs and drug combinations. Most importantly, muscle relaxants do not provide analgesia for painful procedures in animals that are conscious. For those interested in more information please consult the chapters in previous editions of this book. Drug dosages are summarized in Table 13.1.

Table 13.1 Commonly used perianesthetic drugs in crocodilians.

Drug	Dosage (mg/kg)	Species	Remarks	Reference
Analgesia				
Morphine	0.8 IM	*Crocodylus porosus*		Kanui & Hole (1992)
Meperidine	1–2 IM	*C. porosus*		Kanui & Hole (1992)
Meloxicam	0.1–0.2 IM or PO every 2 days			Whiteside & Black (2004); Wellehan (2006)
Tramadol	5 PO every 5 days			Baker et al. (2011)
Ketoprofen	2 IM every 1–2 days			Tuttle (2006)
Butorphanol	0.1–0.2 IM		May cause sedation but not analgesia Usually combined with other drugs	Sladky et al. (2007, 2008); Fleming (2012) Mosley (2011)
Anesthestics				
Ketamine	11–110 IM		Variable response when used alone	Jacobson (1984); Loveridge & Blake (1972)
Medetomidine	0.13–0.17	Adult *C. porosus* 150–370 kg	Reversed with atipamezole 0.09–0.12 mg/kg IM	Olsson & Phalen (2012a)
Medetomidine	0.5	Juvenile *C. porosus* 2.0–4.8 kg	Reversed with atipamezole 2.5 mg/kg IM for 50 minutes Rapid temperature-dependent induction and recovery at body temperatures above 22°C No induction at 17°C	Olsson & Phalen (2013a)
Ketamine/ Medetomidine	10/0.1 IM			Heaton-Jones et al. (2002); Smith et al. 1998a, b and c
Medetomidine/ Ketamine/ Sevoflurane	0.3/15		Juvenile Nile crocodiles Adequate anesthesia for minimally invasive surgery	Monticelli et al. (2019)
Ketamine/xylazine	7.5–10/1–2 IM			Idowu & Akinrinmade (1986)
Ketamine/ dexmedetomidine/ midazolam	3–5/0.02–0.05/ 0.1–0.3 IM, IV			
Ketamine/ dexmedetomidine/ hydromorphone	3–5/0.02–0.05/ 0.1–0.2 IM, IV			
Alfaxalone	3 IV	Male juvenile *C. porosus* and *C. johnstoni*	Adequate induction at various environmental temperatures, but apnea common	Olsson et al. (2013)
Alfaxalone/ dexmedetomidine/ ketamine	5/0.05/5 IV		22-month-old American alligators Intubation within 10 minutes	Aymen et al. (2021)
Alfaxalone/ Dexmedetomidine/ Midazolam	5/0.05/1 IV		22-month-old American alligators Intubation within 10 minutes All became apneic	Aymen et al. (2021)
Tiletamine/ zolazepam	5–15 IM			Jacobson (1984)
Propofol	Dosage is size dependent: small crocodilians 5–6, large adult crocodilians 1–2 If administered in tail may take up to 15 or more minutes for full effect		Physiologic effects dose and rate dependent with similar effects observed in mammals and birds	

Table 13.1 (Continued)

Drug	Dosage (mg/kg)	Species	Remarks	Reference
Midazolam	0.1–01.5 IM or IV		Usually combined with other drugs Reversed with flumazenil (0.1 mg/mL) equal or twice the volume of midazolam (5 mg/mL) Dosage inversely related to size	Olsson & Phalen (2013a)
Diazepam	0.22–0.62 IM		Poor IM absorption Use has been superceded by midazolam	Loveridge & Blake (1972)
Reversal				
Atipamezole	5 mg/1 mg of medetomidine or 10 mg/1 mg of dexmedetomidine			Heaton-Jones et al. (2002); Smith et al. (1998a–c)
Flumazenil	Equal or twice the volume (0.1 mg/mL) to midazolam (5 mg/mL) IM, IV			
Naltrexone	100 times the dose of potent opioid			Fleming (pers. comm.)
Neostigmine	0.03–0.06 IM	*Crocodylus niloticus*		Jacobson (1984); Flammard et al. (1992); Fleming (1996)
Inhalant anesthetics				
Isoflurane	1–5%		2–3% for maintenance	
Sevoflurane	3–8%		Higher than isoflurane for maintenance	Bertelsen et al. (2005)
Muscle relaxants				
Gallamine *Not recommended on humane grounds*	1–2 IM	*C. niloticus*	**No analgesia!**	Fleming (1996); Jacobson (1984); Lang (1987); Loveridge (1979)
Succinlycholine *Not recommended on humane grounds*	0.33–5 IM		**No analgesia!** Also painful muscle contractions before relaxation that may lead to marked hyperkalemia and lactic acidemia	Blake (1993); Jacobson (1984); Spiegal et al. (1984)

IM, intramuscular; IV, intravenous; PO, oral administration.

Etorphine Hydrochloride

Crocodilians and other reptiles are very resistant to the immobilizing effects of potent opioids. Similar to the comments above about muscle relaxants, this author does not recommend their use.

Effective etorphine dosage varies considerably between and within crocodilian species. For example, American alligators weighing 1.6–3.9 kg required a dose of 1.3–3.1 mg/kg, while larger alligators weighing 39.5–68.0 kg required only 0.03–1.3 mg/kg (Hinsch & Gandal 1969). American alligators administered 0.29–0.51 mg/kg IM were immobilized within 20–25 minutes and were recovered in 60–180 minutes with no reversal drug (Hinsch & Gandel 1969). A 0.11-kg caiman administered the larger dosage of 44 mg/kg was immobilized at 11 minutes and recovered by 40 minutes. Intraperitoneal administration is effective, reducing induction times while having a similar duration of effect as IM administration. However, in Nile crocodiles dosages as high as 8 mg/kg IM were ineffective and only produced pupillary dilatation (Loveridge 1979). Without administration of reversal drugs crocodilians recover within 1–3 hours (Lang 1987). There is no report of using either naloxone or naltrexone to reverse etorphine in crocodilians.

Dissociative Anesthetics

Ketamine Hydrochloride

Ketamine alone has variable effectiveness (Table 13.1). It has been used to anesthetize spectacled caiman (44–50 mg/kg), juvenile American alligators (11–12 mg/kg) (1-hour induction; Beck 1972; Stoskopf 1993), and adult American alligators (45–70 mg/kg, 20-minute induction; Stoskopf 1993). In American alligators (Heaton-Jones 1996; Loveridge 1979) immobilization was only achieved at the higher dosage of 50 mg/kg. Similarly, ketamine alone (18–45 mg/kg) had little effect in Nile crocodiles. Even higher dosages (59–110 mg/kg) caused death in several animals (Loveridge 1979). Consequently, ketamine is usually combined with other drugs to reduce the dosage. This reduces the adverse effects and prolonged recoveries, while still benefiting from its anesthetic effects. There is presently no reversal agent for ketamine and recovery times vary with dose, taking up to several hours.

Tiletamine and Zolazepam

Tiletamine/zolazepam (15 mg/kg IM) in American alligators did not produce complete immobilization (Jacobson 1984). Palpebral reflexes were unaffected, hindlinb withdrawal was slow, and episodes of paddling were noted. Righting reflex was achieved 3 hours post injection, however with higher doses reversal times may be prolonged. In the absence of other alternatives, tiletamine/zolazepam (4–6 mg/kg) alone is the best choice for safe immobilization/sedation in crocodilians. It also has the benefit of being sold as a dry powder in a vial, allowing for variation in concentration. This allows reduction of injection volume when a darting or pole syringe system is used. In a warm environment this author has made up solutions approaching 230 mg/mL (compared with the recommended concentration of 100 mg/mL). To further reduce the volume needed ketamine can be used as a substitute for the diluent.

Partial reversal of tiletamine/zolazepam using flumazenil (1 mg per 20 mg of zolazepam) has been described (Lang 1987). Flumazenil, however, is seldom indicated in partially reversing Telazol because it is expensive, its effects may not last, and it may expose the adverse effects of tiletamine, which may include seizures.

Barbiturates

Barbiturates are not recommended for use in crocodilians except for euthanasia. The first report of pentobarbital in a crocodilian was an oral dose of 200 mg/kg, followed by 15 mg/kg intracoelomic, in a Nile crocodile for removal of a gastric foreign body. It was later demonstrated in this species that 28 mg/kg had an induction time of 2 hours and a recovery of 12 days; 53 mg/kg could cause death (Loveridge 1979). Pentobarbital administered to spectacled caiman at 8.8–15.4 mg/kg IM resulted in induction times of 30–45 minutes and recovery times of 1–5 days.

Alpha-2 Agonists

Xylazine alone has variable to no effect in crocodilians. In Nile crocodiles, a combination of xylazine (1–2 mg/kg IM) followed 30 minutes later by ketamine (20 mg/kg IM) resulted in effective surgical anesthesia for 50 minutes with a 3–4-hour recovery (Idowu & Akinrinmade 1986).

Medetomidine (131–220 μg/kg IM) was first described to provide effective immobilization of American alligators either alone or in combination with ketamine (7.5–10 mg/kg) (Heaton-Jones et al. 2002). As with other anesthetic drugs, juvenile alligators required higher dosages. Mean induction times were 19.6 and 26.6 minutes for juveniles and adults, respectively. Total anesthesia times were 61–220 minutes, with any procedure over 120 minutes requiring supplemental gas anesthesia. Olsson and Phalen (2012a,b) describe the use of medetomidine alone for the sedation/immobilization of both juvenile and large estuarine crocodiles (Table 13.1). Medetomidine (150 μg/kg) resulted in bradycardia and bradypnea (Smith et al. 1998a–c).

Yohimbine hydrochloric acid has a low therapeutic index and is not presently commercially available. Since there is a more effective and reliable alternative (atipamezole), yohimbine is not recommended for use in crocodilians.

The selective alpha-2 adrenergic antagonist atipamezole is an effective reversal drug for medetomidine in crocodilians and other reptiles at five times the dose of medetomidine. It should be only given IM to avoid potential adverse circulatory effects, including hypotension and cardiac asystole. Reversal times vary depending on dose and body temperature, but in the above alligator study this was achieved in 35–37 minutes (Heaton-Jones et al. 2002).

Intravenous Anesthetics

Propofol

Propofol's main disadvantage is that it must be injected intravenously. This author also feels there is an increased risk of morbidity and mortality when it is used in

crocodilians. Recommended dosages are size dependent: small crocodilians receive 5–6 mg/kg while large animals may only require 1–2 mg/kg IV to produce sedation/immobilization. When administered by the recommended IV route (ventral coccygeal vein) induction times may be as long as 15–20 minutes to peak effect.

As with all IV anesthetic drugs, propofol should not be administered into the spinal vein unless it is being used for euthanasia. This is because the spinal vein is in close association with the subdural space and there is great potential for accidental injection directly into the Cerebrospinal fluid.

As with other animals, adverse cardiopulmonary effects are directly related to the rate of administration and dosage. Propofol is also not analgesic and must be combined with analgesics for painful procedures.

Alfaxalone

Olsson et al. (2013) describe the successful use of alfaxalone in juvenile estuarine crocodiles. The benefit of this drug is that it can be given IV or IM. The main disadvantage for its use in adult crocodilians is its low commercial concentration precluding its use as the sole immobilizing agent. The present author uses it at low dosages (0.5 mg/kg IM) and injection volumes for its sedative effects as part of a hand-injected multidrug regimen. The cardiopulmonary effects and need for added analgesia are identical to those for propofol.

Other Injectable Agents

Tricaine methanesulphonate (MS-222) is not recommended for anesthesia of crocodilians. It has been used in juvenile American alligators (88–99 mg/kg IM), producing immobilization in 10 minutes and recovery in 9–10 hours (Brisaben 1966). A higher dosage (150 mg/kg) anesthetized an American alligator for 30 hours (Coulson 1983). It has also been used in spectacled caiman at 110–154 mg/kg IM with no effect (Johnson 1991).

Inhalant Anesthesia

As mentioned above, this author prefers parenteral anesthesia with or without local/regional analgesia for crocodilian anesthesia. In certain circumstances an inhalant (isoflurane) is used to supplement anesthesia. The main reason for using parenteral anesthesia has been faster recoveries, especially when some of the drugs can be reversed. Additionally, in many cases animals anesthetized using these combinations spontaneously breathe during a procedure, although at a sometimes slow respiration rate (1 breath/2–4 minutes).

Since crocodilians are capable of long periods of apnea, mask induction is contraindicated. Consequently, parenteral anesthetics are used for induction to allow safe access for intubation.

Crocodilians have complete tracheal rings and cuffed endotracheal tubes, if over inflated, may cause avascular necrosis of the tracheal mucosa. For endotracheal tube placement first open the mouth by grasping the snout with two hands and flexing the head and neck into a dorsal position. The mandible and maxilla can then be more easily separated and a block of wood or other speculum can be placed. A dog leash placed around the upper and lower jaws may provide greater safe leverage for opening the jaws.

For intubation, a light source (i.e., laryngoscope) is necessary to visualize the glottis. The gular flap will also usually need to be depressed to allow the glottis to be identified. The glottis will be closed unless the animal is exhaling or inhaling. The bevel of the endotracheal tube can be gently used to open the glottis. Application of local anesthetic to the glottis will reduce the response to intubation. It should be noted, however, that glottal paralysis could be prolonged. There is the potential for inhalation of water if the animal is returned to water too soon.

Positive pressure ventilation at a rate of 2–4 breaths per minute is adequate for crocodilians. A capnograph is useful for providing assessment of adequacy of ventilation, as well as the return to complete spontaneous ventilation at the end of a procedure. The end-tidal CO_2 level usually starts at 20 mm. Levels above 30 or below 10 are considered hypercapneic and hypocapneic, respectively. Monitoring chest wall movement is an insensitive guide to spontaneous ventilation compared to capnography.

Once the surgical or painful part of the procedure is completed, ventilation can be switched from oxygen to room air and an ambu bag used to inflate the lungs if necessary. In large crocodilians a double-demand valve (Horne et al. 2001) can be used with pressurized room air (scuba tank) for ventilation.

For crocodilians weighing <5 kg a nonrebreathing system is indicated, with a flow of 300 mL/kg/min. For crocodilians >5 kg, a circle system of 1–2 L/min for maintenance is recommended.

The most commonly used inhalant anesthetics are isoflurane and sevoflurane (Monticelli et al. 2019). Halothane is no longer available. This author usually uses isoflurane, primarily because of its cost compared to sevoflurane. The advantage of sevoflurane for faster recoveries is not clinically significant with careful adjustment of the isoflurane

vaporizer settings during and towards the end of a procedure. This author also occasionally uses nitrous oxide (50–66%) as a carrier gas for its rapid uptake and removal, and additional analgesia (Bertelsen et al. 2005).

A major issue when using inhalant anesthetics in crocodilians is shunting of blood away from the lungs, thereby blocking uptake and removal. In alligators it has been shown that administration of epinephrine at a resuscitation dosage will hasten recovery from isoflurane anesthesia without any apparent adverse effects (Gatson et al. 2017). This may be due to altering the pulmonary shunting, but could also be due in part to increased cardiac output and blood flow. Interestingly, this effect seems to also hasten recovery from parenteral anesthesia. This author routinely uses epinephrine IM during recovery of crocodilians.

Anesthetic Protocols

In formulating an anesthetic protocol (Table 13.1) it is important to factor in the species, medical condition, enclosure, temperature, staffing, and ultimate goal of the immobilization. The importance of capture and restraint has also been emphasized previously and it is recommended that Chapter 14 be used as a beginners' guide to techniques and required equipment.

This author prefers a combination of parenteral drugs for most sizes and ages (Aymen et al. 2021). For example, in medium to large crocodilians I use medetomidine (or dexmedetomidine) (30–70 μg/kg IM) combined with ketamine (3–5 mg/kg IM) and either midazolam (0.2 mg/kg IM) or hydromorphone (0.2 mg/kg IM) (Aymen et al. 2021; Monticelli et al. 2019). This combination is usually administered by hand, even to large crocodilians that are restrained, allowing multiple and occasionally large volume injections in the triceps muscles. Alfaxalone can also be added or substituted for midazolam. Onset of maximum effect may take up to 30–45 minutes.

Alternatively, a combination of zolazepam/tiletamine (Telazol) (4–8 mg/kg IM), as described above, will not be sufficient to reach surgical anesthesia, but should allow safe moderate immobilization sufficient for intubation. For adequate surgical anesthesia the animal may need to be intubated and maintained with 0.5–3% isoflurane in oxygen. To reduce a prolonged recovery the dosage can be reduced to 2–4 mg/kg and combined with medetomidine (or dexmedetomidine) (30–50 μg/kg), which can be reversed with atipamezole at the end of the procedure. When recovery is slow, care should be taken not to immerse the crocodilian in deep water until full recovery.

As discussed previously, propofol and alfaxalone are also appropriate for induction (and perhaps constant rate infusion) in small to medium-sized crocodilians.

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14

Crocodilian Capture and Restraint

Kent A. Vliet and Gen Anderson

Introduction

Anesthesia and chemical immobilization of crocodilians usually requires some form of confinement and physical restraint for safe drug administration and to prevent them seeking refuge in their aquatic environment. Anesthesia and immobilization are discussed in Chapter 13. The following is a description of capture and restraint techniques that work to minimize injury to handlers and animals.

Crocodilians are dangerous; they are capable of injuring, scarring, maiming, and even killing handlers. This is not to imply they are bad, loathsome, or evil. It is simply the result of being large, tremendously powerful, predatory, agile, and adaptable. No-one can safely work with these animals until this is fully comprehended. Furthermore, you must remind yourself of this every time you work with them; complacency is our greatest threat.

There are many safe ways to capture and restrain even very large crocodilians. There are even more incorrect ways. Each capture is different and always has the potential to go wrong. There are many variables that must be taken into account in successfully capturing and restraining a crocodilian.

Ultimately, no amount of detail in this chapter, training, or experience will guarantee no harm to those working with these animals. If you cannot personally accept this liability, you should neither attempt any of the techniques discussed in this chapter nor should you work with crocodilians. Accepting this liability is part of the commitment necessary to work with these magnificent animals.

For larger captive crocodilians, the trend is to reduce contact with the keeper staff by providing shift enclosures and training the animals to use them. This is much preferred over physically capturing and restraining an animal. While the former (shifting) is strongly encouraged, the latter (capture and restraint) will form the body of this chapter. Manual restraint is a necessary tool in professional crocodilian management when maintained under human care for medical purposes, data collection, movement, and changes in social dynamics (Molinaro et al. 2022).

Few publications describe techniques for the safe capture, restraint, and handling of captive crocodilians. Most descriptions are of free-living species, for example the American alligator (*Alligator mississippiensis*) (Chabreck 1963; Jones 1965; Joanen & Perry 1972; Murphy & Fendly 1974; Forster 1991; Jones & Hayes-Odum 1994; Wilkinson 1994), the American crocodile (*Crocodylus acutus*) (Mazzotti & Brandt 1988), the Nile crocodile (*C. niloticus*) (Pooley 1984; Hutton et al. 1987; Kofron 1989), and the saltwater crocodile (*Crocodylus porosus*) (Webb & Messel 1977; Walsh 1987). While useful insights and methods are gleaned from these papers, most describe traps that are of little practical application in the captive environment. Electro-stunning is widely used on commercial farms, particularly with *C. porosus* and *C. niloticus* (Franklin et al. 2003; Sa 2020). This efficient capture technique renders the crocodilian unconscious while minimizing stress to the animal and increasing safety for staff. Electro-stunning is used primarily for commercial slaughter as opposed to zoological purposes.

A detailed list of equipment and techniques used in alligator research is found in McDaniel and Hord (1990). Fowler (1978) makes brief mention of restraint of smaller captive crocodilians. Almandarz (1986) describes physical restraint techniques for reptiles, including crocodilians. The most comprehensive reference is that of Wise (1994). This article contains many pertinent and useful insights that serve as a valuable reference for anyone interested in developing the skills necessary to safely work with these animals. The following discussion builds on and expands the contributions of the above references.

This chapter does not detail all the possible techniques for capture and restraint. The authors have included those they are experienced with, are accustomed to, and

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which they believe provide enhanced safety of staff and while minimizing stress on the animal. The primary author has had the opportunity to capture 24 crocodilian species during several thousand captures over multiple decades, in both captive and free-living situations. Techniques evolve and new, better practices come into use. Others may have different, and even better, methods than those presented here.

Capture Equipment

Crocodilians frequently damage and destroy capture equipment. Consequently, restraint is either an expensive exercise or one develops equipment that is easy and inexpensive to manufacture. The latter allows an adequate supply of equipment to always be available. The standard equipment the authors and staff of the St. Augustine Alligator Farm Zoological Park use for crocodilian capture and handling is described below.

Ropes

Ropes are essential for most captures; they are used to gain a hold on, to restrain, and for the safe release of animals. Several ropes are always available for any capture. The size used depends on the crocodilian to be captured. Smaller animals require smaller diameter ropes, while larger crocodilians necessitate thicker and stronger ropes. Too small a diameter ropes may cinch too tightly on the animal or burn into a keeper's hands during a struggle. Ropes of too great a diameter will not close tightly enough over the neck or jaws, allowing the animal to work itself free.

For adult animal captures, the preferred rope diameter is either 1.6 (5/8) or 1.9 cm (3/4 inches). Ropes have different tensile strengths; the strength must be adequate for the size and mass of the animal to prevent breakage and animal escape. Nylon ropes are generally the strongest, but do not perform as well as the preferred polyester in wet environments. Cotton and sisal work well for many purposes, but rot if not allowed to dry after use or are not stored appropriately. This leads to problems during captures of large animals; the rope may separate under tension, allowing the animal to go free and resulting in the keepers falling back and possibly injuring one another. Woven or braided ropes are less likely to kink or fail than twisted ropes. Many ropes float on the water surface, preventing their placement under the head of a submerged crocodilian. Consequently, ropes should be assessed before purchase for their ability to sink when soaked. The best ropes the authors have used are those designed for arborists. They are soft and pliable yet strong, and they do not tend to "burn" hands when jerked by a crocodilian. At first glance, arborist rope may be cost-prohibitive, but the quality of product and usage capabilities make it worthwhile.

Rope length depends on the intended use. Excessive length makes it difficult to gather and control during hectic moments in captures. Staff may also get tangled up in too much rope. The primary author frequently lassos crocodilians from a distance. For large crocodilians, several people are needed to pull a roped animal from the water or to a position where it can be safely secured. For these purposes, the author uses 8–9 m (25–30 ft) ropes.

Smaller diameter and shorter ropes are ideal for restraint. Ropes of 0.6 (1/4) or 1 cm (3/8 inch) diameter may be used to tie the legs together off the ground. This technique may be implemented to prevent movement and injury, especially of larger individuals, or tie an animal to a ladder or restraint board (Valverde et al. 2021; Buah-Kwofie et al. 2018). Leg restraint must be performed cautiously as it can be risky due to joint damage caused by possible dislocation, unintentional use of a limb as a handle, or too tight bindings. Prolonged restraint using this technique can also lead to muscle damage (exertional rhabdomyolysis) and is not recommended.

Jaw ropes are used to tie the jaws shut or remove the tape from an animal's jaws as it is being released. They are generally small diameter, 0.3 (1/8) to 0.5 cm (3/16 inch), and shorter, 3 (10) to 3.7 m (12 feet), ropes. Cotton clothesline works well for this purpose.

Poles

The primary use of a defensive pole is for the protection of the handler(s). Poles must be of sufficient diameter and heft to maintain a safe distance between the holder and crocodilian during capture, but comfortable for the holder to manage. When charged or lunged at by an overly enthusiastic animal, the pole is used to block the animal's advance.

Poles serve many other purposes. Animals can be discouraged from advancing toward a handler by lightly laying a pole on the soft tissues of its nostrils or against its earflap. Animals can be gently encouraged to move out of the way by touching their hind legs and base of tail, allowing access to a particular animal for capture. In addition, a pole can be used after capture to manipulate and position the animal (e.g., move legs, lift jaws, clamp the jaws shut, etc.) without getting too close.

Defensive poles are generally wooden; if an animal bites them they do not cause significant damage to the teeth. The authors prefer a sturdy, 1½-inch diameter length of solid bamboo or eucalyptus, approximately 1.2 (4) to 1.8 m (6 feet) in length.

Poles greatly increase safety while working in close proximity to crocodilians. However, care must be taken when using them with larger crocodilians. Poles can become dangerous to personnel if grabbed and held in the crocodilian's jaws. When the animal swings its head from side to side, the pole may strike and injure a person. Care must also be taken when recovering a pole from a crocodilian.

A variety of catchpoles are used to grab and hold. They all include a long rod with a cable loop or snare at one end. For larger animals (>2 m) poles are designed so the loop and rope attachment separates from the rod. Commercial catchpoles are used when no other poles are available. They are sturdy and give very good control over the animal. However, even relatively small crocodilians (≥1.5 m) roll or spin violently enough during capture to twist and kink the cable snare, thereby destroying it. Furthermore, during a struggle, the metal rotating cuff adjacent to the snare could push into the animal's head and neck, causing injury. Frequent use of commercial catchpoles is not recommended because of initial purchase cost and the expense and time of repeated repair and maintenance.

Alternatively, it is easy, quick, and very inexpensive to make catchpoles. There are three commonly used simple designs. A "break-away" rope loop can be secured to the end of a pole with electrical tape. Once the rope is placed over the head and neck of the animal, the pole is pulled free and removed from the capture area. Recommended poles for this design are long (3–5 m), 3–4 cm (1½ inches) diameter wooden rods or lightweight aluminum electrical conduits. Swimming pool net poles also can be used; they are lightweight, long, and extensible.

Schedule 40 PVC pipes can also be used to make catchpoles. Snares are made of twisted metal cable and affixed to the end (Fig. 14.1). A metal swivel coupled to an eyebolt through an end cap attaches the snare. The cap is glued onto the end of the PVC pipe (Fig. 14.2). An advantage of this design is that snares of different diameter, or that have become damaged during a capture, can be rapidly exchanged during a capture. A small wire can be attached to the snare base to keep it open until in place on the animal. Surprisingly, jacketed cables with plastic coverings cause more skin damage than exposed metal cables.

The simplest homemade catchpole for animals ≤2–3 m (8–9 feet) in length consists of a ¼-inch polyester, nylon, or cotton rope run through a length of 1-inch PVC pipe (Fig. 14.3). The rope is secured through a hole drilled in the pipe wall close to the end, then run out of the pipe and back in again, to form the loop, and then down the length of the PVC. When the loop is placed around the animal, the rope extending from the back end of the pole is pulled tight and bent back against the pole for added friction. PVC pipes bend and fracture if they are used to lift animals.

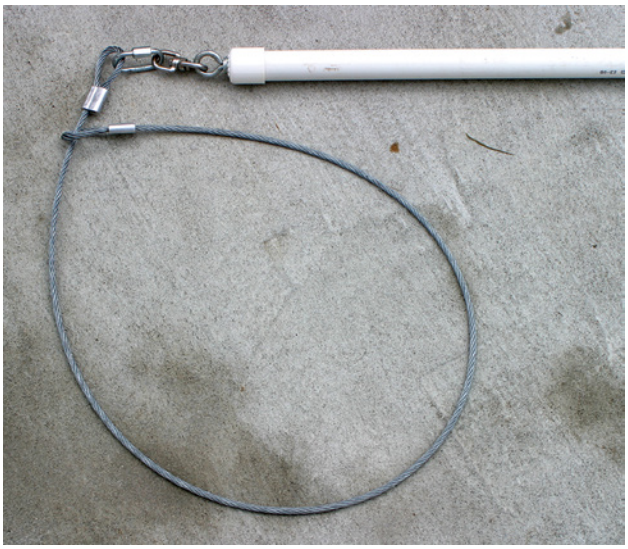


Figure 14.1 A home-made cable snare used for catching small to medium-sized crocodilians. The catchpole is made of PVC piping.



Figure 14.2 A home-made rope snare used for catching small to medium-sized crocodiles. It can also be used as a jaw noose; the rope is placed around the upper and lower jaws and either twisted or the rope pulled at the distal end to tighten. The pole is made of PVC piping.

Once secured with the noose, the handler pulls back in line with the direction of the pipe to pull the animal for positioning and restraint.

The rope catchpole is commonly referred to as a "mouth pole" as it is ideal for safely securing jaws. A shorter version of the loop design works exceedingly well for closing and securing the jaws of captured crocodilians prior to taping or tying. The loop is placed around the maxilla and tightened. Once the jaws are shut, the pole is twisted several times to add more tension to the loop. A person then steps in to quickly secure the jaws.



Figure 14.3 Physical restraint of a small crocodilian (*Crocodylus mindorensis*). Note the electrical tape placed around the jaws and the hand grasping the neck and forelimbs.

Tape

Tape is essential after capture and during restraint; jaws can be safely secured and heavier tapes can be, but are rarely, used to immobilize legs to prevent movement. The most commonly used are silver duct and black PVC electrical tape. Always have a sufficient amount on-hand. PVC electrical tape is preferred as it sticks to itself, not the animal, and has some stretch to ensure proper jaw restraint and handler safety.

Cable Straps

Nylon cable straps or ties (zip-ties) are very useful for securing the jaws of some crocodilians (i.e., narrow-jawed species) before one captures the animal. These come in various lengths and tensile strengths; the largest can resist a force of 100 kg. This temporary method of jaw restraint reduces damage risk during capture and is a useful technique to for slender-snouted species.

Shelf Mats, Rubberized

Shelf mats are made of rubber-coated, woven fabric. They are used as nonskid shelf coverings and are readily purchased. The mats are cut into 5–10-cm (2–4-inch) wide strips to wrap around the snout or the entire head. They are used for this purpose because they do not slip in a wet environment. The crocodile jaws are held shut with a mouth pole or by hand, wrapped with the mat and then taped over. The sponginess of the mat prevents the tape from binding too tightly. Also, the nonslip nature of this material prevents jaw tape from slipping forward and covering the nostrils during transport. Vet wrap is a suitable alternative, but caution must be used to assure the stretchy fabric is not applied too tight. Both methods greatly protect the jaws of slender-snouted species and those with teeth that project outside of the jawbones during manual restraint and transport.

Eye Cloths

The eyes are covered before or after capture with a cloth, towel, or other available fabric such as burlap bag or shirt. This has a calming effect on the animals and likely reduces stress during the capture period. The blinded crocodilian is much less likely to avoid capture and to struggle following capture. Additionally, if the animal does attempt to strike it is undirected and less likely to injure. Eye cloths are safely and gently placed over the eyes using a hook. The cloth is soaked before placement so it will more completely cover the eyes and stay in the proper place on a partially submerged or basking crocodilian.

Eye cloths are secured with a couple of wraps of PVC electrical or duct tape. Crocodilian eyes can be voluntarily withdrawn down into the skull, but some caution must be used when taping the eye cloth. Do not press the eyes too hard or apply too much pressure with the tape. If the eyes are to be covered for an extended period, gauze pads or a folded paper towel are placed over them before taping.

A visual obstruction study on juvenile American alligators by Finger et al. (2018) demonstrated no significant difference in corticosterone levels 30 minutes post capture. Jaws were secured with rubber bands and eyes covered with electrical tape. As crocodilian behavior frequently results in a calmer demeanor after covering eyes with a damp cloth, future research is needed involving other stress indicators to improve crocodilian welfare during capture and restraint.

Hooks

Hooks are absolutely essential tools when working with crocodilians. They facilitate work around the animals by allowing placement of ropes, manipulation of legs, etc. without bringing human appendages within striking range. The authors have used several different hook types. Heavy snake hooks (e.g., python hooks) are sufficiently robust for positioning ropes around a crocodilian's head, lifting legs, lifting the jaws, etc. Hooks are also useful for removing and retrieving ropes during release.

The preferred option is long, very lightweight fiberglass hooks designed for livestock showing. These break fairly easily, but are also inexpensive. They are not substantial enough to manipulate an animal, but are excellent for capture equipment placement and positioning. When

capturing a submerged crocodilian, it is often possible to carefully position a rope loop over and around the head with these hooks without disturbing the animal and causing it to move. Tongs are not recommended as they are often used for feeding crocodilians and may elicit an ill-timed feeding response. Hooks are also handy for retrieving items safely from unsafe locations.

Restraint and Transport Devices

Once captured and the jaws secured, there are many ways to confine or restrain a crocodilian (e.g., bags, buckets, ice chests, shipping crates, ladders, platforms, and cargo nets or marine mammal slings). The restraint technique and equipment selected depends on (1) animal size, (2) duration of confinement, and (3) distance to be transported.

Knives and Other Tools

Cutting implements should always be available during a capture for emergency use. Knives are used to cut tape, frayed rope, etc. Wire cutters are used to cut through cable straps when used on the snouts of some specimens. Not having suitable cutting tools on hand in a timely fashion can result in injury and/or safety concerns for both handlers and animals.

Trauma Kit

If the capture techniques described in this chapter are followed, the risks to personnel are minimized. Depending on the size and species, a bite from a crocodilian can result in minor injuries or severe trauma and death (Savu et al. 2021). The capture team should always be prepared for someone being injured during a crocodilian capture. This includes having a well-stocked trauma kit on hand to provide immediate aid. This kit should include at minimum a pry tool, medical gloves, tourniquet, blood clotting sponge, and scissors (for the removal of clothing and cutting of bandages). A well-stocked trauma kit is not intended to provide proper medical care, but to minimize human blood loss prior to the arrival of paramedics. In the event of limb removal, quick access to a cooler with ice can help preserve the amputated appendage. Wrap with gauze, then place in a plastic bag first before setting on top of ice.

How to Catch a Crocodilian

As described above, crocodilians can be massive, powerful, and often react violently to physical restraint. During capture, the safety of personnel is paramount, followed closely by the welfare of the animals. The techniques favored by the authors restrain the animals completely to limit the possibility of self-injury to the animal and personnel injury. The essential components of successful capture are planning, communication, caution, and knowledge of the animals.

Planning and Preparation

Capture and restraint of small specimens is usually routine and does not necessitate much planning or preparation. This is absolutely not the case when attempting to capture and restrain a larger specimen (i.e., ≥2 m [6 feet] in total length). Preparation includes careful planning, discussion, and oversight. One person (the team or crew leader) is designated the leader and directs everyone else what to do, where to be, etc. Each person's role or roles is discussed and clearly understood before the operation commences.

Many plans, however, are quickly rendered moot if the capture subject is uncooperative. Each capture experience is different; it is not possible to foresee all of the variables likely to be encountered. Flexibility and strategy, the ability to change capture plans in mid-course while still maintaining a safe working environment, are essential. As handlers become more experienced with captures they develop a greater repertoire of techniques to apply to specific situations.

Communication is essential before, during, and after a capture to ensure the safety of the staff and the animal. Each team member must listen for and continue to receive instructions from the team leader throughout the procedure. The team leader must also continually look out for crew safety, make sure staff are in their proper positions, performing their assigned roles, ensure everyone is outside of the strike zone of the animal and escape routes are kept clear at all times.

Environmental Assessment

The first stage of preparation is assessment of the capture environment. If the animal is in a more basic medical enclosure or housed individually, this may be fairly straightforward. However, an animal in a complex habitat full of opportunities (= obstacles) and companions requires more forethought. It is important to answer several questions when assessing the capture environment.

Where are the Escape Routes?

This is perhaps the most important question. More than one route is preferred, but often not available. All team members must be aware of these routes, and they must be left clear at all times during the capture. Personnel must

refrain from blocking escape routes themselves and with extra capture equipment.

What is Physically Possible?

The geography of the enclosure habitat will determine personnel access and the capture techniques used. For example, enclosure structure, landscaping, and furniture such as logs and bridges, can make it difficult to quickly capture a crocodilian (Molinaro et al. 2022).

Is the Animal Trained to Shift?

Many institutions provide adjacent shift areas, similar to those used for mammalian carnivores or large hoofed stock. Crocodilians can be rapidly trained with food to utilize these shifts and to transfer into transport crates. This training facilitates working with these animals and reduces the need for stressful and potentially injurious captures. If a crocodilian does not require a physical examination and or samples to be taken, then a hands-off approach is best for everyone involved.

Will the Animal be Caught in Water or on Land?

The habitat should be assessed to determine whether staging the capture on land or in the water is the best, safest option. In many enclosures, the land surface is insufficient or too crowded with vegetation and furniture to allow a well-coordinated capture. Similarly, some water features make it difficult to gain access to the animal. If the plan is to catch in the water, will the staff be on shore or down in the pool or both?

The characteristics of any water feature must be known to make a proper assessment of its utility in catching an animal. Important variables to know include the total pool area, the water depth, whether the water can be lowered without emptying the pool, the slope of pool sides, and whether staff can easily get out of it.

Land capture requires sufficient space for both the team and the animal, and must allow the staff to stay safely outside the strike zone and out of each other's way. If the animal is on land, the plan should include a contingency for capturing it in the water. Unless caught immediately, crocodilians will seek refuge in water. If either land or water offer ample opportunity for capture, consider choosing to catch in the water. On land, crocodilians feel threatened and cornered. Water is a natural refuge and they often lay more passively, allowing easier placement of the rope and positioning of personnel.

Where will the Animal be Restrained?

In some situations the crocodilian is removed from the enclosure to provide enough space to safely work around the animal. Back areas can be more open due to the needs of maintenance vehicles. In other situations, the jaws are secured while the animal is in the exhibit, then it is removed from the habitat before full restraint or loading into a crate.

Are there Other Animals Present?

Other crocodilians can obstruct access or pose a significant and potentially serious threat to staff and the animal to be captured. If possible, these animals should be shifted out of the way before beginning. Additional staff may be needed to monitor companions; these animals may become involved as the target animal and catch team move about the enclosure. The heightened stress or anxiety in the enclosure associated with the capture may cause the companions to strike out. Care is taken to avoid injury to all animals and staff members involved.

Animal Assessment

Not all techniques are appropriate for all species or size classes. It is required to have natural history knowledge of the animal to be captured; crocodilian species are known for differences in temperament and their capabilities. Saltwater crocodiles (*C. porosus*) and Cuban crocodiles (*C. rhombifer*) are especially dangerous; they may charge and are powerful and agile jumpers. However, this does not imply other species are less dangerous. There are also individual animal differences; some usually mild-mannered species can be unexpectedly belligerent. Ideally, all crocodilians are approached with the same degree of caution. There must be a healthy understanding and respect for the physical abilities of these animals.

Other aspects of the animal's biology, particularly snout morphology, are also considered when preparing for a capture. Slender-snouted species (e.g., *Mecistops cataphractus* and *Gavialis gangeticus*) are more prone to serious snout damage during capture than are species with broader, more robust snouts. As a result, special precautions are necessary in preparing for the capture of these more fragile species. Protecting the jaws prior to capture with cable straps may reduce disfiguring injuries. Conversely, exceptionally robust or broad-snouted species (e.g., the broad-snouted caiman, *Caiman latirostris*) are often difficult to safely secure because there is relatively little purchase area for hands or mouth poles.

The "toothiness" of the animal to be captured should be noted. Protruding teeth cause damage, or even serious injury, when accidentally caught on a hand or arm or forcefully slammed into a team member during a struggle. This danger persists even after the jaws have been secured. Captive crocodilians occasionally have abnormal tooth development resulting in misaligned teeth protruding from the jaws. In some species (e.g., the false gharial, *Tomistoma schlegelii*) the teeth are long, slender, sharp, and naturally

interdigitate, making them very difficult to handle. In these animals it is necessary to wrap the entire jaw line in vet-wrap bandaging tape, a bath towel, rubberized shelf mat, or other material to prevent injury.

Strike Zones

The crocodilian head is its most dangerous part. Many people unfamiliar with these animals believe the tail is the main area to be avoided. While it is true the tail can cause injury, it is the head that has a mouth full of 70–80 teeth and a very high bite force. *C. porosus* has the highest recorded bite force of any extant animal at 3700 psi (Erickson 2013).

The stocky body form and heavily ossified skin of crocodilians limits their flexibility. However, they can and will strike sideways with exceptional speed. In most crocodilians on the ground, the strike zone is defined by the arc of the head swinging from side to side. It is therefore much safer to approach an animal secured by a rope around its neck from the front than the side. Always remember that this is not a steadfast rule when considering the extensive breadth of the current 24 described species. Review the natural history and consider the locomotion capabilities for various crocodilians.

In the process of swinging its large, massive head rapidly to the side, a crocodilian generally swings or slaps with its tail. The tail is solid and strong, and can knock a person off his or her feet or push them toward the jaws. Consequently, catch personnel must also avoid the tail arc.

Roping

Captures generally begin with the securing of a snare or rope noose to the animal. There are two basic variations of this procedure.

Neck Lasso

This technique involves placing the rope over the head and cinching it around the neck. It is usually used for alligator, caiman and heavy-bodied crocodiles. These animals have fairly large jowls at the back of the head behind which the rope loop can take hold. Crocodilian necks are thick, heavily muscled, and usually capable of enduring without injury the forces that occur during struggling. In captivity, where it is often possible to carefully place the rope before closing the loop, some prefer to also hook the noose under one forelimb so it does not cinch tight around the neck. This technique is necessary in very large, heavy specimens that have to be pulled up and over a steep bank or the lip of a pool. This is to prevent too much force being applied to the neck and spine.

Top-jaw Noosing

Top-jaw noosing is used in species with body profiles too slim to allow a neck noose. The rope is caught in the teeth and held firmly. It is of a narrower diameter (≤1.3 cm, 1/2 inch), allowing it to bind more closely around the upper jaw.

A clear advantage of this technique is the greater control of the head, since there is restraint of the snout. However, a major disadvantage is that when the crocodile jerks, twists or shakes, which they do with tremendous force and speed, all of the forces are transmitted through the rope into the hands of the holder. Those who use top-jaw noosing usually secure the jaws with a narrow rope. Two people stand on either side of the head, outside of the strike zone, with the rope stretched between them. This is placed under the lower jaw, and then the ends of the jaw rope are wrapped around one another and exchanged. As the rope is pulled, the jaws are forced together. One person then steps in and holds the knot while the second ties a securing knot. A safer alternative is the use a mouth pole.

Securing the Jaws

Depending in part on the size of the crocodilian, the jaws can be secured with a variety of materials.

Tape

Once the jaws have been closed (by hand in very small specimens or a mouth pole in larger animals), their jaws are usually secured with tape.

Black PVC electrical tape can be used to secure the jaws of crocodilians ≤3 m (10 ft) for short periods of time. It is very quick to apply and sticks well to itself. Most other tapes do not adhere well to crocodilians, especially when wet. During application the tape must be wrapped around the snout and taped to itself to provide a good hold. A general rule is one wrap of electrical tape for each foot (0.3 m) of animal (i.e., for a 5-ft or 1.6-m alligator, wrap the tape five times around the snout). Two rows of tape are applied for large heads.

Do not leave a crocodilian taped for more than a few hours. Electrical tape has a lot of stretch and can be applied with enough force to block the blood flow to the skin. If it remains in place for too long it will cause ischemic skin damage, resulting within a few days in scabbing, sloughing, and scarring.

The author has also used the heavy, bright red tape used for drywall seams. This has excellent adhesive force and a small amount of stretch. However, it does not tear readily, making it necessary to cut it with a knife. The great advantage of this tape is that it is highly visible, making it immediately obvious when an animal has thrown its tape and its jaws are unsecured. This is an added safety measure, especially when transporting several animals at once.

Silver fabric duct tape can be used on larger crocodilians. This also comes in a variety of colors, such as red. It has reasonably good adhesion to itself, but animals otherwise unrestrained are usually able to work it off their jaws within a few hours. A major advantage is it has very little stretch, making it difficult to apply too tightly.

Always create a tab on the top when taping an animal; fold back the end so that it is easy to see and grasp. This facilitates removal of the tape during the release.

Cable Ties

Cable ties (also known as cable straps zip-ties) are frequently used on slender-snouted species (e.g., *Tomistoma*, *Gavialis*, *Crocodylus intermedius*, *C. johnsoni*). There is an increased risk they will damage or even break their snout/lower jaw during capture. This often happens when the animal bites on something in the exhibit and then rolls, applying torsion to the jaws. Securing the jaws shut before a capture reduces the chances of injury. The captures also move more rapidly; staff can restrain the animal in a shorter period of time, further reducing chances of injury and minimizing stress.

To perform the cable strap technique, first make a loop by inserting the tip of the strap through the locking mechanism. Then, drill or punch a small hole through the tip of the strap and thread a string, wire or monofilament line through and tie it. The string and the tip of the cable strap loop are then run through a length of 0.6- (1/4-) to 1.3-cm (1/2-inch) PVC pipe to serve as a catchpole. The loop can be accurately placed over the jaws without touching them. A rapid tug on the string will close the loop and pin the jaws shut, often without disturbing the animal. Alternatively, the cable tie loop is suspended from the string and lowered into a position around the jaws. A swift jerk tightens the strap around the jaws.

This technique is also used with other crocodilian species, but it is more difficult to zip-tie the jaws of broad-snouted species. However, in many species there is a notch or depression in the jaw (e.g., behind an enlarged tooth) into which the cable tie can take hold and tighten down onto the snout.

Caution must be used with these nylon cable ties. Do not trust them; they often are not affixed tightly and can easily slip, releasing the jaws. They also become more brittle with time and prone to breakage; buy new ones before each capture. For a temporary jaw restraint method on slender-snouted species before applying a more secure technique, this method is invaluable.

Other Binds

Less frequently, jaws are bound with rubber bands or heavy cord. Strong, heavy, rubber bands made by cutting tire inner tubes into rings can be used for crocodilians ≤3 m (10 feet) in length.

Eye Coverage

Cover the eyes whenever you restrain a crocodilian. Use an eye cloth or, if the animal is fully restrained, cover the eyes with your hand. During a capture drop an eye cloth in place with a hook. This prevents the animal from seeing your movements, makes it less likely the animal will become unruly, and prevents the animal from directing a strike toward a capture team member. Covering the eyes also keeps the animal quieter and may reduce the stress of the experience for the animal. Though visual obstruction has been proven not to minimize elevated corticosterone levels in juvenile American alligators (Finger et al. 2018), staff observations have confirmed it makes a significant difference in behavior during capture and further research is needed.

Rule #1, Go to the bathroom

There is no delicate way to state this and it seems an odd thing to mention in a discussion of catching crocodiles but, before beginning any major capture operation, make sure each person on the catch team has visited the restroom. These operations can be time-consuming and can be tense for the staff involved. The necessities of bodily functions can arise making a team member uncomfortable and distracted. This can result in actions being rushed or mistakes being made.

Capture and Restraint

Hatchling/Juvenile (Less Than or Equal to 1 m)

Hatchling and small juvenile-sized crocodilians can inflict a painful bite, so caution is still necessary when working with these animals. Biting a keeper is also stressful to the animal and may damage teeth or jaw structures. Also, the animals are small enough that no matter where you grab them, you are never very far from the mouth.

This size of animal is easily grasped by hand. Approach from behind and grab and hold firmly by the neck, over the shoulders, or on the front half of the torso (Fig. 14.3). To reduce the chance of a bite use a hook, a small pole, or any visual barrier such as a broom to push the head away from the hand and block as the animal is picked up. Pillstrom tongs, a standard tool for most herpetologists (Chapter 12), do not work well with crocodilians. The bony armor on the neck and dorsum prevents the tongs from gaining a firm

purchase and the animals can twist, roll, and wrest themselves free. There is also a natural tendency to squeeze the tongs more firmly to prevent this, resulting in injury to the animal.

Once the animal is in hand the jaws must be secured. The animal is held firmly around the neck with one hand, and the other hand is advanced from behind keeping it close to the body. It is placed around the neck and slowly slid forward while gently squeezing. As it moves up onto the head it will slowly close the jaws. The eyes are covered and the head held with this hand. The jaws are then secured shut with tape (even transparent tape will work on this sized animal, a rubber band, or a short length of cotton clothesline) (Fig. 14.3).

Subadults (≤2 m)

Subadult crocodilians or the adults of smaller species (e.g., Chinese alligator, *Alligator sinensis*; African dwarf crocodile, *Osteolaemus tetraspis*; both species of the caiman genus *Paleosuchus*) are perhaps the most difficult size class to capture and handle safely. These animals are large and powerful enough to provide a large struggle, yet still agile and quick enough to turn rapidly and snap.

The tool of choice for these animals is a catchpole made by running a loop of rope through a length of PVC pipe. The loop is placed over the animal's head and around the neck and pulled tight. The rope is bent back against the PVC pipe for added friction. PVC does have some flexion so the animal is not completely controlled. However, the animal can easily be dragged and positioned with this device. Greater control of the animal is achieved if a second person grabs the tip of the tail and pulls the animal. This stretches the animal between the catchpole and the second handler. Maintaining pressure on the tail prevents the animal from twisting or turning to bite. A mouth pole is used to close and secure the jaws. With the animal still controlled by the catchpole, the mouth pole is placed over the snout and the rope pulled tight. It is preferable to stand at the side and slightly behind the animal's head when doing this. The jaws are closed with pressure applied by pulling the rope. When the jaws are completely shut, the mouth pole is twisted several times to add pressure to the jaws. When the jaws are secure and the mouth pole is holding, another crew member steps in and tapes the jaws.

Adult (≥2 m)

Capture and restraint of larger crocodilians is as much a matter of manpower and logistics as it is of proper procedure and safety. A sufficient number of staff is a necessity for a safe and efficient operation. Two people are plenty for a 2-m (6-foot) specimen. Generally, it is best to have at least three or four team members for a 2.5–3-m (8–9-foot) animal. Four or even more people are needed for specimens greater than 3 m (10 feet).

Not to belabor the point, it is ideal when working with these large specimens that they be trained to shift and move into a crate. This provides substantial daily or weekly safety benefits to keeper staff and removes most of the trauma and anxiety of a physical capture. If this is not an option, or if the animal fails to shift when needed, than one may have to proceed with a capture.

As described above, before beginning capture of a large crocodilian make sure ropes that are not frayed or worn and have been soaked are available. Wet ropes not only sink better to position them around an animal, but they do not burn the skin of the animal as dry ropes often will during a struggle.

Catching Adult Crocodilians in Water

If the plan is to catch the crocodilian in the pool the following are some suggestions for techniques to use. If it is possible to lower the water, drop it to a level that just covers the back of the animal (~25 cm [10 inches]). This depth limits the animal's mobility within the water feature while still allowing it to submerge its head. It also provides better visibility of the animal and any obstacles. It is important to keep enough water in the pool for the animal to remain submerged. As long as it can keep its eyes underwater, it is much less likely to become violently defensive.

There are various means of securing an animal in this situation. Most commonly, a rope is placed around the head and neck, and possibly one of the forelimbs. Hooks greatly facilitate safe rope placement and positioning of the noose. Alternatively, a wide lasso is thrown over the head, or a break-away noose or a cable snare catchpole are used to get a line on the animal. If the animal is slender-snouted, or if there are many obstacles in the environment on which the animal might injure itself, the jaws are first secured with a cable strap.

If the team is familiar with the temperament of the animal and it is not reacting violently, it is often possible to manipulate the animal when the water is shallow. Large nets or marine mammal slings may be used to slide under the animal, envelop it, and lift it out of the pool area, greatly reducing the animal's struggles and chances for injury. Animals may also be able to be pushed or herded into a crate or a large-diameter PVC pipe that has been placed in the pool (Saumure et al. 2002).

A common disadvantage of catching in the water is most pools are hard-sided. They are generally constructed of concrete or gunite and readily damage the side of the head of a struggling crocodilian. Attempt to keep the animal

away from the pool sides as it struggles, and move it past these structures as rapidly as possible. Sealed foam rubber gym mats or other shock absorbing materials can be placed against the side of a pool to protect the animal.

Catching Adult Crocodilians on Land

Once the rope is placed on a crocodilian on land there will be a struggle. They are able to generate a tremendous amount of resistance with their short legs forced into the ground. It is best to have sites already identified where one can tie off the rope (fence posts, trees, etc.). Trees must be of sufficient diameter to resist the force of the animal; larger crocodilians will uproot a small tree. Tying off the rope restricts the animal's movements, facilitates repositioning of the handlers to provide further restraint, and, perhaps most importantly, saves energy. Tired or exhausted catch crews are more likely to make mistakes. Successful techniques used for capture of crocodilians on land include the following.

The use of a rope to secure a hold on the animal is most common. Rope lassos can be tossed over the head or the rope is placed with a hook or catchpole. Once the rope is secure, the crocodilian is pulled to the designated work area. The animal is tied to a tree or post. Most carefully prepared capture plans unravel when the crocodilian begins to roll. This tangles ropes, scatters equipment, moves the animal into areas that compromise it or the catch staff, and generally messes up an otherwise well-organized process. Catch leaders must recognize and concede when a plan has been disrupted. Most often it is best to pause momentarily, regroup, reorganize, and then begin again. Once an animal is tied off, it may be possible to cinch a second rope to the tail. Stretch the animal and tie off the second line. This may help prevent the animal from rolling. Once the animal is restrained, a mouth pole is used to close and secure the jaws.

If there is a tree or post within the area, try to pull the animal up to it so that the head is pulled up against the tree. This acts as a stubbing post and can greatly restrict the movement of the head, making it safer to work around the animal.

Most crocodilians, when roped, will pull against the rope in an attempt to escape. A few may be more bold or aggressive and lunge at the staff on the other end of the rope. If this appears to be a possibility, either control the animal by catching it up with a rigid catchpole or place a second rope over the head and stretch the animal.

Mounting

There are situations in which it is necessary to straddle over or "mount" a large crocodilian. With caution, the correct procedure, and experience this is a fairly safe technique. However, the level of security it offers personnel is much less than that of other methods recommended in this chapter (i.e., shifting, working at a distance with hooks and poles, or physical restraint on a backboard). If any of these other methods satisfy the purpose use them instead.

Mounting allows one person to control the animal and its head, take blood or other samples, and facilitates measurement. Once in position on top of the animal the handler is relatively safe. Even with vigorous twists from side to side, the animal should be unable to bite. Care is taken to prevent the animal from rolling. The best technique to prevent this is for other catch crew to keep the tail straight and pull the hindlimbs back and off the ground. Some species (especially caiman) are quite capable of and prone to snapping their heads straight up when a handler leans over them. This is extremely dangerous and can cause serious injury; sit up straight while straddled on the animal.

To attain this position the handler must move into the animal's strike zone, hence the danger of this technique. To do this safely, the animal must be tightly roped and the rope tied securely in front of the head. This prevents the animal from twisting back. The handler moves up along the axis of the animal's body, essentially straight up the tail and the back. Stay as close to the body as possible. If the animal thrashes unexpectedly this will reduce the impact and help maintain your balance. The author finds it useful to nudge the animal with his foot before he proceeds. This tests whether the animal is ready to burst into a struggle. When ready to mount, move forward quickly and deliberately. Place one foot against the base of the tail just behind a hind limb. Move forward rapidly, place the other foot against the other side of the torso at midbody and quickly drop into a seated position on its back, with the knees planted behind the forelimbs of the animal (Fig. 14.4). Cover the eyes with your hand, and keep your



Figure 14.4 Physical restraint of a small to medium-sized crocodilian by straddling the body. Note the covering of the eyes and the noose used to capture the animal.

other hand on the top of the head and snout. Do not let fingers trail off the side of the face as this might elicit a snap to the side.

When ready to dismount make sure the path behind is clear and quickly step back off the animal in the same manner you approached: place your feet against the body and step back along the body axis.

Restraint and Transport

Once the crocodilian is captured and the jaws safely secured, the techniques for safely and efficiently moving it vary. The method of transport depends, obviously, on the size of the specimen and the distance it must be transported. For transport within the institution smaller specimens are simply carried or placed in a bag, pillowcase, duffel bag, bucket, or ice chest. However, even small crocodilians can deliver a painful slap with the tail. This is prevented by placing the tail underneath the arm while holding the animal around the neck and supporting its weight on your arm.

Larger specimens can be heavy, at least unwieldy if not often combative, and difficult to lift and carry. There is a natural tendency to try to lift these specimens by their legs. This can be injurious and must be avoided. The shoulder and hip joints of crocodilians are relatively shallow. It is not difficult to pull a limb out of the joint when lifting its leg. If an animal must be lifted, reach underneath and support it from below the torso and tail. However, crocodilians are not accustomed to being off the ground; they will often struggle, twist, and attempt to roll. The head must always be controlled. Even with the jaws taped shut it is dangerous. Always keep it directed away from others and keep your head away from it.

Ideally, larger crocodilians are either placed into a shipping crate or strapped to a backboard, platform, or aluminum ladder for transport (Fig. 14.5). They must be thoroughly restrained to prevent them from struggling to free themselves and potentially injure themselves or the capture team. Although harsh this has many benefits to the animal as well as to personnel. Some crocodilians will continue to struggle for long periods after capture. This increases their stress and exhausts them. Very large saltwater crocodiles (*C. porosus*) are known to struggle to such an extent that they build up dangerously high levels of lactic acid in their bloodstream (Seymour et al. 1987). This can result in severe acidosis and death. Crocodilians that are completely restrained on a board or platform usually cease to resist. Without the continued struggle there is little chance of the animal seriously compromising itself physiologically.

Restraint can be in the form of nylon cable straps (for smaller specimens), ropes, or cargo straps. The platform can be lifted easily and can be placed on a cart or truck for transport. Straps are placed in several places along the body: over the neck, across the shoulders just behind the forelimbs, across the center of the torso, just in front of



Figures 14.5 Physical restraint of large crocodilians ((a) *Crocodylus novaeguinae,* (b) *niloticus*, and (c) *intermedius*) with restraint board. Cargo straps or plastic seat belts are used to tie the animal to the board. A towel covers the eyes to reduce struggling. Depending on the animal's temperament, even large crocodilians may undergo nonpainful diagnostic procedures, such as this CAT scan, with no to moderate sedation (see Chapter 13). The plastic straps and wood or plastic boards do not interfere with the CAT scan process.

the hindlimbs, on the base of the tail just past the pelvis, and wrapped one or more times across the anterior half of the tail (Fig. 14.5). The head is also secured. If the animal is restrained on an aluminum ladder, it is possible to run the rope through the hollow rungs of the steps to completely secure it to the structure. Cargo straps can be purchased in a variety of widths and strengths. It is best to use those that have a wrenching action to tighten the strap after it is attached.

It is possible to physically restrain even the largest of crocodilians in this manner, assuming the platform and straps are sufficiently strong. However, it can be difficult to release the grip on the buckle of very large cargo straps. A heavy hook is useful for this purpose. For transport to other institutions, crocodilians are generally confined to a shipping crate.

Release Techniques

Releasing an animal that has been captured poses as many safety concerns as the initial capture. One must be concerned not only with the safety of the staff, but also with risks to the animal being released or its enclosure mates.

There is a real possibility the animal may attempt to turn and bite after its jaws have been unbound. Methods should be utilized to put distance between the catch personnel and the animal being released. One such method is the use of a jaw rope. A length of narrow rope is passed underneath the tape or rubber band holding the jaws shut. It is passed from the front to the back so there is no danger of accidentally causing the binds to slip and release the jaws prematurely. The rope is then tied off so that it will grip the binds. With the animal in position, all other restraints are removed, taking care not to trip on or accidentally pull the jaw rope. When all restraints are free and all personnel are well away from the animal, a hard tug on the jaw rope will pull the bindings from the jaws, freeing the animal.

In cases where the animal has been roped around the upper jaw, it will serve as the jaw rope. With the jaws still firmly taped or tied the noose of the top-jaw rope is opened. The length of rope still firmly held in the crocodile's jaws is then used to make several wraps around the snout. This then serves to secure the jaws while the other bindings are removed. When all other restraints are removed and everyone is safely away, the top-jaw rope is unwrapped from the snout. The animal will open its mouth and release the rope.

A rope noose catchpole or mouth pole is ideal for assisting release. The catchpole restrains the animal while the jaw bindings are removed. The pole prevents the animal from moving toward the catch team member holding it. When everyone is safely back from the animal the catchpole is removed.

Immediately after release crocodilians may be highly agitated. If there are other enclosure mates there is a possibility of displaced aggression leading to injury of one or more of the other animals. Before releasing a crocodile make sure it is positioned at a distance from others.

If it is suspected aggression will occur it is possible to release an animal with its jaws still bound and remove the bindings later. Re-tape the jaws and insert a piece of rope or a metal ring under the tape. The rope should float and have a large loop tied in its free end. Once the animals have had sufficient time to calm down after release, a long-handled hook is used to catch the loop in the rope or the metal ring and pull the tape from the jaws.

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Cagebirds (Parrots and Perching Birds)

Michelle G. Hawkins and Peter J. Pascoe

Introduction

The anesthesia of caged (and other species) of birds is unique not only from the aspect of anatomy and physiology, but also due to unique requirements for anesthetic equipment, monitoring, and species-specific pharmacology. It is critical to understand the limitations of currently available technologies when dealing with small patients to plan safe anesthetic procedures.

Preanesthetic Evaluation

The medical history and husbandry of the patient is essential for preanesthetic evaluation. History regarding diet, appetite, previous diseases, and drug therapy should always be collected. Examination of the bird's cage and its contents is useful to assess heavy metal exposure and the bird's droppings. The quantity and quality of the droppings will help determine whether the bird has been eating. Changes in the color or consistency of the droppings suggest abnormalities in the gastrointestinal, hepatic, or urinary systems (Doneley et al. 2006).

Allowing time for acclimation to new surroundings will reduce stress and unmask clinical disease. A complete physical examination including respiratory, cardiac, renal, and hepatic function should always be performed and baseline values recorded for comparison during anesthesia. The bird should first be examined closely in its cage, paying particular attention to respiratory rate and effort. The resting respiratory rate is recorded prior to physical restraint for comparison with rates under anesthesia. The quality of respiration is evaluated by ausculting the air sacs ventrally and the lungs dorsally for evidence of harsh airway sounds or evidence of wheezing. The trachea is also ausculted and gently palpated for any abnormalities. The heart is ausculted carefully for murmurs and a baseline heart rate recorded for comparison during anesthesia. Pulse quality is assessed at either the median ulnar or medial metatarsal arteries, evaluating it for symmetry and strength. The body weight is recorded for calculating accurate fluid and medication dosages.

Accurate assessment of renal and hepatic function is difficult during the physical examination. Urine and urates in the droppings are evaluated for quantity and color. Red-tinged urine could be due to hematuria but may be due to dietary colorings. Green or yellow urate discoloration may be biliverdinuria and a sign of hepatic dysfunction (Doneley et al. 2006). Coelomic palpation is performed to assess for organomegaly, which may mechanically compress the air sacs and lungs.

Hydration status is evaluated and recorded, and dehydration corrected, if possible, prior to anesthesia. Compensatory mechanisms are blunted under anesthesia, exacerbating underlying hypotension and poor peripheral perfusion. Hydration assessment includes examination of the moistness of the cloacal and ocular mucous membranes and the elasticity of the skin at the eyelids and over the keel. Sunken eyes and cool extremities also indicate dehydration. The refill time after digital compression of the median ulnar vein should be immediate; venous refill times of >1 second have been suggested to correlate with >7% dehydration (Steinohrt 1999). The packed cell volume (PCV) will often be increased during dehydration. In pigeons that were water deprived for 72 hours, the plasma urea nitrogen increased 6.5–15.3 times, but the uric acid only showed a 1.4–2 times increase (Lumeij 1987). Clinically, however, it appears uric acid does go up with moderate-to-severe dehydration and will resolve with rehydration.

Ideally, a complete blood count and biochemical profile are performed prior to anesthesia. If one hematocrit tube

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of blood can be collected, a packed cell volume (PCV), whole-blood smear for estimated white blood cell count and differential blood glucose, and several other biochemistry tests can be obtained. There are several biochemical analysis tabletop systems that require only a very small volume of blood to provide a complete biochemistry profile. Any anemias are characterized as either acute or chronic and regenerative or nonregenerative. Acute anemias are corrected prior to anesthesia as birds may not be able to compensate for lowered levels of oxygen delivery. Transfusion is indicated as in mammals if the PCV is <15–20% and the total solids are <3–3.5 g/dL. However, pet birds often have PCV ≥40% so if the blood loss is acute, the authors may perform a transfusion at a higher PCV. Also, avian total protein values may be much lower than those in mammals (2–3 g/dL). There is a poor correlation between total solids measured by refractometer and protein values measured with the biuret method, making the former an inaccurate criterion for avian transfusion (Lumeij & de Bruijne 1985). The type of surgery to be performed and the potential for blood loss are assessed so a fluid plan can be prepared. PCV may decrease 3–5% during anesthesia due to vascular hemodynamic changes associated with certain anesthetic drugs. Hypoglycemia (<200 mg/dL) is supplemented before anesthesia and glucose concentration monitored. Calcium gluconate is commonly administered in African grey parrots prior to induction to prevent hypocalcemia, a common problem in these species.

The gastrointestinal system has a very rapid transit time compared with most mammals. It is therefore important to carefully consider the nutritional plane of the patient. Prolonged anorexia will lead to a negative energy balance requiring nutritional support in the perianesthetic period. Other indications for additional nutritional support include reduced to absent fecal production and significant reduction in body weight. Nutritional requirements differ between species and classes. To calculate nutritional requirements for the critically ill patient, the basal metabolic rate (BMR) is first calculated: BMR (kcal/day) = K ($BW_{kg}^{0.75}$), K = 78 in nonpasserines and K = 129 in passerines. While these two K-factors provide a basic means of estimating avian BMR, many additional factors have been calculated for specific species. The authors refer the reader to appropriate avian nutritional texts for additional detail (Klasing 1998). The maintenance energy requirements are adjustments to the BMR based on hypermetabolism associated with any disease processes. The most common adjustments are 1.2–1.5 times BMR (range 0.5–2.0 times) (McDonald 2006). The chosen diet depends on the patient's nutritional needs. Foods can be blended to a liquid or commercially available enteral products based on the patient's protein, carbohydrate, and fat requirements can be used. Total parenteral nutrition or partial enteral nutrition is not commonly utilized due to catheter-related complications, poor patient tolerance, and lack of appropriate formulations.

Preanesthetic Supportive Care

Fluid Support

Daily maintenance fluid rates are approximately 40–60 mL/kg/day. This range is based on studies where drinking is the main route of water intake. Birds weighing ≥100 g drink approximately 5–8% of body mass/day. This increases at progressively smaller body masses to drinking rates as high as 50% for birds weighing 10–20 g (Bartholomew & Cade 1963; Skadhauge 1981; Zeigler et al. 1972). Estimation of fluid replacement is based on body weight and dehydration percentage: estimated dehydration (%) × body weight (gm) = fluid deficit (mL). One fourth to half the deficit is given in the first 6–12 hours and the remainder over the following 24 hours (Abou-Madi & Kollias 1992).

Oral fluids are only useful for mild dehydration and are contraindicated in head trauma, gastrointestinal stasis, lateral recumbency, or seizuring. Subcutaneous (SC) fluids are commonly used for maintenance and mild-to-moderate dehydration. However, large volumes may not be absorbed due to the paucity of blood vessels in the subcutis and peripheral vasoconstriction. Volumes of up to 10–15 mL/kg/site can be injected into the inguinal folds, axilla, or dorsum. Overdistension of the SC site can result in compromise of the blood supply and decreased fluid absorption. Before each injection, the administration site is inspected for previous delays in absorption. Only isotonic or nonirritating fluids should be given SC. Dextrose solutions ≥2.5% are not given SC as equilibration between the SC fluids and the extracellular fluid will exacerbate preexisting electrolyte imbalances (Abou-Madi & Kollias 1992; Steinohrt 1999).

Fasting

Preanesthetic fasting duration is determined by species, size, and clinical status, with a goal of reducing regurgitation yet minimizing hypoglycemia (Harrison 1991). Fasting times between 2 and 4 hours have been recommended in medium-sized psittacines, whereas birds ≤100–200 g may not be fasted due to high metabolic rates and easily depleted glycogen stores. However, in broiler chickens and adult Japanese quail fasted for 12 and 48 hours, respectively, blood glucose remained within clinically acceptable ranges

(Lamosova et al. 2004; van der Wal et al. 1999). No studies have been performed evaluating the effect of fasting on psittacines. Scheduling procedures as early in the day as possible reduces fasting times. In species with high metabolic rates, clear fluids high in carbohydrates may be provided to maximize calories while minimizing crop and stomach contents prior to anesthesia. The crop contents may be gently aspirated if anesthesia cannot be delayed.

Equipment

Endotracheal Intubation

The main advantages of tracheal intubation are that it provides a patent airway, reduces dead space, and allows easy application of positive pressure ventilation. The disadvantages are that it can be associated with trauma to the airway, it can significantly increase airway resistance, and the tube can become occluded due to mechanical forces or because of secretions. These factors need to be carefully considered when deciding to intubate a patient. There are a handful of species with notable anatomical variations of the upper respiratory tract. Male ruddy ducks (Chapter 21) and both sexes of emus (Chapter 19) have a tracheal sac-like diverticulum that can be confused for a ruptured trachea (King 1989). In emus, this diverticulum arises as a slit-like opening through incomplete tracheal rings from the ventral surface of the caudal one-fourth of the extrathoracic trachea. The caudal end may extend almost to the sternum (King 1989). This sac allows for the booming call of the emu. In the ruddy duck, a pear-shaped sac opens from the dorsal tracheal wall just caudal to the larynx and extends between the esophagus and trachea (King 1989). This sac is only found in the males and may be involved in the bill-drumming display. In both species, positive pressure ventilation will inflate the sac and some anesthetic gas may be sequestered, potentially affecting anesthetic depth. A bandage can be wrapped around the neck over this area to prevent inflation of the sac. A bullous enlargement of the trachea is found in some species of Anseriformes (King 1989). A median septum is present in the trachea of some penguins (Chapter 21) and petrels. This septum divides the trachea from the bronchial bifurcation cranially for variable distances depending on the species. For example, the median septum of the rockhopper penguin is only 5 mm in length (King 1989), but still may allow for unilateral endobronchial intubation. The median septum of the jackass penguin extends to within 1 cm of the larynx, allowing both unilateral endobronchial intubation and the potential for trauma during intubation (Zeek 1951). However, endotracheal tubes can be modified to allow bilateral intubation in species with median septa.

There is significant variation in tracheal length between species, which has important implications for anatomical dead space. The typical bird trachea is reported to be 2.7 times longer than that of a similarly sized mammal, but because it is approximately 1.3 times wider, the net effect is that resistance to air flow is similar to that in mammals (King 1989). Tracheal dead space volume is approximately four times that of comparably sized mammals (King 1989). In some species (e.g., some swans, cranes, spoonbills, and cassowarys), convoluted loops and coils further increase dead space. Healthy, conscious birds compensate for this larger dead space with a larger tidal volume and lower respiratory frequency than mammals. This results in minute ventilation rates that are about 1.5 to 1.9 times those of mammals (Frappell et al. 2001; Powell & Whittow 2000). However, anesthetic drugs can decrease tidal volume and a greater percentage of minute ventilation can become dead space ventilation (Curro 1998; Ludders 1998; Ludders & Matthews 1996).

An increase in airway resistance is of greatest importance in very small patients since the resistance varies with the fourth power of the radius. For example, decreasing the radius from 5 to 3 mm would increase the resistance 7-fold whereas a decrease from 3 to 1 mm would increase resistance >80 times. Since an increased resistance would require the patient to work harder to breathe, this effect can be minimized by providing positive pressure ventilation.

Despite the above cautions, the authors recommend that for any procedure that requires greater than 10 minutes of anesthesia, intubation should be performed. Many types of endotracheal tubes have been used in birds. Cole, noncuffed, and cuffed tubes have all been used successfully in caged birds (Fig. 15.1). Cole tubes have a narrow tip that is static in diameter for a short distance then increases in diameter. The distal end is advanced into the trachea until the larger diameter abuts against the glottis, creating a seal. However, these tubes tend to plug with secretions easily.

Cuffed endotracheal tubes may be used if the inflation of the cuff is carried out using an accepted method. The most careful approach is to place the tube and then inflate the lung to about 15 cm H_2O and listen for a leak. The cuff is inflated in very small increments until the leak is sealed. Overinflation of the cuff on an endotracheal tube can cause tracheal mucosal epithelial trauma due to lack of expansion of the tracheal rings. However, the avian trachea tapers as it proceeds into the thoracic inlet and a seal is often achieved using a noncuffed tube simply by its contact with the tracheal wall as it is advanced down the trachea. In general, a larger uncuffed tube will fit into the trachea than a cuffed tube because of the space taken up by the cuff. Care should be taken not to jam the tube in too forcefully as that can lead

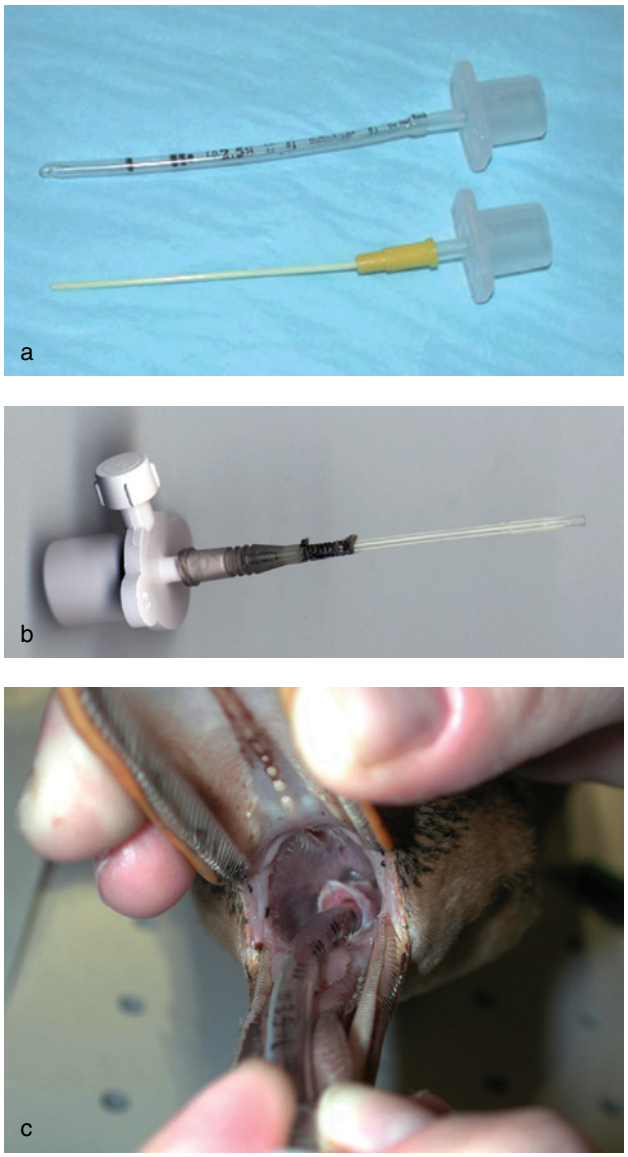


Figure 15.1 Various endotracheal tube types are used in avian clinical practice. Cole, noncuffed, and cuffed tubes have all been used successfully in caged birds (a). Catheters can be modified and used as endotracheal tubes for very small patients (b). Intubation is straightforward as visualization of the glottis is not difficult in most caged birds (c).

to tracheal mucosal damage. The tracheal diameter of many birds is narrower at mid-neck than the glottal diameter. Inflammation of the tracheal epithelium may lead to fibrotic narrowing of the tracheal lumen with complete trans-tracheal membranes (Fig. 15.2). Cuffed tubes without the cuff inflated also have the potential to cause tracheal mucosal damage and inflammation due to the irregularity of the plastic surface of the cuff on the tracheal epithelium. Since this inflammatory process requires time, clinical signs of dyspnea associated with this type of tracheal trauma may not become evident for up to 1 week post intubation. There

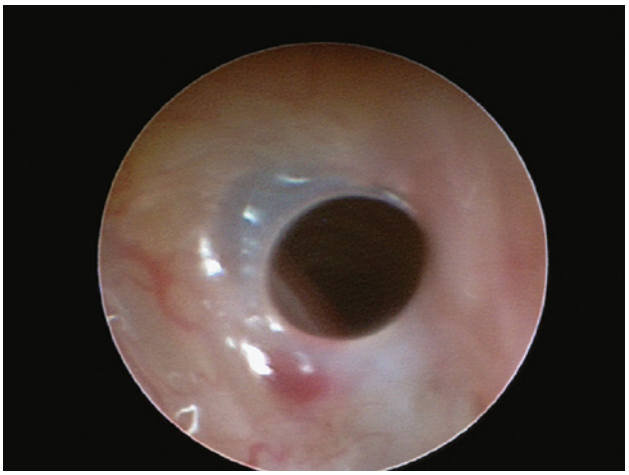


Figure 15.2 Transtracheal membrane occluding approximately 75% of the tracheal lumen in a double yellow-headed Amazon parrot. Note the significant vascularization of the membrane. These membranes have been reported most in birds up to several weeks after intubation with both cuffed and noncuffed endotracheal tubes. Various factors such as overinflation of the cuff, ventilation techniques, and endotracheal tube disinfection protocols have been evaluated but no definitive correlations have been identified to date.

have been a small number of case reports documenting tracheal stenosis or tracheal membrane formation in psittacines post intubation, as well as other species (blue-billed curasow) (de Matos et al. 2006; Evans et al. 2009; Jankowski et al. 2010). These cases have been managed with tracheal anastomosis, with one bird having no respiratory signs for 2 years post resection (Jankowski et al. 2010). Various factors, including ventilation techniques and endotracheal tube disinfection protocols, have been suspected to contribute to this phenomenon and these are factors that are associated with tracheal stenosis in humans (Wain 2009), but no definitive correlation with protocols or procedures has been identified to date.

Although noncuffed tubes are used most, there are several disadvantages to their use. They do not provide a sealed airway, allowing escape of anesthetic gases. This increases the amount of anesthetic gas required and environmental contamination. Also, airway protection from aspiration of secretions or gastrointestinal contents is reduced. This makes it imperative that the oral cavity be clean prior to intubation and monitored throughout the procedure. Elevation of the head and neck may reduce regurgitation of gastrointestinal contents from the crop, proventriculus or ventriculus into the oral cavity. Cuffed tubes have been used in larger avian patients. The cuff is carefully inflated with just enough air to prevent leakage when 10–15 cmH_2O pressure is applied to the breathing circuit (Curro 1998; Ludders & Matthews 1996).

The patient size determines the endotracheal tube size used. The smallest commercial noncuffed tubes have an internal diameter (ID) of 1 mm. However, tubes of <2 mm ID are often highly flexible and kink easily. The smallest diameter cuffed tube is 2.5 mm ID. Very small birds may be intubated with teflon intravenous (IV), red rubber, or urinary catheters. Care is taken to ensure that no sharp edges are present at the end. This is achieved by using a small piece of silicone tubing over the end of the catheter. Ends of catheters can be cut and adapted for use as endotracheal tubes if they are gently filed with an emery board to remove rough edges.

As stated previously, endotracheal tubes with small internal diameters impose significant resistance on gas flow, especially if mucus accumulates. During inhalant anesthesia, copious thick mucus production can occur due to the drying effects of the inspired cold, dry gases. The mucous plug can act as a "flapper" valve allowing air in, but not out. In the authors' experience, humidification of the gases reduces mucus plug formation. Commercially available endotracheal tube humidifiers are available (Humidi-vent Mini Agibeck Product, Hudson RCI, Temecula, CA, USA). Disadvantages of their use include increased dead space and filter plugging with secretions. The use of an endotracheal tube with a Murphy eye, which has both side and end openings, decreases the likelihood of mucus occlusion.

Endotracheal tube obstruction is detected by monitoring the ventilatory pattern. As the airway occludes the expiratory phase duration becomes prolonged (Ludders & Matthews 1996). An anticholinergic (atropine, glycopyrrolate) reduces mucus production and mucus plug formation. However, it also increases mucus viscosity, making it harder to clear secretions from the tube. Some clinicians recommend that the endotracheal tube be removed and replaced after every hour of anesthesia for long procedures.

Extension of the neck, gentle traction on the tongue, and pressure under the mandibular beak will push the glottis forward to aid in endotracheal tube placement. A Q-tip swab is useful to atraumatically pull the tongue forward. Psittacines have a thick, fleshy tongue that makes glottal visualization slightly more difficult. Some birds have very brisk glottal closure reflexes. Intubation in these patients can be facilitated by applying a very small amount of lidocaine to the larynx and waiting 60 seconds. If possible, the tube is secured to the mandibular beak to allow for monitoring the oral cavity during anesthesia. Any portion of the tube extending from the circuit to the glottis is dead space; cutting the tube as close as possible to its entry into the oral cavity will minimize this mechanical dead space.

Inhalant anesthetics can also be administered through a cannula inserted into an air sac for induction and maintenance in birds as small as zebra finches (Fig. 15.3) (Korbel et al. 1993; Korbel 1998a; Mitchell et al. 1999; Nilson

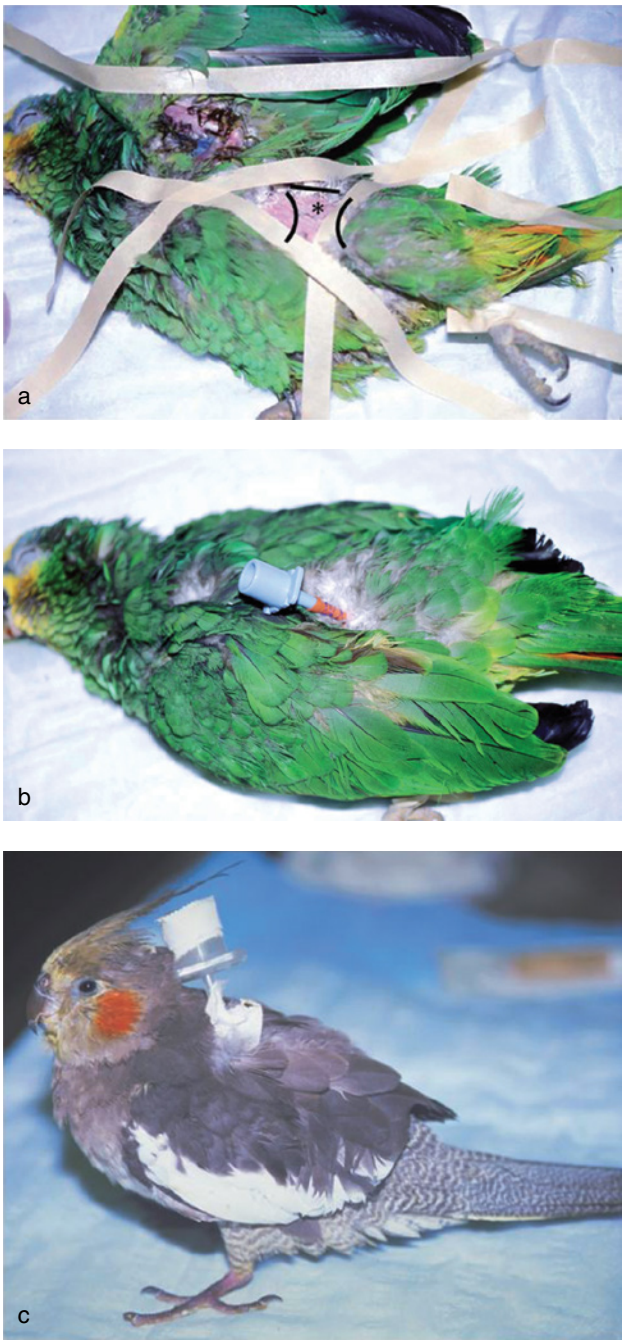


Figure 15.3 Placement of an air sac cannula. Strict asepsis should be observed when placing the cannula. Feathers over the site for cannulation should be gently plucked, contour feathers taped away from the cannula site, and the area should be surgically prepared. The landmarks for air sac cannula placement are caudal to last rib, ventral to the vertebrae, and, in most cases, cranial to hindlimb. The proper site for cannula insertion is marked with * (a). Once the cannula has been surgically placed, it is secured in place with suture (b). A piece of sterile gauze can be used as a filter to minimize contamination of the cannula with particulate matter (c).

et al. 2005; Piiper et al. 1970; Rode et al. 1990; Whittow & Ossorio 1970; Wijnberg et al. 1991). Air sac cannulation provides an airway when upper respiratory tract obstruction is present (e.g., syringeal foreign bodies or granulomas). It is also used for procedures involving the upper airway or cranium (Jaensch et al. 2001; Nilson et al. 2005; Piiper et al. 1970). It is also placed for acute life-threatening obstruction and can be left in place to provide longer-term respiratory support, but not generally for more than 3–5 days without replacing tubes, as inflammatory tissue and cells will accumulate on the tube tip (Korbel et al. 1996; Mitchell et al. 1999).

Materials used for air sac cannulas include sterile endotracheal tubes, large gauge IV catheters (16–18 g), red rubber feeding tubes, and silastic tubing. If the bird is to breathe through the cannula, the tube diameter should be at least equal to the patient's tracheal diameter and short enough to minimize dead space and prevent coelomic soft tissue contusion.

Air sac catheters are usually placed in the left caudal thoracic or abdominal air sac to prevent trauma to the larger right liver lobe. However, catheter placement into the clavicular air sacs has also been reported (Rode et al. 1990; Rosskopf & Woerpel 1990). In sulfur-crested cockatoos (*Cacatua galerita*) caudal thoracic air sac intubation provided stable isoflurane anesthesia without significant respiratory functional changes. Even though caudal thoracic air sac partial pressure of carbon dioxide (PCO_2) decreased to 12.7 ± 7.9 mmHg, spontaneous respiration was still present (Jaensch et al. 2001). Clavicular air sac catheterization was also evaluated but was not successful at either maintaining anesthesia or providing ventilation. In a separate study, clavicular air sac PO_2 and PCO_2 were significantly lower than in the cranial thoracic air sacs, suggesting, at least in sulfur-crested cockatoos, ventilation of this air sac is less than the cranial and caudal thoracic air sacs (Jaensch et al. 2002).

Air sac cannula placement is a relatively simple surgical procedure (Fig. 15.3). For placement into the left caudal thoracic or abdominal air sac, the landmarks are the last rib, the cranial aspect of the femur, and the flexor cruris medialis muscles. Following removal of overlying feathers and aseptic preparation of the skin, a skin incision is made over the desired site. The underlying muscle and air sac membrane are bluntly dissected with a hemostat. The tip of the sterile catheter is grasped with the hemostat and passed into the air sac. The muscle and skin are closed, securing the catheter in place. In an emergency, gas flow and ventilation are provided through an IV catheter placed at the same site and connected to an oxygen source. Care is taken not to advance the catheter needle too far and to limit oxygen flow to prevent hypocapnia. In apneic 1–1.7-kg chickens a flow of 500 mL/min reduced PCO_2 to ≤20 mm Hg (Pascoe, unpub. obs.) so with a small catheter and flow-through ventilation the O_2 flow should probably be <250 mL/kg. Oxygen and anesthetic gases from the cannulated site exit the trachea unless intubated with an occluded endotracheal tube. It is possible to scavenge waste gases by placing a mask or tube over the bird's head and connecting it to an active anesthetic scavenging system.

The most common adverse effects reported with air sac cannulation are apnea, SC emphysema, plugging of the tube, and bacterial contamination with associated coelomitis (Jaensch et al. 2001; Mitchell et al. 1999). Ensure meticulous cleaning/inspection of the tube to prevent plugging. Cleaning is performed with a sterile cotton-tip applicator or Dacron swab. A filter can be designed from small weave gauze (i.e., from the inside of a Hepa-filtered mask) and placed over the end of tube to prevent particulate matter from entering. Although most birds tolerate air sac cannulas, an Elizabethan collar may be required for some. Following cannula removal, the body wall is closed to prevent SC emphysema.

Breathing Systems

Many nonrebreathing systems (e.g., Ayre's T-piece, Mapleson systems, Magill, Jackson-Rees, Norman elbow, and Bain) have and can be used for avian anesthesia. These systems require a relatively high fresh gas flow rate to remove carbon dioxide. These higher flow rates have the added benefit of providing rapid equilibration in inhalant concentration with changes in vaporizer setting. Nonrebreathing systems were traditionally viewed as ideal for small patients because of lower airflow resistance and reduced dead space. Circle systems were believed to have higher airflow resistance because they contain one-way valves and soda lime canisters. However, the primary source of resistance is most likely the endotracheal tube. Studies in infants ≤10 kg (Rasch et al. 1988) and cats (Suter et al. 1989) have shown that resistance was insignificant compared to that produced by the endotracheal tube alone. Circle systems are heavier and bulkier, which predisposes to accidental extubation and difficulty working around the head. For this reason, a nonrebreathing system such as the Bain breathing system is recommended in small birds due to its lightweight design.

Specific flow rates for avian patients have not been defined. As in mammals, 2–3 times minute ventilation appears appropriate when using the T-piece or Norman elbow, but in the Bain circuit a lower flow rate of 150–200 mL/kg/min is effective (Ludders 2001; Ludders & Matthews 1996). The removal of waste gases from the circuit occurs during the pause between expiration and

inspiration. If the respiratory rate is high (shorter pause and therefore more mixing of inspired and expired gases) a higher flow rate is used (e.g., respiration rate >40, increase the flow rate to 300 mL/kg/min). If a capnograph is being used the flow rate can be adjusted to minimize increases in inspired CO_2.

Ventilators

Allometric analyses have been used to predict the effect of body size on respiratory variables associated with gas exchange efficiency between mammals and birds (Frappell et al. 1992, 2001; Maloney & Dawson 1994). A study using 50 avian species found general agreement with the older allometric equations, with some minor differences in coefficients. The variables determined in this study agree with anatomic data and clinical observations, suggesting that irrespective of body size, birds tend to breathe slower and deeper, have lower minute ventilation, and have a greater demand for oxygen when compared with mammals, making the avian respiratory system more highly efficient in terms of oxygen extraction.

Both injectable and inhalant anesthetics cause dose-dependent respiratory depression. Sick or debilitated birds may not be able to accommodate these physiologic changes and require intermittent positive pressure ventilation (IPPV). In mammals, IPPV is associated with reduced cardiac output and hypotension (Steffey & Howland 1977, 1980). In cranes anesthetized with isoflurane, spontaneous ventilation was associated with elevations in arterial partial pressure of carbon dioxide ($PaCO_2$), hypotension, and acidemia compared with controlled ventilation (Ludders et al. 1989). Similarly, there was a significantly reduced $PaCO_2$–to end-tidal carbon dioxide ($PETCO_2$) gradient and no significant difference in mean arterial blood pressure in Hispaniolan Amazon parrots (*Amazona ventralis*) ventilated using IPPV compared to birds breathing spontaneously (Pettifer et al. 2002). It is possible that reduced cardiovascular performance associated with IPPV may not be a concern in birds. However, it is still recommended that cardiovascular variables be monitored closely during IPPV.

Ventilators must cope with the range of tidal volumes in the species of interest. In very small birds this may be ≤1 mL while in a large ostrich it might be ≥2 L. Modern ventilators are usually pneumatic, but control mechanisms may be either pneumatic or electric. If electronically controlled, an auxiliary power source is required if the bird is moved or power fails. The three variables controlled by a ventilator are tidal volume, rate of tidal volume delivery, and respiratory frequency. The method of control varies between ventilators. In volume-limited ventilators tidal volume is set on the machine with the expectation that it will deliver the volume regardless of moderate changes in resistance. Even if the circuit is disconnected the ventilator continues to cycle with no alteration in tidal volume or timing. Some ventilators allow the upper limit for inspired pressure to be set with an alarm. In pressure-limited ventilators the end-inspiratory pressure is set. The ventilator will push gas into the bird until it reaches the set pressure, when the inspiratory phase will terminate and the ventilator allows for passive exhalation. A disconnect or large hole in an air sac is indicated by prolonged inspiration because the preset pressure is not reached. A third method is to set the inspiratory time and achieve different tidal volumes by altering the inspiratory flow rate. This is a form of volume-limited ventilation. The respiratory rate and tidal volume are determined by the gas flow rate. Hence it is necessary to set a faster flow rate for a larger tidal volume. On some ventilators this is set by altering the knob labeled "I:E ratio". This is the inspiratory versus expiratory time and the setting will depend on the number of breaths per minute. If you want inspiration to take 1.5 seconds the I:E ratio would need to be 1:3 for 10 breaths per minute (6 seconds per breath, 1.5 seconds for inspiration:4.5 seconds for expiration) or 1:1 for 20 breaths per minute (3 seconds per breath, 1.5 seconds each for inspiration and expiration). The number of breaths per minute is mostly set by altering a timing device that begins a new inspiration after a set period.

When ventilating birds, it is essential to have a ventilator that can deliver small tidal volumes slowly to give an acceptable inspiratory time. During anesthesia the ventilator should initiate the breath, not the bird, to control the PCO_2. In assisted ventilation mode the bird initiates the breath when its PCO_2 reaches the point set by the central controllers of ventilation in the brain. Since the latter are depressed by anesthetics, assisted ventilation is not likely to decrease PCO_2.

The authors recommend initial inspiratory pressures of 8–10 cmH_2O and rates of 6–10 breaths per minute. Thoracic excursions are assessed as soon as the ventilator is started. The tidal volume is adjusted to achieve an appropriate thoraco-abdominal expansion. The minute volume is lower than in mammals (Frappell et al. 2001) and inspiratory times can be longer. At 6 breaths per minute the I:E ratio could be set to 1:2 to 1:3 (inspiration occurring over 3.3 to 2.5 seconds). During coelomic surgery, when the air sacs have been opened, anesthetic will be pushed by the ventilator into the air being breathed by the surgeons. It is important to avoid or minimize personnel exposure to inhaled agents. In some cases, injectable anesthetics are used if the concerns about using inhalant anesthetics are great.

During positive pressure ventilation, it is possible the direction of gas flow within the lung is reversed. However, the crosscurrent exchange system is not dependent on the

direction of flow and does not significantly affect gas exchange (Ludders et al. 1989; Piiper et al. 1970; Uhart et al. 2020). If a mechanical ventilator is not available, hand ventilation delivered from the reservoir bag provides controlled or assisted ventilation.

Thermal Support

Heat is lost via radiation, evaporation, convection, and conduction. The normal body temperatures of most caged birds range from 39 to 43°C (Dawson & Whittow 2000). Since many birds are small and have a high body-to-surface area ratio they radiate heat rapidly. Once anesthetized, the bird is immobile and relaxed so it will generate less heat from muscle contraction. It is also subject to evaporative loss from the respiratory tract (dry anesthetic gases), skin surfaces (surgical preparations solutions), and open body cavities, conduction of heat via surface contact, and convection of warm gases from around the bird (Wessel et al. 1966). Anesthesia redistributes blood flow and depresses thermoregulatory response, further promoting heat loss. The core body temperature of pigeons with no external heat support dropped ≥8°C in ≤30 minutes of inhalant anesthesia (Harrison et al. 1985). Hypothermia has several adverse physiologic effects. It results in bradypnea and decreased minute ventilation and tidal volume (Moon & Ilkiw 1993). Hypothermia decreases anesthetic requirement and metabolism and will prolong recovery (Ludders & Matthews 1996), therefore monitoring core body temperature and providing thermal support are mandatory to reduce anesthetic morbidity and mortality in the anesthetized and recovering patient.

Body temperature is monitored continuously throughout anesthesia. Prevention of heat loss is essential in the anesthetized patient and supplemental heat sources are used regardless of procedure length. Electronic thermometers and temperature probes provide accurate readings. Cloacal temperatures have been correlated with thoracic esophageal readings, suggesting core temperature may be indirectly monitored (Phalen et al. 1996). However, as cloacal musculature relaxes, peripheral temperature readings are lowered. Esophageal temperature probes provide consistent readings when placed at the level of the heart in the thoracic esophagus. Care is taken to ensure the crop is not damaged during placement and the probe does not back out resulting in incorrect temperature readings.

Since most heat is lost via radiation, the most effective technique to prevent heat loss is to minimize the temperature gradient between the bird and the room. Options include increased room temperature, insulating the patient with clear plastic drapes, and wrapping nonsurgical fields. The surgical time and the amount of time that the body cavities are open are minimized, as are feather plucking and alcohol use for skin preparation. Latex gloves, empty fluid bags or plastic bottles can be filled with water, warmed in a hot water bath or microwave and placed next to the bird. Water bottles are always wrapped in a towel to prevent burns. Circulating warm water blankets insignificantly diminish the rate of heat loss in birds (Phalen et al. 1996; Rembert et al. 2001). Radiant heat lamps are effective at maintaining core body temperature, but the optimal distance between the heat source and the patient differs with patient size, heat lamp strength, and the heat setting (Phalen et al. 1996; Rembert et al. 2001). Forced air warmers (Bair® Hugger) have been thought to be more effective at minimizing hypothermia during anesthesia than other methods (Borms et al. 1994; Machon et al. 1999; Rembert et al. 2001). They are particularly effective when set up to have warm air rising around the patient either by wrapping the patient in the blanket or by using a perforated table. The patient's eyes are well lubricated to prevent corneal ulceration due to drying from the warm dry air. However, one trial showed that an electrical heating method (Hot Dog™, Augustine Medical) was more effective than a forced air warmer (van Zeeland et al. 2012).

Further reductions in heat loss are achieved by warming fluids and reducing respiratory cooling. In pigeons anesthetized for 90 minutes there was no significant difference in heat loss between either a circle system with mechanical ventilator producing heated air, a nonrebreathing system with mechanical ventilator producing nonheated air, and a Bain nonrebreathing circuit (Boedeker et al. 2005). This contrasts with humans, cats, and rabbits in which heated, humidified anesthetic gases reduce or prevent the development of hypothermia (Haskins & Patz 1980; Newton 1975; Shanks 1974; Tausk et al. 1976). In intubated anesthetized ring-necked doves (*Streptopelia risoria*) without thermal support, hypothermia was not lessened by humidification and heating of inspired gases (Phalen et al. 1996). However, in anesthetized pigeons maintained on a facemask, heated inspired gas did minimize hypothermia (Jenkins 1988).

Emergencies

Emergencies during anesthesia should be planned for and anticipated. Many can be averted by careful monitoring of respiratory and heart rates, and body temperature. Emergency equipment (i.e., endotracheal tubes, oxygen, IV catheters and materials for securing them, ventilatory support, and emergency drugs) should always be close by and prepared for use. It is recommended that emergency drug dosages be calculated and 1–2 doses predrawn before

Table 15.1 Emergency drugs used in birds.

Drug	Dosage	Route	Comments
Atropine	0.01–0.02 mg/kg	SC, IM, IV	Most species/preanesthetic
	0.04–0.1 mg/kg	SC, IM, IV, IO, IT	Bradycardia
	0.5 mg/kg	IM, IV, IO, IT	CPR
Glycopyrrolate	0.01–0.02 mg/kg	IM, IV	Slower onset than atropine Most species/preanesthetic
	0.04 mg/kg	IV	Ratites
Epinephrine (1:1000)	0.05–0.5 mg/kg	IM, IV, IO, IT	CPR, bradycardia
Norepinephrine	0.7 µg/kg/min	IV	Increased MAP in Pekin ducks by 11% (Jungbluth et al. 1994)
Dopamine	5 µg/kg/min	IV	Increased MAP in Hispaniolan Amazon parrots by 25% (Schnellbacher et al. 2012)
Dobutamine	5 µg/kg/min	IV	Increased MAP in Hispaniolan Amazon parrots by 17% (Schnellbacher et al. 2012)

CPR, cardiopulmonary resuscitation; IM, intramuscular; IO, intraosseus; IT, intratracheal; IV, intravenous; MAP, mean arterial pressure; SC, subcutaneous.

induction (Table 15.1). Respiratory depression and arrest are treated by turning off the anesthetic and controlling ventilation. Cardiac arrest is usually a result of myocardial hypoxemia and inotropic and chronotropic anesthetic drug effects. Although treatment is often unrewarding (Onuma et al. 2017), administration of epinephrine IV, intratracheal or by intracardiac injection, is recommended. Cardiac massage is nearly impossible due to the heart's anatomical location dorsal to the large bony sternum but should be attempted. Severe bradycardia is treated with atropine, assuming it is due to increased parasympathetic tone. In very small birds, it is possible to see spontaneous ventricular defibrillation as the mass of the heart is small enough that it cannot maintain a fibrillatory pattern.

Hypotension is not a common problem in anesthetized birds but Table 15.1 provides some information on the use of norepinephrine, dopamine, and dobutamine for this purpose (Jungbluth et al. 1994; Schnellbacher et al. 2012). Given that this information is very limited, it is expected that the clinician would use these doses as a starting point and increase/decrease the infusion to achieve the desired outcome.

Anesthesia

Restraint

Correct restraint is essential to minimize patient stress and the time required for anesthetic induction. Stressed birds may die from physical restraint and this risk is magnified in sick or debilitated patients. Appropriate means of physical restraint must be assessed for each patient and appropriate stabilization and supportive care prepared prior to handling. Paper towels, wash cloths, hand towels, large bath towels, or blankets may be used based on the patient size. Hooding calms some species (e.g., raptors and ratites), but care must be taken to ensure adequate air flow. Leather gloves will not protect handlers from the crushing bite of a large parrot. Nets are used to capture birds in larger enclosures or escapees. They should be sized appropriately for the patient to minimize iatrogenic trauma. Once netted, the bird is gently removed to avoid trauma to the wings, legs, or toes. Ear protection for the handler (e.g., cotton balls or ear plugs or noise cancelling headphones) can be used when handling large psittacines (e.g., cockatoos and macaws). Face shields or goggles are used when handling birds likely to inflict ocular damage with the tip of their beaks (e.g., Ciconiiformes).

It is preferable for caged birds to be captured from within their travel cage or hospital enclosure to reduce the chance for injury and reduce stress induced by escape attempts in a room. All perches, toys, and food and water dishes are removed to facilitate capture and minimize trauma, and ambient noise should be reduced. If a patient must be captured from a larger area, this should ideally be done in a small area that is free of windows and doors leading to the outdoors. Alternately, windows can be covered to minimize self-induced trauma if an escape occurs and doors are locked. Some methods to aid capture from a room include placing the bird on the floor or turning off lights as this will often reduce the excitement level of the patient. Regardless of the physical restraint technique employed, care should be taken not to compromise thoracic cage

movement or the ability of the anesthetist to monitor the patient. Movement with the bird in hand should be quiet and calm to reduce fright and stress. The capture is performed expeditiously to minimize stress. If a bird should escape and need to be re-captured or is unduly excited, delay anesthesia until the bird has calmed down.

Once the bird is in hand, a towel is initially placed over the dorsum, then gently wrapped around the wings to restrict flapping and prevent damage to the wings and feathers. Once adequately restrained by the handler, birds are removed from the towel if possible to prevent hyperthermia that can occur subsequent to prolonged restraint. Small birds (e.g., passerines) are restrained with the head between thumb and forefinger, and the body within the palm. Alternatively, in smaller psittacines the head is restrained using a "three-point" technique with the thumb and middle finger supporting the mandible and the index finger on top of the head. Bruising of the face is possible in large macaws and only the minimum pressure necessary to restrict movement is applied. Gentle extension of the bird's neck further limits head movement. Large parrots are strong and will inflict severe wounds if the head and beak are not immediately controlled. Some prefer to encircle the birds neck with their fingers for restraint. A third technique places the thumb under the intermandibular space while the other fingers are placed over the top of the head. This is the author's choice for maintaining full control of the head during restraint. The other hand is placed on the dorsum to secure the wings and legs.

Restriction of the movement of the sternum and thoracic muscles due to overexuberant physical restraint, and dorsal and ventral recumbency are often reported to lead to hypoventilation (Curro 1998; Forbes 1999; Heard 1997; Jaensch et al. 2002; King & Payne 1964; Pettifer et al. 2002) It has been hypothesized that dorsally-recumbent patients have their air sacs and lung openings (ostia) compressed by the internal organs, which may be exacerbated by increasing anesthetic duration (King & Payne 1962, 1964). This hypothesis has led to recommendations to avoid dorsal recumbency in anesthetized birds when possible. Until recently, the only studies of this effect have been in the domestic chicken. The chicken has a very well-developed pectoral musculature that may compress the thorax during respiration in dorsal recumbency more so than lighter-bodied birds. Chickens and other domestic poultry also usually have large amounts of intracoelomic fat that reduces air sac volume. It was shown in a recent evaluation of air sac and lung volume in red-tailed hawks that even birds with significant coelomic fat did not demonstrate a reduction in lung volume, only air sac volume (Malka et al. 2009). Additionally, chickens have a somewhat different gas exchange anatomy that may affect ventilation in dorsal recumbency. While the domestic chicken is not the most appropriate model for flying birds, the recommendation for avoiding dorsal recumbency is also supported by clinical experience (Curro 1998; King & Payne 1964). In a recent study evaluating the effects of positioning on spontaneous ventilation in red-tailed hawks during isoflurane anesthesia, no significant differences were found in minute ventilation, heart or respiratory rates, or arterial blood pressures when birds were placed in either dorsal or lateral recumbency. The PaO_2 was significantly higher in dorsal recumbency (M.G. Hawkins, S.M. Malka, P.J. Pascoe, unpub. data). Any adverse effect of positioning appears to be negated by assisted ventilation.

Preoxygenation

In mammals, the functional residual capacity (FRC) acts to buffer changes in oxygen partial pressures during the respiratory cycle. In the past, it has been suggested that there is little FRC in avian lungs and therefore birds have little mechanism for blunting the effects of apnea on PaO_2 and $PaCO_2$ (McLelland 1989). However, there is a significant reservoir of gas in the air sacs and unidirectional flow of gases through the avian lung may minimize the potential for significant fluctuations in blood gas tensions during short periods of apnea. For example, in chickens, 8 minutes of apnea after breathing 100% oxygen resulted in oxygen blood gas tensions that decreased at a similar rate to that seen in mammals (P.J. Pascoe, unpub. obs.). Having a high concentration gradient (>95% O_2) and small distances to traverse allows for diffusion of oxygen through the lungs as the oxygen is being removed by the blood, accounting for this delayed onset of hypoxia. In a bird breathing room air there is a very small diffusion gradient and because oxygen consumption is higher in birds than mammals any periods of apnea, however brief, must be treated immediately. Normal blood gas values for selected species are presented in Table 15.2. It should be noted that these values are obtained in awake birds on room air. Over a range of 19 species, PaO_2, $PaCO_2$, and pH were noted to average ($\pm$ standard deviation) 91.61($\pm$ 8.5), 31.43 ($\pm$ 4.2), and 7.50 ($\pm$ 0.03), respectively (Powell & Whittow 2000). From these data it is clear birds tend to have $PaCO_2$ tensions that are lower than in many mammals.

The response of birds to hypoxia has been studied in awake animals but not in birds under inhalant anesthesia. Typically, birds do not increase respiratory rate in the early stages of hypoxia but increase minute ventilation by increasing tidal volume (Butler & Taylor 1974). As hypoxia progresses respiratory rate will increase, and oxygen consumption, body temperature, and blood pressure may decrease. Heart rate starts to increase early in hypoxia, but

Table 15.2 Injectable pre-medication/emergency, sedative, tranquilizer, and anesthetic drugs used in birds.

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
Benzodiazepines					
Diazepam	0.2–2.0	IM, IV	Most species Premedication, sedation, anticonvulsant, appetite stimulant	IM administration may cause severe muscle irritation and absorption may be delayed 0.25–0.5 mg/kg has been used as an appetite stimulant and to improve acceptance to novel captive diets for raptors and wild passerines Reversal with flumazenil	Abou-Madi (2001); Samour (2000) Clyde & Paul-Murphy (1994); Suarez (1993) Massey (2003)
	2.5–4.0	PO	Most species/sedation		Ritchie et al. (1994)
	7.3–8.0	IN	Canaries	Dose divided into each nare and given slowly. Dorsal recumbency for ~35 minutes.	Vesal & Eskandari (2006); Vesal & Zare (2006)
Midazolam				In larger macaws the author's have noted regurgitation after doses of >0.3–0.5 mg/kg IM. Water soluble; does not cause muscle irritation with IM use. Reversal with flumazenil	
	0.1–2.0	IM, IV	Most species/ premedication, sedation, appetite stimulant	IM onset 5–15 minutes. Higher dosages may cause profound sedation.	Abou-Madi (2001); Day & Roge (1996)
	2.0–6.0	IM	Quail, sedation	High dosages give greatest sedation without cardiopulmonary effects, but adequate sedation also found with lower dosages, just shorter duration of sedation.	Day & Roge (1996)
	2.0	IM	Canada geese/ sedation	For 15–20 minutes	Valverde et al. (1990)
	2.0	IN	Hispaniolan Amazon parrots	Mild-to-moderate sedation in 3 minutes; reduced vocalizations, struggling and defensive behaviors for 15 minutes; reversed with IN flumazenil	Mans et al. (2012, 2010)
	7.3–8.0	IN	Canaries, ring-necked parakeets	Dose divided into each nare and given slowly. Dorsal recumbency for approx. 17 minutes. Flumazenil reduced time to recovery.	Vesal & Eskandari (2006); Vesal & Zare (2006)
Flumazenil				Benzodiazepine reversal agent	
	0.02–0.10	IM, IV	Most species		Abou-Madi (2001); Day & Roge (1996); Machin & Caulkett (1998a,b)
	0.05	IN	Mallard ducks		Machin & Caulkett (1998b)
	0.13–0.15	IN	Canaries, ring-necked parakeets	Dose divided evenly between nares and given slowly	Vesal & Eskandari (2006); Vesal & Zare (2006)

(*Continued*)

Table 15.2 (Continued)

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
α-2 Adrenergic agonists					
Detomidine	0.3	IM	Rock partridges	Marked sedation/significant decrease in HR, RR, decrease in cloacal temperature, prolonged recoveries (260 ± 18 minutes)	Uzun et al. (2006)
	12	IN	Ring-necked parakeets	Dose divided into each nare and given slowly; sedation <3 minutes but did not allow dorsal recumbency or manipulation; reversal with atipamezole significantly reduced time to recovery	Vesal & Eskandari (2006)
	12–15	IN	Canaries	Dose divided into each nare and given slowly; higher dose prolonged sedation but could not place in dorsal recumbency; prolonged duration of effect (258 ± 2 minutes) but completely reversed with yohimbine IN	Vesal & Zare (2006)
Dexmedetomidine				Use half the recommended dose of medetomidine Reversal with same dose of atipamezole	
	0.025	IM	Common buzzards	Adequate restraint to prevent reaction to handling, but did not allow for intubation. Completely reversed with atipamezole. Mean times to loss of righting reflex = 3.5 ± 1 minutes in common buzzards. No arrhythmias noted on ECG. No excitement or major adverse effects observed in either group.	Santangelo et al. (2009)
	0.075	IM	Common kestrals	Adequate restraint to prevent reaction to handling, but did not allow for intubation. Completely reversed with atipamezole. Mean times to loss of righting reflex = 7 ± 1.2 minutes in common kestrels	Santangelo et al. (2009)
Medetomidine	0.01–0.035	IM	Pigeon, yellow-crowned Amazon	0.08–2 mg/kg IM associated with inadequate sedation. Profound respiratory depression may occur. Much higher dosages appear to be required in some avian species when compared with mammals.	Clyde & Paul-Murphy (1994); Pollock et al. (2001); Sandmeier (2000)
	0.025–0.035	PO	Chickens	Sedation	James et al. (1999)}

Table 15.2 (Continued)

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
Xylazine				Not recommended by itself for tranquilization and seldom used in pet birds due to adverse effects – excitement, convulsions, bradycardia, arrhythmias, bradypnea, hypoxemia, hypercarbia, death when used alone; most useful in ratites	
	1.0–10.0	IM, IV	Most species, tranquilization in combination with ketamine for anesthesia	Adequate sedation often with <4 mg/kg, in smaller psittacines dosages up to 10 mg/kg may be required	Carpenter (2000); Clyde & Paul-Murphy (1994); Huckabee (2000); Ludders, Rode, Mitchell, et al. (1989); Samour (2000)
α-2 Adrenergic antagonists					
Atipamezole				Alpha-2 adrenergic antagonist; 1:1 volume reversal of dexmedetomidine/medetomidine is the general rule; although the same effects would be expected as with medetomidine, there are no data available on the efficacy of atipamezole reversal of dexmedetomidine in birds	
	0.25–0.5	IM	Psittacines, pigeons, raptors, geese	Righting reflex regained 2–10 minutes after administration	Machin & Caulkett (1998b); Pollock et al. (2001); Samour (2000); Santangelo et al. (2009)
	1.3–1.6	IV	Chickens		James et al. (1999)}
	0.18–0.28	IV	Mallard ducks		Machin & Caulkett (1998b)
	6.0	IN	Ring-necked parakeets	Dose divided evenly between nares and given slowly, significantly reduced recumbency time after detomidine administration	Vesal & Eskandari (2006)
Yohimbine	0.1–0.2	IV	Psittacines, raptors, waterfowl, ratites	Reversal for xylazine	Carpenter (2000); Heard (1997); Jensen et al. (1992); Keffen (1993); Raath et al. (1992); Samour (2000)
	1.0	IV	Most species, including psittacines, guinea fowl		Teare (1987)

(*Continued*)

Table 15.2 (Continued)

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
	0.1–0.2	IM, IV	Raptors		Huckabee (2000)
	0.11–0.275	IM	Budgerigars		Heaton & Brauth (1992)
	0.1–1.0	IM	Most species		Abou-Madi (2001)
Dissociative Anesthetics					
Alfaxalone	20–30	IM, SC	Small birds (e.g. budgerigars, finches, quaker parrots)	Addition of midazolam or butorphanol to alfaxalone hastened induction but prolonged anesthesia time and recovery	Perrin et al. (2017); Romano et al. (2020)
	10	IM	Pigeons	Alfaxalone was administered with xylazine (10 mg/kg and medetomidine 0.2 mg/kg)	Susanti et al. (2019)
	2	IV	Flamingos	Induction and recovery were shorter and smoother than when isoflurane was used alone	Villaverde-Morcillo et al. (2014)
Ketamine				Usually combined with an alpha-2 adrenergic or with a benzodiazepine to improve relaxation, depth of anesthesia Not recommended as a sole anesthetic agent due to reports of poor muscle relaxation, myoclonic contractions, opisthotonus and violent recoveries	
	20–50	SC, IM, IV	Psittacines, pigeons, ratites, poultry, waterfowl Restraint 30–60 minutes	Smaller species require a higher dose, large birds tend to recover more slowly	Beynon et al. (1996); Fowler (1995); Heard (1988, 1997); Jensen et al. (1992); Lawton 1996); Samour (2000)
	50	IO	Pigeons	Provided effective analgesia	Kamiloglu et al. (2008)
	5–30	PO	In bait, for ducks		Forbes (1991, 1999)
	50–100	PO	In bait for raptors		Samour (2000)
Ketamine/ diazepam	(K)5–30 + (D)0.5–2.0	(K)IM, (D)IM, IV	Most species	Ketamine should be given 5–15 minutes after diazepam for adequate muscle relaxation.	
	(K)20 + (D)1.0	IV	Toucans	For short procedures (15–20 minutes), give slowly.	Cubas (2001)
	(K) 75 + (D) 2.5	(K)IM, (D)IV	White leghorn cockerels	Diazepam administered 5 minutes before ketamine for typhlectomy; smooth induction/recovery, some limb contracture, hypothermia, hypoxia, hypercapnia	Maiti et al. (2006)

Table 15.2 (Continued)

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
Ketamine/ midazolam	(K)10–40 + (M)0.2–2.0	SC, IM	Most species, including psittacines		Mandelker (1988); Marx & Roston (1996)
	(K)40–50 + (M)3.65	IN	ring-necked parakeets	Dose divided into each nare and given slowly; onset of action <3 minutes, dorsal recumbency for 71 ± 47 minutes, recovery times reduced with flumazenil IN	Vesal & Eskandari (2006)
	(K) 50 + (M) 2.0	(K)IV, (M) IM	White leghorn cockerels	Midazolam administered 5 minutes before ketamine for typhlectomy; hypoxia, hypercapnia, torticollis, dyspnea, salivation noted; prolonged recovery (92–105 minutes)	Maiti et al. (2006)
Ketamine/ xylazine	(K)25 + (X)3.0 + (D)4.0	K, X, D-IM	Roosters	Use with caution: significant decreases in HR, RR, cloacal temperatures and prolonged recoveries (up to 4 hours)	Mostachio et al. (2008)
	(K)15 + (X)2.5 + (M)0.3	K, X, M-IM	Guinea fowl	Midazolam improved anesthetic quality	Ajadi et al. (2009)
Propofol	2.9–4.7 (induction); 0.4–0.55 (mg/kg/min) (maintenance)	IV	Red-tailed hawks and great horned owls	Minimal blood pressure effects, but ventilation was significantly reduced. Prolonged recoveries with moderate-to-severe excitatory CNS signs may occur in these species with an infusion	Hawkins et al. (2003)
	5.0 (induction); 1.0 (mg/kg/min) (maintenance)	IV	Hispaniolan Amazon parrots	Recovery times (15.4 ± 15.2 minutes) were prolonged when compared with isoflurane; 6/10 birds had agitated recoveries. Light anesthetic plane in 8/10 birds	Langlois et al. (2003)
	5.0 (induction); 0.5 (mg/kg/min) (maintenance)	IV	Wild turkeys		Schumacher et al. (1997)
	8–10 (induction); 1–4 as bolus PRM	IV	Mallard ducks, canvasback ducks		Machin & Caulkett (1998a, 1999)
	8.0 (induction); 0.8–0.9 (mg/kg/min) (maintenance)	IV CRI	Mute swans	Smooth inductions, minimal excitation on recovery	Muller et al. (2011)

D, diazepam; ECG, electrocardiogram; HR, Heart rate; IM, intramuscular; IN, intranasal; IO, intraosseous; IV, intravenous; K, ketamine; M, midazolam; PO, Per OS; RR, respiration rate; SC, subcutaneous; X, xylazine.
Note that these are suggested dosages based on published information and the author's clinical experience. Species and individual variation in response to a given drug can be uncertain so the dosage should be adjusted depending on the clinical response of the animal.

bradycardia ensues during severe hypoxia. This hyperventilation, associated with hypoxia, can decrease $PaCO_2$ but birds can tolerate values <10 mmHg because cerebral blood flow is maintained (Bickler 1992). The responses to hypoxia vary between different species, especially in those adapted to high altitude (Lague et al. 2017).

Preoxygenation is performed whenever possible and when hypoxemia may occur (i.e., upper respiratory obstruction, cardiac, pulmonary or air sac disease). It replaces nitrogen in the respiratory system and can produce an oxygen reservoir 4–5 times normal in the air sacs. The benefits are achieved in ≤1 minute of high inspired oxygen concentration in the healthy bird but may take ≥5 minutes in a bird with compromised respiratory function. Preoxygenation is accomplished with an oxygen cage or an induction chamber in the unrestrained bird, or a facemask in the physically restrained bird. Levels rise more slowly in an unprimed oxygen cage or induction chamber than in a tight-fitting facemask with minimal deadspace. If the bird is allowed to breathe room air the parabronchial oxygen levels can fall precipitously if the bird becomes apneic.

Mask or Chamber Induction

Inhalant anesthesia induction is often performed with either a mask or induction chamber. Before using a mask check the bird is able to breath through its nose when its mouth (beak) is closed. Commercially available veterinary inhalant masks can be used for many species. However, differences in beak anatomy and location of nares require unique masks to be formed from syringe cases, plastic soda bottles, or other materials. The mask is as small as possible, and the entire head of the patient is placed inside the mask. To minimize waste gas release, a seal is developed using a disposable latex glove placed over the mask with a central hole cut for the bird's neck. Although some have suggested that this seal can be used for positive pressure ventilation, it is not recommended by these authors. In addition to increased waste gas release, this technique will introduce gas into the gastrointestinal tract.

Facemask induction in some birds (i.e., waterfowl) is associated with apnea and bradycardia that may last for 3–5 minutes (Ludders & Matthews 1996). This response may even occur from placing a facemask snugly onto the face and beak without inhalant anesthetic. This response is a stress response that appears to be mediated by stimulation of trigeminal nerve receptors in the beak and nares of diving ducks (Butler 1988; Jones et al. 1988; Woakes 1988). Premedication with a benzodiazepine may avert this response. If this response occurs, discontinue inhalation anesthesia, remove the mask, and provide 100% oxygen until bradycardia resolves.

Commercially available induction chambers sized for mice up to small dogs can be utilized for birds as small as hummingbirds. The advantages of these appropriately sized chambers are reduced waste gas and shorter induction times. In stressed birds, the chamber is covered with a towel to darken it. Alternatively, an animal carrier or the front of a hospital cage is sealed with a plastic bag and inhalant anesthetic administered for induction of large or stressed patients. Disadvantages of induction chambers include the inability to auscult the patient, gas pollution when the chamber is opened, and trauma due to flapping during the excitement phase of anesthesia. The latter is reduced by padding the induction chamber and minimizing chamber size to reduce movement. Gas flow rates are adjusted to chamber size to provide an optimum rate of rise of the anesthetic concentration. This might be as low as 0.5 L/min for a 1-L chamber up to 15 L/min for a 60-L chamber. The efficiency of the respiratory system makes high inhalant induction concentrations unnecessary, for example isoflurane vaporizer settings rarely need exceed 3%. The bird is promptly removed after the righting reflex is lost. The final phase of the induction is accomplished using a mask to facilitate monitoring.

Vascular Support

During anesthesia or emergencies IV or intraosseous (IO) fluids are used to provide replacement fluids. Sites for IV catheters include the basilic (ulnar), medial metatarsal, or jugular veins (Fig. 15.4). Small bore over-the-needle catheters (≤24 g) are used. If blood is to be repetitively collected from the catheter, it should be placed in either the jugular (small patients) or a large peripheral vessel. The increased fragility of avian blood vessels, the lack of soft tissue support, and patient temperament make catheter maintenance difficult. The catheter site is gently plucked and aseptically prepared. Catheters are secured with a bandage tape butterfly and sutured with an everting mattress pattern. The catheter site is bandaged for additional security. Complications of long-term, indwelling catheterization include infection and possibly fatal hemorrhage. Jugular catheters require 24-hour monitoring because fatal hemorrhage can occur if the bird pulls or chews on the catheter and damages the vessel.

IO catheterization is used in smaller patients or during cardiovascular collapse (Aguilar et al. 1993; Lamberski & Daniel 1992; Ritchie et al. 1990; Valverde et al. 1993). IO catheter maintenance is easier to achieve due to stability in the medullary cavity. Products that can be utilized include 18–24-gauge, 2–5-cm spinal needles or 18–25-gauge, 2-cm hypodermic needles. The length of the catheter should be long enough to extend a third to a quarter of the length of



Figure 15.4 Sites for intravenous (IV) catheters include the ulnar (basilic) vein (a), medial metatarsal vein (b) or jugular vein. Small bore over-the-needle catheters (24 gauge or smaller) are most often necessary for avian patients.

the medullary cavity. A wire stylet may be necessary with hypodermic needles to reduce the potential for a bone core. The sites most often used include the distal ulna and proximal tibiotarsus. Pneumatic bones (i.e., the humerus and femur) are avoided. Feathers are gently plucked and the site surgically prepared. Wearing gloves, the sterile IO catheter is positioned at the center of the cnemial crest of the tibiotarsus or slightly ventral to the dorsal condyle of the distal ulna and parallel to the bone. The bone is held firmly with one hand while the other applies firm pressure combined with slight rotation (Fig. 15.5). Once the cortex is penetrated, the catheter should advance easily with little resistance. If there is further resistance, the opposite cortex has most likely been penetrated. The cannula is flushed with heparinized saline and should flow easily. Fluids will be seen flowing through the basilic vein when the cannula is correctly placed in the distal ulna. The insertion site is covered with antibiotic ointment and the cannula secured with a bandage tape butterfly at the exit point in the skin and sutured. A bandage can be placed over the cannula site for additional security to prevent trauma or damage to the catheter. Although IO catheters are reported to remain patent for 72 hours without flushing (Ritchie et al. 1990), it is recommended that the catheter be gently flushed with heparinized saline twice daily.

Complications associated with IO catheterization include penetration of both cortices, failure to properly enter the medullary cavity, and extravasation of fluids with associated pain. Extravasation has been observed even with proper catheter placement after 1–2 days of use (Steinohrt 1999). IO catheterization is contraindicated in septic patients and those with metabolic bone disease. Osteomyelitis may occur due to duration or placement of the IO catheter (Steinohrt 1999). Administration of alkaline or hypertonic solutions may also contribute to osteomyelitis and will cause pain and transient microscopic changes in the bone marrow (Lamberski & Daniel 1992; Ritchie et al. 1990). These solutions are therefore diluted prior to administration and the catheter is flushed with heparinized saline after any drug injection.

Crystalloid fluids (e.g., 0.9% NaCl [Baxter, Deerfield, IL, USA], lactated Ringer's [Abbott Laboratories, North Chicago, IL, USA}, Normosol-R [CEVA Laboratories, Overland Park, KS, USA], and Plasmalyte-A [Baxter]) are commonly used for IV volume support, maintenance, and rehydration. Fluids are warmed to body temperature (38–39°C) to minimize hypothermia.

Fluid rates of 3–10 mL/kg/h are recommended for healthy anesthetized patients. This rate is based on studies in human patients. While this is a starting point, it is recognized rates in very small patients may need to be considerably higher, but caution should be exercised to not fluid overload small patients. Each patient is assessed individually for their fluid needs. Fluid boluses of 10–20 mL/kg over 5–7 minutes are well tolerated (Abou-Madi & Kollias 1992). For severe hemorrhage whole-blood transfusion (volume for volume) should be provided. If this is not available, it has been recommended to provide crystalloid fluids at three times the volume of blood loss. However, this recommendation is based on mammals

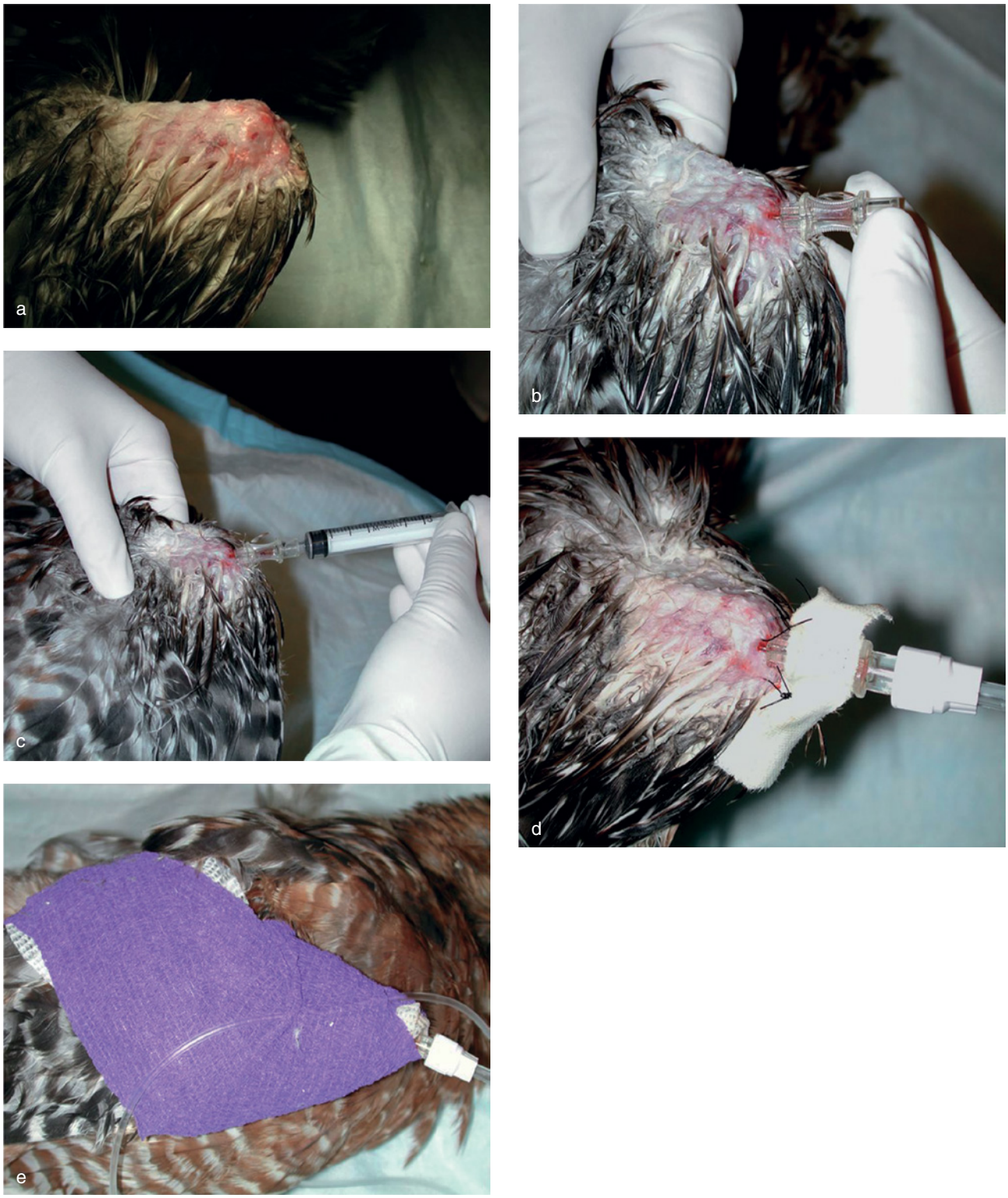


Figure 15.5 Intraosseous (IO) catheter placement in the distal ulna of a bird. Strict asepsis should be observed when placing the catheter. Feathers over the site should be gently plucked and the site should be surgically prepared (a). Wearing sterile gloves, the sterile catheter is positioned slightly ventral to the dorsal condyle of the distal ulna and parallel to the bone (b). The bone is held firmly with one hand while the hand other applies firm pressure combined with slight rotation (c). The cannula should be flushed with heparinized saline and should flow easily (d). The insertion site should be covered with an antibiotic ointment and the cannula should be secured with a bandage tape butterfly at the exit point in the skin and suture (d). A bandage can be placed over the cannula site for additional security and to prevent possible trauma or damage to the catheter (e).

where the interstitial space is twice the vascular volume. In birds, the interstitial space is four times the plasma volume (Skadhauge 1981). Replacement fluid volumes may need to be greater than three times blood loss. Dextrose solutions are added to fluids for treatment of hypoglycemia. Parenteral dextrose use is minimized to prevent compartmental shifts in electrolytes and water leading to hypovolemia (Abou-Madi & Kollias 1992).

Hypertonic fluids (e.g., 7.5% NaCl) are used to expand intravascular volume during resuscitation following acute severe hemorrhage. Hypertonic saline has been evaluated in birds primarily for studying renal sodium excretion and the role of osmotic thirst in the control of normal drinking. In several studies, plasma osmolality increased after bolus infusion (Leary et al. 1998; Yeomans & Savory 1988). The major benefit of hypertonic saline is intravascular volume expansion at a quarter of the volume of isotonic solutions. The mammalian dosage (4 mL/kg) given over 10 minutes is used in birds. However, due to osmotic diuresis and rapid redistribution of sodium cations the intravascular effect is transient (<30 minutes) and additional fluid therapy with a crystalloid or colloid must be used. Hypertonic fluids are contraindicated in dehydration, hypernatremia, and head trauma with intracranial hemorrhage. The sustained use of hypertonic saline is not recommended because hypernatremia and hyperchloremic acidemia, increased bleeding, and exacerbation of underlying cardiac and pulmonary disease due to fluid overload may occur.

Small patient size and species diversity often preclude the use of natural colloids such as homologous or heterologous plasma. The indications for the use of synthetic colloids (e.g., hydroxyethyl starch solutions) are the same as hypertonic saline although the benefits last longer. All are cleared through the kidneys, so they are used with caution in patients with cardiac or renal impairment. They do not provide albumin, thrombocytes, or coagulation factors. Potential adverse effects include anaphylactoid reactions and blood coagulation abnormalities. In critically ill raptors boluses of hetastarch (10–15 mL/kg 6%, every 8 hours) for ≤four treatments) were well tolerated (Stone & Redig 1994). It is suggested that the dose should not exceed ≤20 mL/kg/day.

Reported circulating blood volume percentage based on bodyweight varies considerably (Campbell et al. 1994): 5% in ring-necked pheasants (Campbell et al. 1994), 7.5 ± 1.5% in quail (Takei & Hatakeyma 1987), 16.3–20.3% in the racing pigeon (Campbell et al. 1994), 10.6 ± 2.9% in the galah (Jaensch & Raidal 1998), and 5.4 ± 10.5% and 13.1 ± 2.3% in two strains of chickens (Makinde et al. 1986). Hemorrhage is better tolerated than in mammals. However, when severe (>30% blood volume) or the PCV <20%, whole-blood transfusion is indicated. Heterologous blood cells (e.g., from pigeon or chicken) transfused into parrots last only 12 hours, causing a significant metabolic drain on the recipient as the body utilizes energy to destroy the foreign cells (Finnegan et al. 1997; Sandmeier et al. 1994). The half-lives of homologous and autologous blood transfusions were 8.5 and 9.9 days in conures (*Aratinga* spp.; Degernes & Crosier 1999), 12.5 and 12.2 days in cockatiels (*Nymphicus hollandicus*; Degernes et al. 1999), and 7.1 and 26.8 days in pigeons (Sandmeier et al. 1994), respectively. In pigeons, PCV and total solids were elevated ≥102 hours following homologous transfusion (Finnegan et al. 1997).

The storage of whole blood or blood products has been little studied to date (Morrisey et al. 1997) and transfusions with fresh whole blood are recommended. The anticoagulants citrate phosphate dextrose adenine and acid citrate dextrose are used most at a ratio of 1:9 whole blood:anticoagulant. If given rapidly the citrate can decrease ionized calcium and decrease myocardial contractility. It may be necessary to give calcium gluconate or chloride to the patient to reverse this effect. Donors are screened for infectious diseases. A major/minor crossmatch is performed prior to transfusion. Sixty-six per cent of major crossmatches performed between different species were positive for agglutination or hemolysis whereas between the same species they were all negative (Stauber et al. 1996). Mammalian protocols are presently followed for blood collection and administration. Pediatric blood filters have been evaluated for their ability to cause hemolysis in chicken blood and an 18-μM filter did not cause hemolysis compared to a nonfiltered control (Jankowski & Nevarez 2010).

Standard micro-drip fluid sets used in small animal veterinary practice (60 drops/mL) will not allow appropriate infusion rates in very small patients. Instead, fluid infusion and syringe pumps are used for accurate fluid administration (Fig. 15.6).

Routes of Drug Administration

Drugs can be administered orally in solid or liquid form or even gavaged into the crop. Any drug administered orally in a solid form (tablet or capsule) must be disintegrated and then dissolved before it can be absorbed. Most absorption occurs in the small intestine because of the high surface area and relatively neutral pH. Lipophilic drugs may be able to pass from the intestinal lumen to the blood by simple diffusion but there are enzymes present in the mucosal cells that can metabolize many drugs. These processes and those present in the liver contribute to the first-pass effect where the amount of drug reaching the systemic circulation may be considerably less than the amount absorbed due to intestinal or hepatic breakdown.

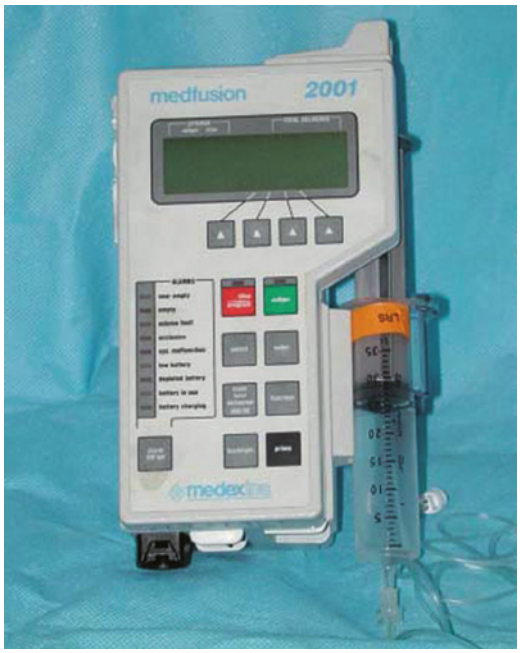


Figure 15.6 To provide accurate infusion rates for small avian patients, fluid infusion pumps and syringe pumps are required.

This can be modified by including another drug that inhibits the specific metabolism of the first drug (e.g., drugs that inhibit cytochrome P450 enzymes). The intestinal mucosa also contains transporters, which can enhance the absorption of a drug, as well as proteins that will eject drugs from the cell back into the lumen. The transporter processes may be saturable such that they limit the uptake of the drug beyond a certain dose and the ejector systems may be overwhelmed by excess drug so that it gets absorbed when it would normally be removed. Inflammatory processes may alter the oral absorption of drugs by damaging the normal barriers. In general, drugs administered orally will take longer to reach peak effect and the dose may need to be altered to account for the bioavailability of that drug.

Oral transmucosal administration is difficult in most birds because it is much more likely that the bird will swallow the drug before it is taken up through the mucosa. However, a study evaluating the oral transmucosal use of pentobarbital for euthanasia in wild birds showed uptake is quite successful (Gardhouse et al. 2021).

Bird skin is much thinner than the skin in mammals and there is often less of a subdermal layer. The most common SC injection site used in birds is in the inguinal area, where there is more redundant skin than elsewhere on the avian body. Do not attempt to use the patagium as a SC site in a flighted bird as this can lead to inflammation and potential contracture of the patagium. There is little redundant skin dorsally and there are anecdotal reports of the needle being advanced too far and intra-spinal cord or pulmonary injection occurring instead. The uptake of a drug from SC administration will depend on its lipid solubility, the osmolality of the solution, and its effects on circulation. A drug like buprenorphine, which is highly lipid soluble, may be absorbed into the SC fat and not be taken up very rapidly. This can be used to advantage to provide a prolonged uptake with buprenorphine when injected subcutaneously in a concentrated form (Simbadol). Diazepam is dissolved in propylene glycol and the solution has a very high osmolality (>9000 mosm/L), making absorption less likely because the solution tends to attract water from the body. Alpha-2 agonists are vasoconstrictors and so SC injection of these drugs reduces uptake by decreasing the blood supply to that area.

Intramuscular (IM) injection tends to provide a more rapid onset than SC because of the greater blood supply, but the same limitations apply regarding osmolality (see above). The most common site used in most birds is the pectoral muscles, but these muscles are much smaller in flightless birds and so care must be taken not to penetrate down to the keel. There is a vascular sinus close to the keel, making it good practice to always inject in the center of the muscle and aspirate before injecting a drug to avoid intravascular injection. The thigh muscles are used in larger birds but concerns have been raised that drugs entering the circulation from this area could be removed by the renal portal system. To date none of the studies that have examined this have shown altered pharmacokinetics compared with pectoral muscle injections (Carvalho et al. 2007).

IO access is used in small birds where IV injections are difficult. Drugs injected by this route will enter the circulation as if they had been injected IV although the onset may be slightly slower (Bakhshi et al. 2019; Valverde et al. 1993). Drugs should not be highly acidic or alkaline because they might damage the bone marrow. This route has been used to maintain anesthesia with propofol (Guimarães et al. 2006).

IV injection is more difficult in birds because the vessels are often very small and it can be difficult to restrain a bird safely and effectively for IV injection. The median ulnar vein (where it crosses the radius and ulna) and the median metatarsal vein are used for injection most commonly during anesthetic events.

Intranasal (IN) administration has been used extensively with the expectation that there will be transmucosal absorption and even transfer into the brain through the cribriform plate. This has been effective with several sedatives and anesthetics, but it is essential that the volume of drug is limited in order not to drown the bird. Drugs that are very acidic (e.g., ketamine) may be quite painful if administered by this route.

To the authors' knowledge, there have not been any studies reporting intracloacal uptake of sedative, analgesic, or anesthetic drugs in birds. Several poultry vaccines have been effectively absorbed via this method (Abaza et al. 2020) whereas poor intracloacal uptake was shown for some anesthetic and sedative drugs in chelonians (Scarabelli & Di Girolamo 2022).

Intraperitoneal (IP) injection has been used in birds in a laboratory setting for several agents. The uptake of drugs from this site can be quite rapid but it is a risky method of administration because of the abdominal air sacs. It is essential when using this method to aspirate before injection to ensure that neither air nor blood are withdrawn.

Preanesthetics

Parasympatholytics

Several authors question the necessity of routine premedication with parasympatholytics in birds. Atropine and glycopyrrolate reduce mucus production and plug formation, but increase viscosity (Ludders & Matthews 1996). Additionally, some practitioners avoid using anticholinergics in birds because they increase heart rate, cardiac work, and myocardial oxygen demand. Therefore, the use of these agents should be weighed against their potential adverse effects as premedications.

Sedatives and Tranquilizers

Sedatives and tranquilizers are used to decrease anxiety and fear during induction, but most tranquilizers lack analgesia. Additionally, most require injection and the handling and restraint may be as much as required for anesthetic induction. The merits of premedication must be weighed against this additional stress in birds.

Benzodiazepines

Diazepam may cause excitement, tachycardia, and tachypnea in birds if given intravenously. Uptake of diazepam from IM or SC injection is erratic but effective by the IN route (Bigham & Zamani Moghaddam 2013; Sadegh 2013; Vesal & Zare 2006). Midazolam (0.2–2.0 mg/kg IM) has been used as a sole sedative for minor, nonpainful procedures (i.e., radiographs) (Valverde et al. 1990). Low doses in this range are most often used for preanesthetic sedation. In pigeons, very high doses of midazolam (14–16 mg/kg IM) induced profound sedation and reduced isoflurane minimum anesthetic concentration (MAC) by approximately a third (Smith et al. 1993; Smith & Muir 1992). IN midazolam (5 mg/kg) caused sedation but not loss of righting reflex (Hornak et al. 2015). The MAC of isoflurane was decreased by 19% and 28% by IM midazolam at 1 and 2 mg/kg, respectively, in Quaker parrots (Zaheer et al. 2020). In quail midazolam (2–6 mg/kg IM) produced chemical restraint and 40–60 minutes of sedation at higher doses (Day & Roge 1996). Sedation with midazolam shortly after capture increased the postsurgical survival of female surf scoters (*Melanitta perspicillata*) surgically implanted with intracoelomic transmitters (Net et al. 2019). A study of 17 psitaccids showed that the combination of midazolam (0.5 mg/kg) and butorphanol (1 mg/kg) decreased the time to intubation with isoflurane, improved the quality of induction, and decreased the required concentration of isoflurane during the procedure by about 30% (Kubiak et al. 2016). In cockatiels midazolam at 3 mg/kg with or without butorphanol induced sedation and the combination was more effective than midazolam alone (Doss et al. 2018).

IN administration of midazolam (0.5 mg/kg) has been used by clinicians to facilitate physical examination, beak trimming, and sample collection in many birds. In ring-necked parakeets (*Psittacus krameri*) midazolam administered intranasally alone or in combination with ketamine produced sedation that allowed dorsal recumbency and adequate sedation for minor procedures (Vesal & Eskandari 2006). In blue-fronted and orange-winged Amazon parrots, IN midazolam (2 mg/kg) resulted in rapid onset (5 minutes) and about 25 minutes of sedation in most birds, but three out of 10 blue-fronted parrots had no sedation (Schaffer et al. 2017). Another group using the same dose of midazolam intranasally in Hispaniolan Amazon parrots found that birds were easier to capture and handle (Mans et al. 2012). In budgerigars (13.2 mg/kg) and finches (13 mg/kg), IN midazolam induced a rapid loss of righting reflex (1–1.3 minutes) and sedation lasting 30–60 minutes (Bigham & Zamani Moghaddam 2013; Sadegh 2013). Sedation duration is significantly reduced after IN flumazenil administration (Mans et al. 2012). The authors recommend titrating the dose to avoid the reversal of the beneficial anxiolysis, sedation, and muscle relaxation.

Midazolam IM did not produce major alterations in cardiopulmonary function in Canada geese (Valverde et al. 1990), quail (Day & Roge 1996), and racing pigeons (Smith et al. 1993; Smith & Muir 1992). Midazolam/ketamine IV produced anesthesia with full recovery in 23 minutes (Machin & Caulkett 1998b). Midazolam reduced mean corticosterone and median lactate concentrations in spectacled eiders (*Somateria fischeri*) by approximately 30%, but blood pH was reduced, likely resulting from sedative-induced respiratory depression. This was easily treated with intubation, mechanical ventilation, and administration of flumazenil. This drug

has been associated with decreased gastrointestinal transit times in cockatiels at 6 mg/kg (Martel et al. 2018), which could result in regurgitation. In pigeons a concentrated formulation of midazolam (50 mg/mL; Zoo-Pharm,Inc. Windsor, CO, USA) resulted in substantially less injection volume when compared with the standard midazolam concentration for IM injection and exhibited the same efficacy, but the study did not evaluate adverse effects such as muscle bruising after injection (Martel et al. 2021).

Alpha-2 Adrenergic Agonists

Xylazine and medetomidine are the most reported alpha-2 adrenergic agonists in birds. However, as the use of dexmedetomidine supplants that of medetomidine, more information on the use of this agent will become available. This drug is the dextro-enantiomer of medetomidine and has twice the potency of the racemic mixture, medetomidine, since levomedetomidine has no action at alpha-2 receptors. To aid dosing for practitioners, dexmedetomidine (0.5 mg/mL) is supplied at half the concentration of medetomidine (1.0 mg/mL) and dosing charts are available for dogs and cats. One study has examined the use of dexmedetomidine in two raptor species at a dose of approximately 25 μg/kg for common buzzards (*Buteo buteo*) and 75 μg/kg for common kestrels (*Falcon tinnunculs*) (Santangelo et al. 2009). The authors noted loss of righting in both species within approximately 8 minutes and sedation was sufficient to allow handling. In the study above, atipamezole was used for reversal at a total dose of 250 μg and provided rapid reversal of sedation. It should be noted atropine was administered in conjunction with dexmedetomidine in this study, which has been reported to cause increases in mean arterial blood pressure, heart rate, and the occurrence of cardiac arrhythmias in dogs and is not recommended for coadministration with dexmedetomidine (Congdon et al. 2011). In pigeons a combination of midazolam (5 mg/kg) and dexmedetomidine (80 μg/kg) administered intranasally produced more profound sedation than midazolam alone but this was accompanied by bradycardia and a decrease in respiratory rate and body temperature (Hornak et al. 2015).

The major advantage of these agents is they can be reversed with atipamezole, yohimbine or tolazoline. Alpha-2 adrenergic agonists can have profound cardiopulmonary effects including respiratory depression, second-degree heart block, bradyarrhythmias, and increased sensitivity to catecholamine-induced cardiac arrhythmias (Altman 1980; Ludders 2001; Ludders & Matthews 1996; Machin & Caulkett 1998a; Maiti et al. 2006; Varner et al. 2004). When used alone at high doses, xylazine is associated with respiratory depression, excitement, and seizure-activity (Ludders 2001; Ludders & Matthews 1996; Machin & Caulkett 1998a; Varner et al. 2004) and is not recommended for sedation. In Pekin ducks xylazine produced significant respiratory depression resulting in hypoxemia and hypercapnia and behavioral changes (i.e., moving, paddling, and picking at their enclosures) that lasted ≤ 45 minutes (Ludders et al. 1989). In mallard ducks xylazine/ketamine/midazolam IV resulted in cyanotic membranes and apnea in three; two died and the surviving animal was reversed with atipamezole (Machin & Caulkett 1998b). Xylazine (10 mg/kg) in rock partridges produced profound sedation only 2–5 minutes post administration and marked hypoventilation, but did not produce a significant decrease in heart rate (Uzun et al. 2006). In roosters undergoing typhlectomy, xylazine (3 mg/kg) induced a loss of righting response in 3–4 minutes. When diazepam (4 mg/kg) and ketamine (25 mg/kg) were given subsequently, significant decreases in heart rate, respiratory rate, and cloacal temperature were observed. A lack of response to painful stimulus was maintained for approximately 1 hour (Mostachio et al. 2008). Xylazine was also evaluated in guinea fowl in combination with ketamine. The addition of midazolam to the combination appeared to improve the duration and quality of analgesic effect (Ajadi et al. 2009).

Much higher dosages of medetomidine appear to be required compared with mammals. In pigeons and yellow-crowned Amazon parrots, medetomidine (2 mg/kg IM) alone did not induce reliable sedation (Sandmeier 2000). Similarly, in pigeons medetomidine (0.2 mg/kg) alone produced only moderate sedation, but significant bradycardia and bradypnea (Pollock et al. 2001). Also in pigeons, a medetomidine (0.2 mg/kg), butorphanol, and ketamine combination produced profound sedation. However, significant bradycardia, bradypnea, and hypothermia were observed (Atalan et al. 2002). Arrhythmias in three out of eight pigeons resolved after atipamezole reversal.

In mallard ducks medetomidine/midazolam/ketamine provided anesthesia and analgesia for 30 minutes' duration when given IV, but not IM (Machin & Caulkett 1998b). Also in ducks, medetomidine/midazolam/ketamine IV produced respiratory depression, apnea, and acidemia; one of 12 died and three required assisted ventilation (Machin & Caulkett 1998a). Very high medetomidine dosages (≤10 mg/kg) in mallard ducks did not increase sedation over 0.2 mg/kg (Machin & Caulkett 1998b). One clinician reported seizures in canvasback ducks with medetomidine IV (N. Caulkett, pers. comm.).

Since medetomidine appears to require combination with other injectable drugs for reliable effect, the advantages of rapid and smooth reversal with atipamezole are negated. Although the mammalian dosage of atipamezole

(five times the medetomidine dose) has been shown to exhibit excellent reversal in some birds (Machin & Caulkett 1998a), a lower ratio (2.5 times) also produces effective reversal (Machin & Caulkett 1998b; Sandmeier 2000). Based on the many adverse effects and disadvantages reported for this class of drugs in birds, it is recommended they be used with great caution. It should also be noted that the doses provided in this chapter for medetomidine can be used at half the value if using dexmedetomidine. A potentially revolutionary peripheral alpha-2 antagonist, vatinoxan, has been studied recently in several mammal species that can reverse the peripheral cardiovascular effects without changing the central sedation (Einwaller et al. 2020; Honkavaara et al. 2020; Pypendop et al. 2019). With the advent of this new peripheral alpha-2 antagonist, new studies in birds using this antagonist directly with dexmedetomidine should be evaluated.

Injectable Anesthetics

There are several situations in which injectable anesthetics are preferable to inhalants. Surgeries involving the beak, mouth, glottis, or trachea are complicated by the presence of an endotracheal tube. Surgery within the coelomic cavity, respiratory system, or pneumatic bones exposes personnel to high levels of inhalant anesthetics. Injectable anesthetics are almost always associated with longer recoveries than inhalants (Mehmannavaz et al. 2015). Also, if it is possible, the injectable drug should be discontinued and replaced with an inhalant as soon as the procedure will allow. Injectable anesthetics are more commonly used in the field due to the ease of transport compared to inhalant anesthetic delivery equipment.

Many injectable drugs are highly variable in their effects between species and individuals (Machin & Caulkett 1998b; Samour et al. 1984). Some of these effects may include poor induction, inadequate muscle relaxation, cardiopulmonary depression, and prolonged or violent recoveries (Langlois et al. 2003; Ludders & Matthews 1996; Samour et al. 1984). Different delivery routes also affect efficacy and dosage. For example, in mallard ducks IM administration of many anesthetics is not effective, suggesting poor drug uptake from the pectoral musculature. Also, no effect was identified when evaluating many drugs given intranasally to mallard ducks (Machin & Caulkett 1998b). Elimination of injectable anesthetics depends on drug distribution, and hepatic and/or renal biotransformation and excretion (Paul-Murphy & Fialkowski 2001). Due to the potential for side effects, patients must be weighed accurately and monitored closely.

Dissociative Anesthetics

Ketamine alone is not recommended due to poor muscle relaxation, myoclonic contractions, opisthotonos, and violent recoveries. It is usually combined with an alpha-2 adrenergic agonist or benzodiazepine or both to improve relaxation and anesthetic depth (Muir 1988). Ketamine may produce convulsions, excitation, and salivation in vultures, but these signs are rarely observed in other species (Muir 1988; Salerno & van Tienhoven 1976). Ketamine/alpha-2 adrenergic and ketamine/benzodiazepine combinations are used for short procedures (i.e., physical examination, minimally painful diagnostics) or induction as part of balanced anesthesia (Boever & Wright 1975; Borzio 1973; Kolias & McLeish 1978a; Ludders, Rode, Mitchell, et al. 1989; Machin & Caulkett 1998b; McGrath et al. 1984; Raffe et al. 1993; Redig & Duke 1976; Vesal & Eskandari 2006).

IM administration of ketamine induces immobilization within 5–10 minutes and lasts for 5–20 minutes, with recovery in 40–100 minutes. These times are dependent on size, dose given, body temperature, and health status (Paul-Murphy & Fialkowski 2001). In mallard ducks midazolam/ketamine IV produced anesthesia with recovery in 23 minutes (Machin & Caulkett 1998b). In another group of ducks ketamine/xylazine (15/5 mg/kg) was compared with ketamine/xylazine/diazepam (KXD; 15/2.5/2.5 mg/kg) administered intramuscularly and the KXD combination produced a more rapid onset and a longer duration of effect (Ahmad et al. 2018). In chickens ketamine (120 mg/kg IM) produced no significant change in respiratory rate, but did induce bradycardia (Salerno & van Tienhoven 1976). As noted above, ketamine (15 mg/kg IM) in combination with xylazine (2.5 mg/kg IM) produced lateral recumbency in 3 minutes that lasted approximately 56 minutes in guinea fowl. The duration of recumbency was significantly longer (91 minutes) with the addition of midazolam (0.3 mg/kg IM) (Ajadi et al. 2009). In ring-necked pheasants a pilot study was used to define doses needed for about 30 minutes of anesthesia. The researchers used 200 μg/kg medetomidine or 3 mg/kg xylazine followed by 80 mg/kg ketamine, 5 minutes later, administered IM (Kaya et al. 2019). The administration of medetomidine was associated with a significant increase in respiratory rate and seven out of 15 birds became apneic following the ketamine injection.

In red-tailed hawks (*Buteo jamaicensis*), ketamine (30 mg/kg IM) produced no significant effect, compared to awake birds, in arterial blood gas or acid-base values, but did produce mild hyperventilation (Kollias & McLeish 1978a). A combination of ketamine (30 mg/kg), xylazine (1 mg/kg), and midazolam (0.2 mg/kg) produced adequate

chemical restraint in eagles (Sadegh et al. 2011). The effects of IO versus IM administration of ketamine were compared in domestic pigeons and both the onset of anesthesia and recovery times were found to be shorter with IO administration. Heart rate decreased significantly in both groups (Kamiloglu et al. 2008).

Propofol

Propofol produces a rapid and smooth anesthetic induction but must be administered intravenously. Because propofol takes about 2 minutes to reach peak effect, the authors suggest a calculated propofol dose be given in quarter increments each administered over 30–60 seconds. This will allow more accurate dosing and minimize apnea and hypotension. In pigeons (Fitzgerald & Cooper 1990) and chickens (Lukasik et al. 1997) propofol had a very narrow margin of safety and respiratory depression. However, at much lower dosages in turkeys (Schumacher et al. 1997) and mallard ducks (Machin & Caulkett 1998a,b) propofol is effective and safe if cardiopulmonary function is monitored and ventilatory support provided. Respiratory depression and significant apnea are common (Hawkins et al. 2003; Langan et al. 2000; Langlois et al. 2003; Machin & Caulkett 2000). In mute swans, propofol provided as a constant rate infusion (CRI) was compared to multiple boluses for short procedures. The overall dose provided by boluses was lower, but the anesthesia was less predictable and the birds were prone to sudden awakening. On recovery, about 50% of the birds in both groups demonstrated a few minutes of excitement. Notably, these birds were maintained on room air, but did not experience a significant change in oxygen saturation (Muller et al. 2011). However, ventilatory support is recommended for any bird anesthetized with propofol, regardless of whether bolus or CRI techniques are utilized. Prolonged recovery, with or without moderate-to-severe central nervous system excitatory signs, has been reported particularly after the use of a CRI (Hawkins et al. 2003; Langan et al. 2000; Langlois et al. 2003). However, one study evaluating its use in the field showed smoother recoveries than with isoflurane anesthesia (Machin & Caulkett 2000). The need for ventilatory support and the potential for excitatory and/or prolonged recoveries limit its use as a sole anesthetic. However, it has been proposed that balanced anesthesia may produce propofol-sparing effects that may reduce these disadvantages (Langlois et al. 2003). In a study in chickens a CRI of propofol was used for an ulnar osteotomy and pinning. Propofol alone was compared with the addition of methadone (6 mg/kg), nalbuphine (12.5 mg/kg), and fentanyl (30 μg/kg loading dose + 0.5 μg/kg/min). The methadone and the nalbuphine resulted in lower infusion rates of propofol (~20% reduction) but the fentanyl did not. The authors did not show that these opioid doses were equivalent. The birds breathed spontaneously and maintained end-tidal CO_2 in the 55–65 mmHg range and recovery to standing was not different between the groups (45–50 minutes) (Santos et al. 2020).

Alfaxalone$_2$

Alfaxalone is a neurosteroid anesthetic that was first developed in the 1970s. At that time, it was licensed for use in animals as a mixture of alfaxalone and alphadolone, mixed in a castor oil base (Saffan®). The latter tended to cause histamine release in many species so the drug was withdrawn from the market. More recently alfaxalone has been dissolved in a cyclodextrin and this base has had very few adverse reactions reported (Alfaxan®). One of the major advantages of alfaxalone over propofol is that it can be administered intramuscularly or even subcutaneously and still have an effect. When administered to mallard ducks IM the bioavailability was 100% and the elimination half-life was around 15 minutes (Kruse et al. 2019). Alfaxalone is a cardiopulmonary depressant but at doses needed for sedation and anesthesia there appears to be minimal depression (Romano et al. 2020). Some investigators have reported transient decreases in heart rate and apnea with higher doses (Baldrey et al. 2014; Balko et al. 2017; Escalante et al. 2018; Romano et al. 2020). Reported doses for small birds (e.g. budgerigars, finches, quaker parrots) are in the range of 20–30 mg/kg, with 10 mg/kg for pigeons, and 2 mg/kg for flamingos (Perrin et al. 2017; Romano et al. 2020; Susanti et al. 2019; Villaverde-Morcillo et al. 2014). The speed of induction and the degree of relaxation have been improved by the addition of other drugs such as midazolam or butorphanol (Perrin et al. 2017). Alfaxalone has been associated with rough recoveries in dogs and cats, and some hyperexcitation during recovery has been reported in birds (Villaverde-Morcillo et al. 2014).

Inhalant Anesthetics

Inhalant anesthetics offer rapid induction and recovery, the ability to rapidly change anesthetic depth, and their use does not require an accurate body weight. Very little of the agent is metabolized, reducing the impact on hepatic and renal function, and recovery is independent of either. Disadvantages include pollution of the work environment and the expense of the anesthetic and associated equipment.

Endogenous catecholamines are released during stress and pain. They can have a significant impact during anesthesia because some inhalant anesthetics sensitize the

myocardium to catecholamine-induced arrhythmias (Aguilar et al. 1995; Greenlees et al. 1990; Joyner et al. 2008; Ludders & Matthews 1996). Clinical observations suggest manipulation of fractured bones, especially the pectoral girdle, causes significant bradycardia and arrhythmias in some patients. However, it is unknown whether this is a vagotonic or baroreceptor effect. Hypercapnia, hypoxemia, and some anesthetics can depress cardiovascular function.

The MAC necessary to prevent purposeful movement in response to a noxious stimulus in 50% of avian patients is used as a measure of inhalant anesthetic potency. MAC for many species is very similar; most birds require approximately the same concentration of inhaled anesthetic for an equivalent amount of stimulation as mammals.

Isoflurane

Isoflurane causes less cardiovascular depression than halothane (Jaensch et al. 1999; Ludders 1992; Ludders et al. 1990; Miller 2005). In mammals, it produces peripheral vasodilation and negative inotropic effects, possibly explaining the dose-dependent hypotension it induces in birds (Goelz et al. 1990; Greenlees et al. 1990; Ludders et al. 1990; Ludders, Rode, & Mitchell, 1989). When isoflurane was compared to sevoflurane and desflurane in red-tailed hawks, isoflurane caused a lower respiratory rate than desflurane. However, $PETCO_2$ did not change and the difference in respiratory rate is unlikely to be clinically significant (Granone et al. 2012). The MAC is 1.32% in chickens, 1.30% in Peking ducks, and 1.34% in sandhill cranes (Ludders et al. 1990; Ludders, Rode, & Mitchell, 1989; Miller 2005). The isoflurane concentration required to produce apnea in ducks was 1.65 × MAC and in cranes was 2 × MAC (Ludders et al. 1990; Ludders, Rode, & Mitchell, 1989). These values are less than those in dogs, cats, and horses (Miller 2005). If surgical anesthesia is achieved in 95% of patients at 1.3 × MAC, isoflurane anesthesia has a low safety margin for apnea.

In addition to cardiopulmonary depression, inhalant anesthetics may cause cardiac arrhythmias. Cardiac arrhythmias have been noted in 35–75% of bald eagles (*Haliaeetus leucocephalus*) anesthetized with isoflurane (Aguilar et al. 1995; Joyner et al. 2008). In both of those studies, second-degree heart block was the most prevalent arrhythmia. In one study, it occurred during induction and recovery in 80% of the cases (Aguilar et al. 1995). Catecholamine release was suspected to be the cause. Cardiac arrhythmias are also commonly detected in other species (Aguilar et al. 1995; Goelz et al. 1990; Korbel et al. 1996), but in the authors' experience arrhythmias are most common in raptors. Cardiac stability is a perceived advantage of isoflurane anesthesia in birds compared with halothane. However, where an electrical fibrillation model was used to investigate myocardial irritant effects of isoflurane and halothane, the former had a lower threshold for electrical fibrillation than halothane (Greenlees et al. 1990). Clinically, arrhythmias appear to be uncommon, but do occasionally occur and warrant vigilant monitoring.

Sevoflurane

Sevoflurane is potentially more useful than isoflurane due to an even lower solubility than isoflurane or halothane. Low solubility allows for faster induction and recovery, as well as more rapid changes in anesthetic depth (Miller 2005; Thurmon et al. 1996). In pigeons, induction and recovery times were more rapid than with isoflurane (Korbel 1998b). This trend was also noted in bald eagles, with faster recovery times compared to isoflurane. A similar number of arrhythmias were noted with each agent (Joyner et al. 2008). In red-tailed hawks, only the time to visual tracking was faster with sevoflurane (and desflurane) compared to isoflurane. Induction time and time to extubation did not vary significantly. All recoveries were noted to be excellent or good (Granone et al. 2012). Sevoflurane administered at 3.5% provided adequate anesthetic plane in crested caracaras (*Caracara plancus*) with significant decreases in respiration rate, arterial blood pressure, cloacal temperature, and blood pH (Escobar et al. 2009). Time to induction and time to recovery were not recorded. Additionally, in several psittacine species recovery times (time to extubation, sternal, and standing) were not significantly different between the two agents, but the birds subjectively appeared less ataxic (Quandt & Greenacre 1999). The time to intubation was longer with sevoflurane (≥4.4 minutes) than isoflurane. However, this was attributed to administration of sevoflurane below the suspected MAC in birds. In Hispaniolan Amazon parrots the time to intubation (38 ± 2 seconds) was rapid with sevoflurane, which was attributed to the higher concentration used during induction. The time to extubation was also rapid (2.3 ± 0.4 minutes) (Klaphake et al. 2006).

In chickens, the MAC of sevoflurane was found to be 2.21% ± 0.32%, which is within the mammalian range (Naganobu et al. 2000), 3.0 ± 0.6% in pigeons, 3.44 ± 0.25% in Amazon parrots, 2.03 ± 0.32% in crested serpent eagles, and 2.9 ± 0.1% in guineafowl (Botman et al. 2016; Chan et al. 2013; Escobar et al. 2012). At this concentration, heart rate did not change significantly and cardiac arrhythmias were not observed up to 2 × MAC (Naganobu et al. 2000). In another study in chickens, hypotension was observed during both spontaneous and controlled ventilation; dose-dependent hypotension was observed only during controlled ventilation (Naganobu et al. 2003). Tachycardia occurred during spontaneous ventilation while the heart

rate remained unchanged during controlled ventilation. However, in Hispaniolan Amazon parrots, bradycardia was observed after 25 minutes using controlled ventilation (Klaphake et al. 2006). Increases in $PaCO_2$ (≤86 mmHg) occurred with increased sevoflurane concentration during spontaneous ventilation. Hypercapnia-induced increases in sympathetic tone were suggested to account for the maintenance of the arterial blood pressures and heart rate in the spontaneously ventilated birds (Naganobu et al. 2003). In both chickens and Hispaniolan Amazon parrots, a significant bradypnea was observed (Klaphake et al. 2006; Naganobu et al. 2003).

Sevoflurane has a less irritating smell than other inhalants. In human pediatric patients it is routinely used for mask induction to prevent struggling due to smell. While the agent cost is higher than isoflurane, many practitioners use sevoflurane for induction then switch to the more cost-effective isoflurane for maintenance.

Anesthetic Adjuncts

In other domestic animals, infusions of other drugs may be used to decrease the dose of inhalant with the expectation of decreasing the cardiovascular and/or respiratory effects of the inhalants. These drugs are often not anesthetics so they have been called adjuncts to anesthesia. Partial IV anesthesia is also used to describe this approach. Opioids, alpha-2 agonists, ketamine, and lidocaine have been investigated in a number of mammals but to date the only studies in birds have involved fentanyl infusions. In red-tailed hawks and Hispaniolan Amazon parrots target concentrations of 8, 16, and 32 ng/mL resulted in similar reductions in the MAC of isoflurane (30–55%) (Pascoe et al. 2018). Based on the data from these studies, a fentanyl infusion rate of 0.3–0.4 μg/kg/min would be required in red-tailed hawks and 5–6 μg/kg/min in Hispaniolan Amazon parrots to achieve about a 50% reduction in MAC. In the red-tailed hawk there was minimal effect on the measured cardiovascular variables (HR, BP) but fentanyl was associated with a decreased HR and BP in Hispaniolan Amazon parrots (Pascoe et al. 2018). The effectiveness of such anesthetic adjuncts needs further evaluation in birds.

Local Anesthesia

There are few studies evaluating local anesthetics in birds. In chickens, successful brachial plexus nerve blocks using lidocaine 2% or levobupivacaine were observed for 30–60 minutes in most birds evaluated (D/Otaviano de Castro Vilan et al. 2006). Another investigator compared local blocks using lidocaine and bupivacaine in chickens and noted a longer duration of sensory blockade in the chickens treated with bupivacaine, but this difference was not statistically significant due to a large amount of variation (Figueiredo et al. 2008). Brachial plexus blocks using ropivacaine (7.5 mg/kg) provided sensory and motor blockade for approximately 2 hours (Cardozo et al. 2009). However, attempts to perform brachial plexus block in mallard ducks with lidocaine and bupivacaine resulted in no consistent alteration in compound nerve action potentials or sensory nerve conduction velocities, suggesting ineffective nerve blockade (Brenner et al. 2010).

Historically it has been stated in the literature that birds may be more sensitive to the toxic effects of local anesthetics than mammals. Toxic effects of lidocaine were reported in birds at lower total doses (2.7–3.3 mg/kg) than in dogs (Hocking et al. 1997), but the authors could not obtain the original work showing this specific range. More recent studies suggest higher doses before toxicity occurs: an effective dose 50 (ED_{50}) of about 6.3 mg/kg was recorded for the onset of a 30% reduction in HR or BP and a massive 29 mg/kg for respiratory arrest in chickens (Brandao et al. 2015; Imani et al. 2013). In a similar study with bupivacaine in chickens the ED_{50} was around 2 mg/kg IV (Imani et al. 2013). Toxic effects are like those reported in mammals and respiratory arrest, seizures, and cardiac arrest have been reported with higher dosages in birds (Ludders 1994). Other adverse effects include depression, drowsiness, muscle tremors, vomiting, hypotension, and arrhythmias as well as CNS signs such as ataxia and nystagmus.

Appropriate lidocaine dosing is difficult in the small avian patient, but toxicity can be prevented by using appropriate concentrations and volumes. This often requires the commercial lidocaine solution (2%, 20 mg/mL) be diluted 1:10 (Ludders 1994). It is unknown whether this dilution allows either appropriate tissue drug levels for analgesia or the expected duration of analgesia to occur (Farley et al. 1994).

Bupivacaine is used conservatively due to concerns that its toxic effects may take longer to resolve. In mammals the maximum recommended dosage of bupivacaine is 2 mg/kg. In mallard ducks (*Anas platyrhynchos*) bupivacaine (2 mg/kg SC) was shorter acting than in mammals (Machin & A., 2001) and showed a faster absorption versus elimination rate. In addition, sequestration and redistribution suggested by increases in plasma concentrations at 6 and 12 hours may delay toxicity. A 1:1 mixture of bupivacaine and dimethyl sulfoxide applied to amputated chicken beaks immediately

after amputation improved feed intake (Glatz et al. 1992). Intra-articular bupivacaine (3 mg in 0.3 mL of saline), was effective for treating arthritic pain in 1.5-kg chickens (Hocking et al. 1997).

EMLA is an acronym for "eutectic mixture of local anesthetic" and is a mixture of 2.5% lidocaine and 2.5% prilocaine for topical use. The depth of penetration of EMLA cream is dependent on the contact time with the skin. In humans, toxicity from EMLA cream is associated with improper administration (i.e., application to large surface areas, prolonged contact time, and application to damaged skin or mucous membranes). Common side effects in humans include skin blanching and local erythema. Less common side effects include methemoglobinemia or neurologic signs, generally when EMLA is applied to a large surface area for a prolonged time. Optimal use in humans requires application and occlusion for 1 hour prior. However, shorter times appear to be effective. There have been no studies evaluating shorter contact times in animals with thin skin, as in birds. The maximum dosage must be calculated prior to administration to prevent toxicity. Systemic uptake may be increased after feather plucking due to skin damage and exposed feather follicles.

For some procedures involving the caudal coelom, a caudal spinal anesthesia technique has been established for chickens (Kazemi-Darabadi et al. 2019). There is no epidural space caudal to the thoracic region of the coelom because there is a general attachment of the vertebral periosteum to the dura mater (Kazemi-Darabadi et al. 2019). In contrast, the arachnoid space is well developed in the synsacral spinal cord (Azcoitia et al. 1987). As a result, epidural injection is not possible in the lumbosacral area of the chickens, but spinal injection can be performed (Kazemi-Darabadi et al. 2019; Khamisabadi et al. 2021). While having delayed onset compared with lidocaine, bupivacaine produced approximately 55 minutes of spinal anesthesia in broiler chickens, much longer than the 18 minutes of spinal anesthesia provided by 2 mg/kg lidocaine (Khamisabadi et al. 2021).

Monitoring

Due to the rapid rate at which birds may decompensate under anesthesia, monitoring is the most important aspect of avian anesthesia. Additionally, many monitors are not built for the small size and rapid heart rate of avian patients and may be more unreliable than in dogs and cats. This means having one person dedicated to consistent, hands-on monitoring and ensuring the anesthetist has a clear view of the patient are critically important.

Cardiovascular

Heart rate is widely variable between individuals and species. Knowledge of expected species values is important, but trends in rate during anesthesia are of more significance. Sudden bradycardia is an indication to decrease anesthetic depth and provide supportive care, such as fluid boluses.

Heart rate and rhythm are monitored by an external or an esophageal stethoscope, electrocardiograph or peripheral pulse rate. Peripheral pulse rates are determined at the brachial, medial metatarsal artery, or carotid artery by direct palpation or with a Doppler ultrasonic probe. The Doppler probe is placed against the palatine artery on the dorsal palate of some species (Fig. 15.7).

ECG limb leads are placed close to the body. Due to the delicate nature of avian skin, the alligator clips are attached to needles or stainless-steel suture passed through the skin, rather than directly attaching to the skin. Heart rate and the presence of an ECG trace are insensitive indicators of anesthetic depth.

Blood pressure may be subjectively assessed by palpating the pulse at the median ulnar or medial metatarsal artery. Changes in pulse pressure and velocity are also reflected in sound.

There is an increasing awareness of the need to monitor blood pressures in avian patients during anesthesia as techniques for monitoring improvement. However, when direct blood pressure measurements are compared across a variety of species in different orders, there are significant differences. This can make it difficult to determine what values are normal for a particular species. There appears to be a trend for Galliformes and pigeons to have lower pressures than Psittaciformes, which also appear to average lower than raptorial species, but this is based on a low number of species. Blood pressure is the result of cardiac output and peripheral vascular resistance. Both are affected by several factors, including autoregulatory control and humoral, hormonal, and neural influences (Smith et al. 2000). Very short-term adjustments are mainly the result of reflex responses within the small arteries and arterioles. Tissue production of metabolic products, including CO_2, H^+, and others, may cause a functional hyperemia in local tissues (Smith et al. 2000). Circulating hormones such as epinephrine, norepinephrine, and angiotensin II also have significant effects on peripheral vascular resistance (Smith et al. 2000). There has not been sufficient research into the differences in these multitude of factors between species to know which is responsible for the differences in resting blood pressures noted clinically. This means that monitoring trends for a particular patient under anesthesia is more important than the actual blood pressure value.



Figure 15.7 In addition to the medial metatarsal artery, peripheral pulse rates can be determined in many birds by placement of a Doppler flow probe over either the brachial artery (a), the carotid artery (b) or over the palatine artery (c) on the dorsal palate of some species of raptors and waterfowl.

Direct arterial pressure monitoring can be performed. The most common sites include the brachial and carotid arteries (Fig. 15.8). The catheters are usually placed percutaneously, but a cut-down procedure is sometimes required to confirm arterial location. Significant arteriospasm may occur in some species. In this author's experience, cutaneous application of a small amount of EMLA 30 minutes prior to percutaneous catheterization reduces arteriospasm. Alternatively, diluted 2.5% lidocaine is applied directly over the artery during a cut-down procedure. Occasionally a profound bradycardia is associated with catheterization of a brachial artery.

Indirect blood pressure monitoring is performed using a Doppler ultrasonic probe to detect arterial flow, a pressure cuff for occlusion, and a sphygmomanometer to measure pressure (Fig. 15.9). Recently, there have been several publications investigating the accuracy and precision of indirect blood pressure (iBP) monitoring in multiple avian species. In Hispaniolan Amazon parrots, iBP measurements obtained with a size 1 neonatal cuff (30–40% of limb diameter) did not provide adequate correlation with direct arterial measurements (Acierno et al. 2008). In red-tailed hawks, iBP measurements were found to more closely approximate MAP measurements over a range of blood pressures and values obtained with a cuff 40–50% of the limb diameter did not differ significantly between wing or leg placement (Zehnder et al. 2009). A study evaluating the precision of multiple iBP measurements in awake psittacines found significant variability between repeated measurements when iBP cuffs were applied multiple times to the same limb (Johnston et al. 2011). Oscillometric devices have demonstrated high failure rates and unreliable measurements in avian patients and are not recommended for iBP monitoring (Acierno et al. 2008; Zehnder et al. 2009). From the studies that have been done, it seems that an appropriately sized cuff and sphygmomanometer can be

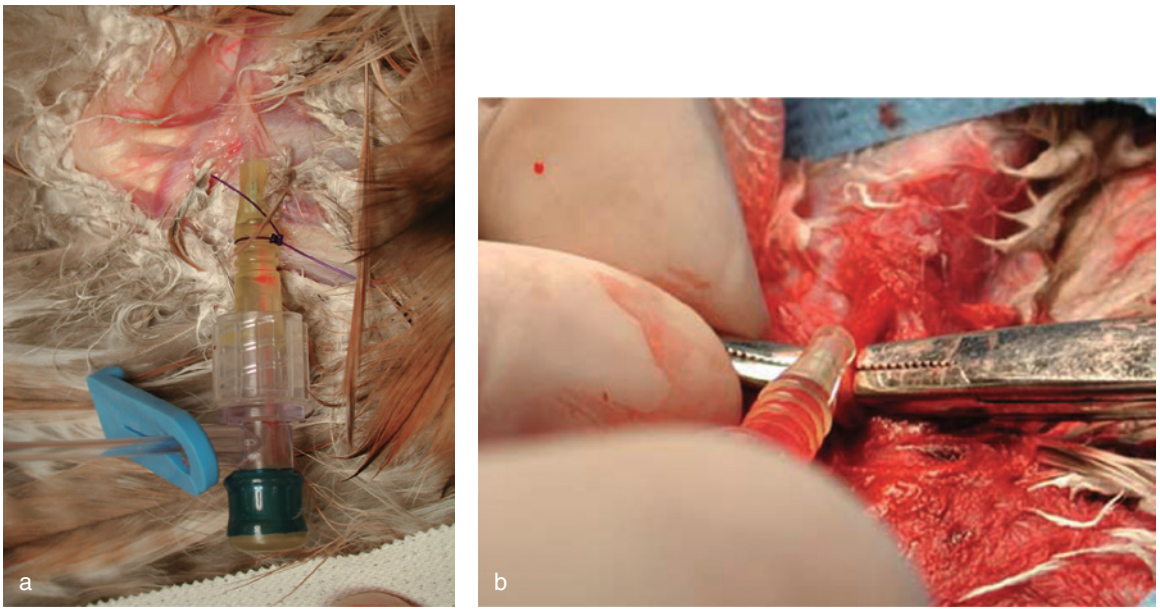


Figure 15.8 Arterial catheterization of the brachial artery in a bird. The brachial (a) and carotid arteries are the most common sites for arterial catheterization in birds. Percutaneous placement is utilized most, but sometimes a surgical cut-down procedure is required to confirm the location of the artery (b).



Figure 15.9 Indirect blood pressure monitoring can be performed using a Doppler ultrasonic probe to detect the arterial flow, a pressure cuff to occlude arterial blood flow and a sphygmomanometer to measure pressures.

used to evaluate trends in iBP during an anesthetic episode, but that repeated sampling that involves different cuff placements (as in different hospital visits) may be unreliable.

Respiratory

Respiratory rate and character should be closely monitored throughout anesthesia as these may be the first indication of problems and are a good sign for early intervention. Ventilation is assessed by observing the frequency and range of sternal motion and reservoir bag movement. Substituting balloons for regular reservoir bags will facilitate visualization of movement in patients with small tidal volumes. However, assessment of adequacy of ventilation by these methods in birds is inaccurate. A sudden change in respiratory pattern involving increased respiratory effort may indicate obstruction of the endotracheal tube, a particular concern in very small patients. Normal ventilation is associated with little to no respiratory tract noise. Whistling, wheezing or harsh sounds may also indicate obstruction. Many birds (e.g., ducks) will normally have an expiratory syringeal noise during IPPV. Apnea ≥10–20 seconds is an indication to decrease anesthetic depth and provide assisted ventilation. The time between respiratory and cardiac arrests may be ≤1–2 minutes. Respiratory monitors that detect gas flow increase mechanical dead space.

End-tidal carbon dioxide ($PETCO_2$) monitoring is used to determine ventilatory efficacy. This can be done using either main-stream or side-stream technology. Main-stream detectors are placed on the end of the endotracheal tube and contain sources of infra-red light and detectors used to measure CO_2 concentration. This means that the displayed waveform is synchronous with the bird's respiration. In birds <5 kg a pediatric adapter should be used with the main-stream adapter to minimize dead space but in small birds (<500 g) this added dead space to the airway is excessive. Side-stream technology draws gas from the airway and passes it through a detector in the monitor so there is always a slight delay between the bird's

breathing and the displayed waveform. This method allows the dead space to be minimized by drawing gas from an endotracheal tube adaptor or from within the airway Ideally the sampling port is located inside the endotracheal tube, but it should not increase airway resistance. Sidestream capnographs draw samples at a rate of 50–200 mL/min. This rate is usually fixed, but some capnographs allow alteration. In small birds even this low flow may exceed minute ventilation so care should be taken to account for this removal of gas by the monitor.

There is relatively good correlation between $PETCO_2$ and $PaCO_2$, with $PETCO_2$ slightly exceeding $PaCO_2$ (Edling et al. 2001; Hawkins et al. 2003; Pettifer et al. 2002). In a study evaluating the accuracy of $PETCO_2$ in multiple raptor species, the authors found that sidestream $PETCO_2$ overestimated $PaCO_2$ at low levels, with the reverse trend at higher levels (Desmarchelier et al. 2007). This can occur in the avian parabronchus, but is impossible in alveolar gas exchange (Powell & Whittow 2000). Carbon dioxide diffusion occurs across the length of the parabronchus, with a higher diffusion rate at the inspiratory end and a lower rate at the expiratory end. Since arterialized blood returning to the heart is a mix of capillary blood draining the entire length of the parabronchus, $PaCO_2$ can be less than $PETCO_2$ in ideal cross-current exchange. With very small tidal volumes there may be enough mixing of expired gas with fresh gas that the capnogram reading is artificially low. One way to check this is to administer a larger breath and to check if the $PETCO_2$ increases: if it does then the ongoing reading is not a true reflection of the $PaCO_2$. The capnogram provides important information regarding trends in $PETCO_2$ (Fig. 15.10) and can also be used to detect changes in dead space. If the inspired CO_2 begins to climb, then this indicates increased dead space. If a nonrebreathing circuit is being used this is most often caused by an inadequate flow of oxygen and is mostly seen when the respiratory rate increases. A flow rate that may have been adequate to remove CO_2 at 20 breaths per minute may not be sufficient at 40 breaths per minute due to a reduction in the time between breaths for gas removal. One further

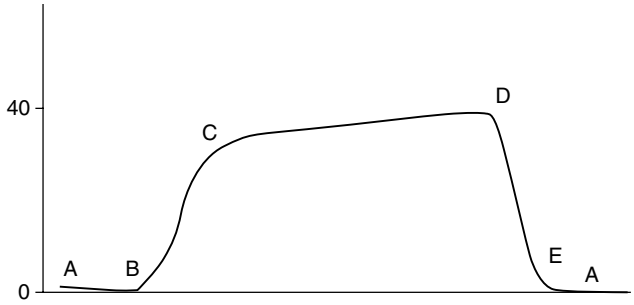


Figure 15.10 Avian capnogram.

complication in birds is that the waveform may suddenly disappear if an air sac is opened because gas is now flowing out of the air sac and not back up the trachea. If an inhalant is being used the surgeons should be notified so that they can potentially close the air sac. If that is not possible then consideration should be given to switching to an injectable technique for anesthesia.

Pulse oximetry has not been validated in birds. The absorption characteristics of oxygenated and deoxygenated avian and human hemoglobin are different, resulting in underestimation of hemoglobin saturation (Schmitt et al. 1998). In pigeons, hemoglobin saturation trends were consistent, but values did not correlate with those derived from blood gas analyses and calculation (Schmitt et al. 1998). A recent study in Andean geese showed an excellent correlation between SaO_2 and SpO_2 but more studies are needed (Ivy et al. 2018). However, these monitors are often used to provide a pulse rate and some monitors have been adapted to count pulses up to 400 breaths per minute.

Anesthetic Depth

The cere, beak, head, cloaca, and digits are used to assess response to pain. Surgical incisions and needle pricks evoke less response under anesthesia than for mammals. Withdrawal reflexes include toe pinch, stimulation of the interdigital tissue, pinching the scaly areas of the skin, cloacal pinch, and feather plucking. Slight corneal and palpebral reflexes are maintained at a surgical plane; their absence may indicate excessively deep anesthesia. In raptors anesthetized with propofol, contour feather plucking did not initiate a response in any bird at any time during the CRI (Hawkins et al. 2003). Rather, toe clamping was a better guide to anesthetic depth.

Glucose

Blood glucose is monitored when possible, particularly during prolonged procedures. In auklets, the values determined by four handheld human glucose monitors were comparable to Chemstrip BG. However, values for all systems were 33% less than those determined by a reference chemistry laboratory (Lieske et al. 2002). Blood storage in heparin was preferable to ethylenediamine tetra-acetic acid. Stored blood glucose values were stable for 4 hours.

Recovery

Recovery complications are usually associated with long anesthetic procedures (≥0.5–1.0 hours). This emphasizes the importance of minimizing anesthetic time. The vaporizer is turned off at the end of the procedure and

circle breathing systems flushed with oxygen. This flushing is unnecessary with a nonrebreathing system. The patient remains connected to the breathing system and oxygen if possible. Signs of recovery include muscle fasciculations, then wing and leg movement. Once beak tone returns, the bird is extubated to prevent severing the endotracheal tube. Once extubated, an anesthetic face mask with or without the rubber diaphragm is placed over the bird's head to continue oxygen supplementation. Most birds are placed loosely in a towel and held upright to minimize self-trauma and regurgitation. Respiration is monitored during towel restraint to ensure adequate sternal movement. Once recovered the bird is placed in a warm, well-oxygenated environment for continued recovery. A quiet dark environment minimizes stress and movement.

Analgesia

Pain Recognition

Pain recognition is critical for providing timely analgesic selection for any species. It requires consideration of age, sex, and species differences, as well as individual behavior and environmental factors. Pain assessment must also account for different types and sources of pain (i.e., acute, chronic, visceral, and somatic). Pain is subjective and the emotional component is difficult to translate because birds lack facial expression and do not share verbal language with humans. In humans pain is what the patient says it is but with birds, people's perceptions of the bird's behavior determines what is recognized as pain.

Behavioral changes associated with pain in birds can be very subtle and obscure but are often the earliest signs of pain detected by owners or animal care staff. Behavioral changes do not manifest uniformly among different species of birds; observers must become familiar with the full range of normal behaviors for the species as well as for the individual. It is important to observe birds' behaviors at appropriate times for each species, for example observing nocturnal species at night. Social species exhibit pain behaviors dependent on the group social dynamics. Predatory species exhibit abnormal behaviors more readily than prey species. Painful behaviors attract unwanted attention from predators, requiring masking to survive. The clinician is viewed as a potential predator. Birds either hide painful or exhibit different behaviors outside their home cage. Without knowing the range of normal behaviors, an observer will find it extremely difficult to detect abnormal behaviors.

Pain can change a bird's social interactions, especially in species with complex social systems. This may be an obvious change, such as perching away from the flock, or might be subtle, such as a reduction in social grooming. When birds are housed as single pets, their social interactions with the owner may be reduced or the bird may permit interactions that it would not otherwise allow. Birds in pain may display guarding behavior to protect a painful area, which may manifest as antisocial behaviors. Some forms of aggression have been linked to painful conditions in birds; anecdotal reports have suggested aggressive behaviors are sometimes reduced or dissipate following treatment of the painful condition.

Feather grooming is an avian behavior that runs the full spectrum of behavioral changes associated with pain, both acute and chronic. Grooming activity may decrease when a bird is in pain, but conversely overgrooming and feather destructive behaviors have been associated with chronic pain, which may include neuropathic pain. In a social species housed within a group, a bird in pain frequently isolates itself from others, it may sleep apart from the rest of the flock, and mutual grooming is often decreased (Le Maho et al. 1992). Increased self-grooming activities or preening other birds can be an intentional distraction.

Birds respond to noxious stimuli with a fight-or-flight response (escape reactions, vocalization, excessive movement) and/or tonic immobility. In domestic chickens (*Gallus gallus domesticus*) removal of feathers caused a progression of behavioral changes from an alert agitated response following the initial removal of feathers to periods of crouching immobility following successive feather removal (Gentle & Hunter 1991). In red-tailed hawks (*Buteo jamaicensis*) hospitalized with recent orthopedic injuries, movement, head motions, and beak clacking were significantly reduced when compared to birds without recent orthopedic injuries (Mazor-Thomas et al. 2014). Studies using chickens with experimentally induced arthritis demonstrated that shifting their attention can reduce painful behaviors (Gentle & Tilston 1999).

Many clinical signs are associated with pain, including change in temperament (either aggressive or passive), restlessness, reduced mobility (Mazor-Thomas et al. 2014) or reluctance to stand or perch, lethargy, hunched appearance, sleep deprivation, tachypnea, and lameness. Reduced food consumption may occur, and bodyweight should be monitored. Animals with abdominal pain can exhibit tensing with a "tucked up" or "hunched" appearance. Birds may either avoid a painful body area or bite/chew it. Decreased or overgrooming (feather-picking) may occur at a painful site. In red-tailed hawks both head movements and beak clacking were decreased in birds thought to be in pain (Mazor-Thomas et al. 2014). Vocalization and writhing occur rarely during acute or severe pain. Owners often describe reduced vocalization in birds with traumatic injuries.

Few physiologic variables are consistent indicators of pain. In chickens during feather plucking, heart rates and respiratory rates were variable, but increased blood pressure was a reliable indicator (Gentle & Tilston 1999). Catecholamines are well-recognized humoral indicators of stress but vary between individuals and species because of differences in adrenal content (Harvey et al. 1984). Corticosterone significantly increases in birds following pain, but it also increases with handling (Heatley et al. 2000). The use of noxious stimuli (primarily thermal) as well as induced pain models (Paul-Murphy et al. 2009a) will allow researchers to evaluate the use of analgesics more objectively in birds.

Pain scales and scoring sheets are increasingly used to assess pain, especially when specifically designed for a given species under well-defined conditions. Using pain scales requires an understanding of both normal and pain-related behaviors for the species and individual. Score-sheet descriptions of behaviors must be refined and terms must be clearly defined to reduce interobserver variability and observer bias. In lieu of species-specific pain score sheets, there is tremendous value in using a generic visual analog pain scale of 1 to 10 to evaluate a bird's pain and the response to treatment and recovery from a painful condition. For example, pigeons following orthopedic surgery were evaluated using a detailed numeric rating scale plus a simple 1 to 10 pain scale, and there was significant correlation between both methods (Desmarchelier et al. 2012a). Effective analgesia is expected to show a marked, easily discernable change in posture or behaviors that will effect a reliable change in the subjective pain score. If no change in pain score occurs, then the drugs, dosage, or frequency of administration should be re-evaluated for that patient. Alternatively, a set of universal questions are used to determine if a patient is in pain:

1) Would the lesion or procedure be painful to any species?
2) Is the lesion or procedure damaging to tissues in any species?
3) Does the patient display any abnormal behavioral responses?

If the answer to any of these questions is yes, then the veterinarian must assume that the patient is in pain and an analgesic plan should be developed.

Approaches to the Treatment of Pain

Surgical incisions and other painful procedures in humans induce prolonged nervous system changes that later contribute to postoperative pain. This noxious stimulus-induced sensitization can be prevented or "pre-empted" by administration of analgesic agents prior to tissue injury. Pre-emptive analgesia with opiates, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or local anesthetics can block sensory noxious stimuli from onward transmission to the CNS, thus reducing the overall potential for inflammation and pain and improving the patient's short- and long-term recovery. Combinations of drugs in a multimodal protocol with opiates, NSAIDs, local anesthetics, and/or other drugs acting at different points in the nociceptive system provide a greater effect and potentially less toxicity than individual drugs given alone, which is especially important in avian species for which few analgesic data are available.

Opioids

Most opioid analgesics are used parenterally because of their overall poor oral bioavailability associated with the first-pass effect. Analgesia is species and intra-species variable at equipotent dosages. Opioids are used for moderate to severe pain, such as traumatic or surgical pain. Opioids reversibly bind to specific receptors in the central and peripheral nervous system. These drugs are categorized as full agonists, partial agonists, mixed agonist/antagonists, or antagonists based on their ability to induce an analgesic response once bound to a specific receptor. The action of opioid drugs on these receptors activates G-proteins, leading to a reduction in transmission of nerve impulses and inhibition of neurotransmitter release (Bovill 1997). Agonist drugs have a linear dose–response curve that may be titrated to reach the desired effect, whereas the agonist/antagonist drugs may reach a ceiling effect after which increasing the dose does not appear to provide additional analgesia. During anesthesia, opioids are used to provide perioperative analgesia that may reduce the concentrations of volatile anesthetics (i.e., gas anesthesia-sparing effects). The most common adverse effects reported with opioids are cardiac and/or respiratory depression. In many cases, these drugs may be reversed with antagonists, which will also terminate analgesia. The application and dosages of several opioid formulations have been scientifically evaluated and clinically applied in birds.

Few studies have been conducted regarding the distribution, quantity, and function of each opioid receptor type in birds, and although marked species variability is assumed, further studies are necessary (Duhamelle et al. 2018). In pigeons, regional distribution of μ, κ, and δ receptors in the forebrain and midbrain were like mammals but the κ and δ receptors were more prominent in the pigeon forebrain and midbrain than μ receptors and 76% of opioid receptors in the forebrain were determined to be κ type (Mansour et al. 1988). However, in 1-day-old chicks

receptor distribution was markedly different, suggesting either age or species effect (Csillag et al. 1990). There were small differences in receptor densities between cockatiels and pigeons but these may not be sufficient to make functional changes (Fousse et al. 2020). In conditioning experiments pigeons were able to differentiate μ from κ receptor agonists. Isoflurane-sparing effects of μ and κ agonists are quite variable in mammals and it is likely that similar variability will be evident in birds (Concannon et al. 1995).

Morphine is a μ-receptor agonist that has been infrequently used in avian medicine because early studies in domestic fowl yielded conflicting results and suggested that very high dosages were required to reduce response to the toe pinch (Schneider 1961) or a noxious electrical stimulation (Bardo & Hughes 1978). In one study, it decreased the response temperature in a thermal threshold test (hyperalgesia) in two breeds but increased it another one (Hughes 1990). A study of adult white leghorns that involved the use of the isoflurane-sparing technique found that increasing doses of morphine (0.1, 1, and 3 mg/kg) caused a significant decrease in the isoflurane MAC (Concannon et al. 1995). An intra-articular injection of 1–3 mg morphine in a domestic fowl arthritis model identified no significant antinociceptive effects, but it is unclear whether synovial fluid pH differences may have affected the activity of the drug (Gentle et al. 1999). The pharmacokinetics of morphine at 2 mg/kg IV also have been evaluated in the domestic chicken (Singh et al. 2010). At this dose, chickens cleared morphine at a higher rate than humans or cats, and plasma morphine analgesic concentrations were like humans for approximately 2 hours. In a recent study evaluating the analgesic efficacy of morphine, lame broiler chickens underwent an obstacle course and latency-to-lie test before injection at 30 minutes and 2 hours after injection, to assess their walking and standing ability (Singh et al. 2017). Following 2 mg/kg IV of morphine, chickens had an increase in time to finish the obstacle course and exhibited sedation which confounded assessment of its analgesic effects. The authors indicated that morphine would likely produce analgesia without sedation at lower doses, which would also require a more frequent administration and warrants further investigation.

Hydromorphone HCl is a μ-opioid receptor agonist with an approximate potency five to seven times that of morphine in humans (Quigley 2003). Hydromorphone shows a dose-responsive thermal antinociceptive effect when administered at 0.1, 0.3, and 0.6 mg/kg IM to American kestrels (*Falco sparverius*) for up to 6 hours (Table 15.3) (Guzman et al. 2013). Severe sedation was detected in four birds when administered 0.6 mg/kg hydromorphone, and when the sedated birds were handled they appeared agitated for a few seconds then resumed sedated behavior. The pharmacokinetics of hydromorphone following IM and IV administration in American kestrels

Table 15.3 Analgesic drug dosages commonly used in birds.

Drug	Dosage (mg/kg)	Route	Frequency	Species	Comments	References
Morphine						
	0.1, 1, and 3	IV	Single	Chickens	15%, 40%, and 52% reductions in the MAC of isoflurane	Concannon et al. (1995)
	2	IV	Single	Chickens	Produced enough sedation that analgesia was not evident	Singh et al. (2017)
Hydromorphone	0.1, 0.3, and 0.6	IM	Single	American kestrels and cockatiels	Increased thermal threshold in kestrels but no effect in cockatiels	Guzman et al. (2013); Guzman et al. (2014c); Houck et al. (2018)
	1 and 2	IM	Single	Amazon parrots	Increased thermal threshold but accompanied by significant agitation	Guzman et al. (2020)
Methadone	6	IM	Single	Chickens	30% decrease in the MAC of isoflurane	Escobar et al. (2021, 2016)

(*Continued*)

Table 15.3 (Continued)

Drug	Dosage (mg/kg)	Route	Frequency	Species	Comments	References
	6	IM	Single	Amazon parrots	Increased thermal threshold but accompanied by significant agitation	Guzman et al. (2020))
Fentanyl	0.2	SC	Single	Cockatoos	Affected withdrawal threshold in some birds, hyperactivity noted	Hoppes et al. (2003)
	0.2–0.5 μg/kg/min	IV	CRI	Red-tailed hawks	Reduced isoflurane MAC 31–55% in a dose-related manner, without significant effects on HR, blood pressure, $PaCO_2$, or PaO_2	Pavez et al. (2011)
	1.0–5.0	IM	Single	Hispaniolan Amazon parrots; African grey parrots	Withdrawal thresholds to electrical stimuli reduced after 2 mg/kg IM for 2 hours	Guzman et al. (2011); Paul-Murphy et al. (1999); Sladky et al. (2006)
	75 μg/kg/min	IV	CRI		MAC reduction in psittacines with 3 mg/kg loading dose	
Buprenorphine	0.01	IM	Single	African grey parrots	May not achieve plasma concentrations at this dose; no change in withdrawal response to noxious stimuli	Paul-Murphy et al. (1999, 2004)
	0.25–0.50	IM	Single	Domestic pigeons	Decreased withdrawal from noxious stimulus for 2 hours(0.25 mg/kg) and 5 hours(0.5 mg/kg)	Gaggermeier et al. (2003)
	0.1, 0.3, and 0.6	IM	Single	American kestrels	Dose-dependent increase in thermal threshold	Ceulemans et al. (2014)
Busprenorphine sustained release	1.8	SC, IM	Single	American kestrels	Increased thermal nociceptive thresholds for at least 24 hours	Guzman et al. (2018a, 2017a)
Buprenorphine concentrated	0.3	SC	Single	Red-tailed hawks	Maintained plasma concentrations >1 ng/mL for 24 hours	Gleeson et al. (2018)
	1.8	SC	Single	Red-tailed hawks	Maintained plasma concentrations >1 ng/mL for 48 hours	Gleeson et al. (2018)
Butorphanol	1–2	IM	Single	African Grey parrots	Increased withdrawl threshold to electrical stimulus	Paul-Murphy et al. (1999)
	3 and 6	IM	Single	Hispaniolan Amazon parrots	Increased thermal thresholds	Sladky et al. (2006)
	1, 3, and 6	IM	Single	American Kestrels	No change in thermal threshold Agitation at 6 mg/kg	Guzman et al. (2014a)
	2	IV	Single	Chickens	Analgesia evident from obstacle course test	Singh et al. (2017)

Table 15.3 (Continued)

Drug	Dosage (mg/kg)	Route	Frequency	Species	Comments	References
	2 and 4	IM	Single	Guineafowl	Reduced sevoflurane MAC by 9% and 21%, respectively. At the higher dose administered rapidly IV it caused significant arrhythmias	Escobar et al. (2014); Martini et al. (2020)
	1	IM	Single	Cockatoos	25% decrease in isoflurane MAC	Curro et al. (1994)
	5	IM	Single	Hispaniolan Amazon parrots	Increased thermal threshold for 30 minutes only	Laniesse et al. (2020)
Nalbuphine	12.5	IM	Single		Excellent IM bioavailability; 12.5 mg/kg produced 3 hours analgesia; higher doses did not increase analgesic time	Keller et al. (2011); Guzman et al. (2011)
Tramadol	7.5	PO	Single	Peafowl	Maintained human therapeutic concentrations for 12–24 hours (M1 metabolite)	Black et al. (2010)
	10	PO	q24h	African penguin	Elimination $t_{1/2}$ 7.3 hours	Kilburn et al. (2014)
	15.0	PO	q12h	Red-tailed hawks	Based on 11 mg/kg single dose	Souza et al. (2011)
	5.0	PO	q12h	American bald eagles	PO bioavailability high, based on 11 mg/kg single dose	Souza et al. (2009)
	30	PO	Single	Hispaniolan Amazon parrots	Reduced thermal withdrawal response for ~6 hours	Souza et al. (2010); D.S.-M. Guzman (pers. comm.)
	30	PO	Single	Muscovy ducks	Elimination half-life of 3.95 hours	Bailey et al. (2019)
NSAIDs						
Carprofen					Use caution in Gyps vultures	Cuthbert et al. (2007)
	1.0	IM	Single	Chickens	Improved locomotion of lame birds 1hr post-treatment	McGeowen et al. (1999)
	30.0	IM	Single	Chickens	Painful behaviors (arthritis) reduced for 1 hour	Hocking et al. (2005)
	3.0	IM	q12h	Hispaniolan Amazon parrots	Arthritis pain partially reduced for <12 hours	Paul-Murphy et al. (2009b)
Ketoprofen					Avoid in Gyps vultures; mortalities associated with clinical doses	Naidoo et al. (2010)

(*Continued*)

Table 15.3 (Continued)

Drug	Dosage (mg/kg)	Route	Frequency	Species	Comments	References
	2.0	IV, IM, PO	Single	Quail	Low IM, PO bioavailability	Graham et al. (2005)
	12	IM	Single	Chickens	Painful behavior reduced for 1 hour	Hocking et al. (2005)
	5.0	IM	Single	Mallard ducks	12 hours activity noted	Machin et al. (2001)
Meloxicam	0.1–0.5	IV	Single	Chickens, ostrich, ducks, turkeys, pigeons	Half-life in chickens and pigeons was three times as long as for ostrich, ducks, and turkeys	Baert & De Backer (2003)
	0.2	PO	Single	Brown pelicans	Longest half-life of any avian species to date	Horgan et al. (2020)
	0.5 1	IM PO	Single	African penguin	0.5 mg/kg IM and 1 mg/kg PO results in concentrations above target for approximately 24 and 60 hours, respectively	Morrison et al. (2018)
	1	IV, PO	Single	Cockatiels	Very low (11%) oral bioavailability and shorter half-life than other psittacines	Dhondt et al. (2017)
	1	IM, PO	Multiple dose, q24h for 12 and 7 days, respectively	Grey parrot	Moderate bioaccumulation following IM administration	Montesinos et al. (2019)
	1	IM	q12hr	Hispaniolan Amazon parrots	Improved weight-bearing on arthritic limbs	Cole et al. (2009)
	2	IM, then PO	q12hr	Pigeons	Provided analgesia post osteotomy for 9 days	Desmarchelier et al. (2012b)
	2	IM, PO	Single	Cape Griffon vultures	Short $t_{1/2}$, less than 45 minutes	Naidoo et al. (2008)
	5	SC	Single	Chickens	Thermal threshold increased in lame chickens	Hothersall et al. (2014)
Piroxicam	0.5–0.8	PO	q12h	Whooping cranes	Used for acute myopathy and chronic arthritis	J. Paul-Murphy (pers. Comm.)
Sodium salicylate	100–200	IM	Single	Chickens	Arthritis painful behaviors partially reduced for 1 hour	Hocking et al. (2005)
	25	IV	Single	Chickens, ostrich, ducks, turkeys, pigeons	Rapid clearance except long $t_{1/2}$ in pigeons	Baert & De Backer (2003)

Table 15.3 (Continued)

Drug	Dosage (mg/kg)	Route	Frequency	Species	Comments	References
Local anesthetics						
Bupivicaine	1.33, 1.96	IV	Single	Chickens	1.96 mg/kg IV bupivacaine associated with a 50% probability of a clinically relevant change in MAP and HR, whereas 1.33 mg/kg IV bupivacaine is associated with a 1% probability of causing the same effect	DiGeronimo et al. (2017)
	2–8	Peri-neural		Mallard ducks		Brenner et al. (2010)
Lidocaine	1–3	Local		Most species	Incision site infusion	
Ropivicaine	7.5	Peri-neural		Chickens	Successful brachial plexus block in 15 minutes, ~110 minutes of anesthesia	Cardozo et al. (2009)

CRI, continuous rate infusion; HR, heart rate; IM, intramuscular; IV, intravenous; MAC, minimum anesthetic concentration; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; PO, per os or orally; q12h, every 12 hrs; q24h, once a day; SC, subcutaneous. Note that these are suggested dosages based on published information and the author's clinical experience. Species and individual variation in response to a given drug can be uncertain so the dosage should be adjusted depending on the clinical response of the animal.

found a high IM bioavailability (75%) and rapid elimination, with a short terminal half-life and a rapid plasma clearance (Guzman et al. 2014b). A similar thermal nociception study in cockatiels (*Nymphicus hollandicus*) that were administered 0.1, 0.3, and 0.6 mg/kg IM hydromorphone and saline treatment showed no significant effect on the thermal threshold, and the highest dosages resulted in only a mild sedative effect (Houck et al. 2018). The thermal antinociceptive effect of hydromorphone was evaluated following IM administration to orange-winged Amazon parrots (*Amazona amazonica*) (Guzman et al. 2020). Hydromorphone at 1 and 2 mg/kg significantly increased thermal foot withdrawal response at 0.5, 1.5, and 3 hours, and 1.5 and 6 hours respectively, compared with the response after saline administration. Significant agitation was observed for 1 and 2 mg/kg hydromorphone doses at 0.5, 1.5, and 3 hours. This kind of agitation in response to an opioid in normal birds may not be present in birds in pain. Other significant adverse effects after administration of 1 and 2 mg/kg hydromorphone included nausea-like behavior, ataxia, and pupillary constriction. One bird regurgitated/vomited after receiving the 2 and 1 mg/kg doses at 0.5 and 1.5 hours, respectively. While hydromorphone at 1 and 2 mg/kg IM appears to have desired analgesic effects, the presence of agitation, nausea-like behavior, and ataxia warrants consideration of lower doses for clinical use in orange-winged Amazon parrots. Plasma hydromorphone concentrations were maintained above 1 ng/mL for 6 hours in six out of seven and eight out of eight orange-winged Amazon parrots receiving 1 mg/kg hydromorphone IV and IM, respectively (Guzman et al. 2020). Hydromorphone hydrochloride had a positive pharmacokinetic profile in this species with high bioavailability and rapid elimination after IM administration, with a short terminal half-life, rapid plasma clearance, and a large volume of distribution (Guzman et al. 2020).

Methadone in small animals acts similarly to morphine regarding its degree of analgesia and duration of action (Plumb 2020). Methadone is a μ-opioid receptor agonist that also is a noncompetitive inhibitor of N-methyl-D-aspartate (NMDA) receptors. Methadone can also reduce re-uptake of norepinephrine and serotonin, which may contribute to its analgesic effects. Due to its additional mechanisms of action, methadone potentially may be more efficacious than other μ agonists (e.g., morphine), particularly for neuropathic or chronic pain (Plumb 2018). Methadone is much more lipid-soluble than morphine and approximately 1–1.5 times as potent. In hens, methadone at a dose of 6 mg/kg IM decreased the isoflurane minimum anesthetic concentrations by 30% at 15 minutes post administration. At this dose, in spontaneously breathing hens, methadone produced mild respiratory acidosis, decreased heart rate, and increased systemic blood

pressure, with occasional cardiac arrhythmias (Escobar et al. 2016). The bioavailability was estimated to be 79% for IM administration (Escobar et al. 2021). Methadone at 6 mg/kg IM in orange-winged Amazon parrots resulted in a significant increase in thermal threshold when compared to saline administration, while lower doses of 1 and 3 mg/kg did not result in a significant effect (D.S.-M. Guzman, pers. comm.). Methadone caused significant agitation and nausea-like behavior when compared to saline administration. The IM mean bioavailability was 85.7% with mean terminal half-lives of 2.35 and 2.29 hours after IV and IM administration, respectively (D.S.-M. Guzman, pers. comm.). While methadone at 6 mg/kg IM appears to have the desired analgesic effects, the presence of agitation, nausea-like behavior, and ataxia warrants consideration of lower doses for clinical use in orange-winged Amazon parrots. Further studies are needed to fully determine the analgesic and adverse effects of methadone in psittacine birds and other avian species.

Fentanyl is a short-acting μ-opioid receptor agonist often administered as a continuous rate infusion or as a transdermal patch. Fentanyl administered at 0.02 mg/kg IM did not affect the withdrawal thresholds to electrical or thermal stimuli of white cockatoos (Hoppes et al. 2003) however, a 10-fold increase in the dosage (0.2 mg/kg) administered subcutaneously did produce an antinociceptive response, but some birds were hyperactive for the first 15–30 minutes after receiving the high dose (Hoppes et al. 2003). Fentanyl had rapid absorption and elimination in cockatoos (*Cacatua* spp.), with a terminal half-life of 1.15 hours (Hoppes et al. 2003). Administered as an IV CRI in red-tailed hawks, fentanyl reduced the minimum anesthetic concentration of isoflurane 31 to 55% in a dose-related manner, without significant effects on heart rate, blood pressure, $PaCO_2$, or PaO_2 (Table 15.3) (Pavez et al. 2011). In a similar study with Hispaniolan Amazon parrots, fentanyl administered as an IV CRI reduced isoflurane MAC similarly to the red-tailed hawks; however, approximately 20 times higher dosing was necessary to achieve the same effects and significant effects were detected in HR and BP, suggesting that while this can also be an effective opioid in these birds, close monitoring is recommended (Hawkins et al. 2018). In several breeds of chickens, the plasma concentrations of fentanyl were evaluated following application of 25 μg/h transdermal fentanyl patches (TFP) (Delaski et al. 2017). The TFPs were in place for 72 hours over the left iliopsoas muscle after plucking the feathers in the region. There was a significant degree of interindividual difference in maximum plasma fentanyl concentrations that was attributed to absorption variability, but all chickens achieved human target plasma concentrations of 0.2–1.2 ng/mL within 2–4 hours and had a rapid decrease in concentrations following patch removal. Based on these findings, fentanyl transdermal patch application for chickens targeted to provide 8–10 μg/kg/h fentanyl resulted in plasma concentrations within the range considered therapeutic in people for 72 hours (Delaski et al. 2017). A transdermal fentanyl solution has been evaluated in Helmeted guineafowl (*Numida meleagris*) (Waugh et al. 2016). The solution was placed on the skin in the interscapular region at 5 mg/kg, which resulted in mean plasma concentrations above those considered analgesic for dogs (0.6 ng/mL) from 4 hours through to at least 7 days with no evidence of adverse effects or change in behavior. Unfortunately, this commercial formulation has been discontinued at the time of writing this chapter. Further studies would be needed to evaluate effective and safe plasma concentrations of fentanyl in birds.

Butorphanol is a mixed κ-opioid receptor agonist and μ-opioid receptor antagonist opioid drug. This opioid has historically been one of the most commonly used opioid analgesics in birds, despite many studies suggesting it requires very frequent dosing. There is some evidence to suggest that butorphanol does not produce dose-related respiratory depression in contrast to μ-receptor agonists. Earlier isoflurane-sparing studies using butorphanol (1 mg/kg) produced an isoflurane-sparing effect in cockatoos and African grey parrots, but not in blue-fronted Amazons (*Amazona aestiva*), indicating species variability either in response to the drug itself or to the dose administered (Curro 1994; Curro et al. 1994). In parakeets, butorphanol (3 and 6 mg/kg) reduced the MAC of sevoflurane 10 and 17%, respectively (Martini et al. 2020). Similarly, in guinea fowl butorphanol (2–4 mg/kg) also reduced sevoflurane MAC by 9 and 21%, respectively (Escobar et al. 2014). When the 4 mg/kg dose of butorphanol was administered rapidly IV there were significant arrhythmias in all birds, significant decreases in heart rates and arterial blood pressures, and one bird died (Escobar et al. 2014). Preoperative butorphanol administration (2 mg/kg IM) did not show significant anesthetic (including time to intubation and extubation) or cardiopulmonary changes in Hispaniolan Amazon parrots anesthetized with sevoflurane (Klaphake et al. 2006). In African grey parrots butorphanol (1–2 mg/kg) showed an increased withdrawal threshold in response to electrical stimuli (Paul-Murphy et al. 1999). In a thermal antinociceptive study in which butorphanol dosages of 3 and 6 mg/kg IM were evaluated in Hispaniolan Amazon parrots, both dosages similarly increased thermal withdrawal thresholds (Sladky et al. 2006). The IV, IM, and PO pharmacokinetics of butorphanol were evaluated in Hispaniolan Amazon parrots (Guzman et al. 2011). Oral administration had very limited bioavailability (5.9%) and is not recommended. The $t_{1/2}$ (half life) of IM and IV administration was very similar at 0.51 and 0.49 hours, respectively. Butorphanol administered at 6 mg/kg IM attained high plasma concentrations which

decreased rapidly over time (Guzman et al. 2011). Based on results in Hispaniolan Amazon parrots, butorphanol tartrate administered at 5 mg/kg IV or IM would have to be administered every 2 and 3 hours, respectively, to achieve target plasma concentrations determined in pharmacodynamic studies (Sladky et al. 2006).

In contrast, American kestrels (Guzman et al. 2014a) administered butorphanol tartrate at 1, 3, and 6 mg/kg IM showed no significant increase in foot withdrawal thermal threshold values and no sedative effects were observed. Instead, hyperesthesia or hyperalgesia and agitation were noted in males receiving 6 mg/kg. Because of these findings, butorphanol is not recommended in this species for pain management until further evidence of its analgesic properties is available. One study evaluating the pharmacokinetics of 0.5 mg/kg butorphanol in red-tailed hawks and great-horned owls (*Bubo virginianus*) found terminal half-lives of 0.93 and 1.78 hours, respectively, when given intravenously, and 0.94 and 1.84 hours, respectively, when given intramuscularly, suggesting the drug requires very frequent dosing in these species (Riggs et al. 2008). Likewise, when a dose of 2 mg/kg butorphanol was administered intravenously to domestic chickens, its terminal half-life was shorter in chickens than in humans, dogs, cattle, rabbits, and owls but longer than in red-tailed hawks (Singh et al. 2011). In a recent study in evaluating the analgesic efficacy of butorphanol, lame broiler chickens underwent an obstacle course and latency-to-lie test before injection at 30 minutes and 2 hours after injection to assess walking and standing ability (Singh et al. 2017). Following 2 mg/kg IV of butorphanol, chickens finished the obstacle course faster after the injection of butorphanol and the authors concluded that it may be analgesic in chickens for up to 2 hours. All these data confirm that frequent dosing of butorphanol is necessary in birds. This may be impractical because of lack of personnel to provide frequent dosing and the stress of frequent handling on the patient. In common peafowl, the pharmacokinetics of butorphanol were assessed after administration via an osmotic pump, a novel delivery method (Clancy et al. 2015). Two osmotic pumps containing 2 mL of butorphanol at a concentration depending on body weight of the bird administering the drug at a rate of 247 μg/kg/h each were surgically implanted in 12 birds and removed 7 days later. The osmotic pumps were 5.1 cm in length and weighed 5.1 g. Plasma butorphanol concentration was measured before implantation SC in the left inguinal region for several hours to days after implantation and 3 and 6 hours after the implant removal. Plasma concentration reached 60 ng/mL after 24 hours in most birds, and in most birds stayed above this threshold for 7 days, then decreased rapidly after implant removal. There was no evidence of sedation or adverse effect. This delivery method holds promise for pain management in large birds with the limitation that it will likely require deep sedation or general anesthesia for implantation and removal. Further research evaluating continuous rate infusions of butorphanol is needed to identify whether this is a good drug for use in balanced anesthesia/analgesia protocols.

Buprenorphine hydrochloride has a slow onset of action with longer duration than other opioid drugs and a unique and complex pharmacological profile. Buprenorphine is thought to act as a partial μ agonist but its κ-receptor activities are less well defined. Several studies suggest that buprenorphine demonstrates κ-receptor agonist effects but other evidence in mammals and pigeons (*Columba livia*) suggests that it also displays some κ-antagonistic activities. Buprenorphine has unusual receptor binding characteristics that appear to be the result of slow drug dissociation from opioid receptors. Buprenorphine at 0.1 mg/kg IM in African grey parrots did not demonstrate any antinociceptive effect when tested by noxious electrical stimulus and pharmacokinetic analysis suggests this dose may not achieve effective plasma concentrations determined for mammals (Paul-Murphy et al. 2004). Pigeons administered 0.25 and 0.5 mg/kg IM buprenorphine had an increased withdrawal threshold from a noxious electrical stimulus for 2 and 5 hours, respectively, suggesting that in different species this drug may have some effect at relatively low doses (Gaggermeier et al. 2003). In American kestrels (Ceulemans et al. 2014), buprenorphine did cause a significant dose-dependent thermal antinociceptive response at 0.1, 0.3, and 0.6 mg/kg IM for 6 hours compared with control treatment. At 0.6 mg/kg, a mild sedative effect was appreciated. The pharmacokinetics of 0.6 mg/kg IM and IV buprenorphine were also evaluated in kestrels and high bioavailability (94.8%) after IM dosing and a longer elimination rate than other opioids were identified (Gustavsen et al. 2014). In a pharmacokinetic study in American kestrels, SC and IM administration of 1.8 mg/kg Buprenorphine SR-LAB™ (Wildlife Pharmaceuticals, Windsor, CO, USA) were both characterized by rapid absorption (Guzman et al. 2017b). Forty-eight hours after administration mean plasma concentrations remained above the target concentration of >1 ng/mL. The elimination half-lives were 13.5 and 11.1 hours, respectively, approximately nine times longer than the half-life of 1.5 hours reported in American kestrels receiving 0.6 mg/kg IM standard buprenorphine (Gustavsen et al. 2014). This difference was expected due to the sustained release properties of this formulation and the higher dose administered than in the prior study. SC hematomas in three of the birds that received Buprenorphine SR-LAB™ SC were attributed to traumatic administration but resolved without intervention. A follow-up study evaluating the thermal antinociceptive effects of this formulation in the

same species concluded that 1.8 mg/kg IM requires administration at least every 24 hours to manage pain but might have a longer duration of action depending on the severity and type of pain, adjunctive therapy, and the individual response (Guzman et al. 2018). In red-tailed hawks (*Buteo jamaicensis*), the pharmacokinetics of two doses of the concentrated formulation of buprenorphine (Simbadol®, Zoetis, Kalamazoo, MI, USA) were evaluated after SC administration (Gleeson et al. 2018). Maximum buprenorphine concentration was achieved at approximately 5 and 15 minutes for the 0.3 and 1.8 mg/kg doses, and plasma concentrations were maintained above 1 ng/mL for at least 24 and 48 hours, respectively. Mean elimination half-lives were 6.23 and 7.84 hours, respectively, for the low and high doses. Adverse effects were not noted in any birds. The use of this concentrated buprenorphine formulation might help reduce stress related to repeated handling and administration of treatments in raptors while providing consistent pain management. An additional benefit is that at the same dose this formulation is more cost-effective than the standard buprenorphine formulation, which is a very important factor for wildlife rehabilitation.

In contrast, studies using cockatiels showed no significant difference in thermal withdrawal threshold using the same dosages of buprenorphine hydrochloride as in the kestrel studies, and no sedative effects were observed at any dosage (Guzman et al. 2018). In orange-winged Amazon parrots, the thermal antinociceptive effects of a concentrated formulation of buprenorphine (Simbadol®) after SC administration was evaluated (D.S.-M. Guzman, pers. comm.). Concentrated buprenorphine at 2 mg/kg resulted in a small but significant increase in thermal threshold when compared to saline, while lower doses of 0.1 and 1 mg/kg did not result in a significant effect. No significant effect of buprenorphine on agitation-sedation score was observed at any of the doses evaluated. These results provide evidence of weak efficacy at lower doses for pain management in this species, like previous findings in the cockatiels, and highlights the differences in efficacy compared with the raptors evaluated. Further studies are needed to fully determine the analgesic and adverse effects of buprenorphine in psittacines and warrants evaluation in other species.

Nalbuphine hydrochloride (HCl) is primarily a κ-receptor agonist and is a partial antagonist at the μ-receptor, like butorphanol. It is used in the treatment of moderate pain in humans and has a relatively lower incidence of respiratory depression that does not appear to be dose dependent. Nalbuphine HCl was rapidly cleared after both IM and IV dosing of 12.5 mg/kg to Hispaniolan Amazon parrots and had excellent bioavailability following IM administration, with little sedation and no adverse effects (Keller et al. 2011). This dosage increased thermal foot withdrawal threshold values in this species for up to 3 hours while higher dosages (25 and 50 mg/kg IM) did not significantly increase thermal foot withdrawal threshold values (Sanchez-Migallon et al. 2010).

Tramadol hydrochloride is an analgesic drug often used in avian medicine due to its ability to be dosed orally. It is a synthetic μ-opioid receptor agonist that appears to have variable efficacy depending on the species. The efficacy is thought to be primarily related to the production of the o-desmethyltramadol metabolite (M1). This metabolite acts centrally over the opioid receptor and is thought to have almost 200 times higher affinity for this receptor than the parent drug. Tramadol also has effects on the κ and δ opioid receptors, as well as inhibiting reuptake of norepinephrine and serotonin (Scott & Perry 2000). The conversion to the M1 metabolite is variable among species, but it is produced in the bird species studied thus far (Black et al. 2010; Kilburn et al. 2014; Souza et al. 2009, 2011, 2012). In humans, less respiratory depression and constipation are seen with tramadol than with μ-agonist opioids, but there are no data on these potential adverse effects in other species.

Pharmacokinetic profiles have been reported for American bald eagles (*Haliaeetus leucocephalus*) (Souza et al. 2009), red-tailed hawks (Souza et al. 2011), African penguins (*Spheniscus demersus*) (Kilburn et al. 2014), Indian peafowl (*Pavo cristatus*) (Black et al. 2010), and Hispaniolan Amazon parrots (Souza et al. 2012), and important differences exist with pharmacokinetic parameters between species. Oral bioavailability of tramadol was higher (98%) for American bald eagles than humans and dogs, suggesting this as a useful route of administration for this species. The terminal half-life of tramadol in bald eagles after oral dosing was two times that reported in dogs, but only half that of humans. Tramadol 11 mg/kg PO achieved concentrations in the human analgesic range for 10 hours in five out of six bald eagles; M1 plasma concentrations reached the human therapeutic range only in two eagles at much earlier time points (Souza et al. 2009).

In red-tailed hawks administered 11 mg/kg PO, analgesic thresholds for humans were maintained for approximately 4 hours with a $t_{1/2}$ of 1.3 (±0.6) (Souza et al. 2011). Based on the pharmacokinetic profile, the recommended dose is 15 mg/kg PO q12h (administer twice a day). In Hispaniolan Amazon parrots, doses of 10 or 20 mg/kg orally did not result in significant antinociception to thermal stimuli and human analgesic thresholds were only reached after dosing with 30 mg/kg orally or 5 mg/kg IV (Guzman et al. 2012). Transient bradycardia was noted after IV administration. In adult peafowl gavaged with 7.5 mg/kg, levels of tramadol remained over the human analgesic threshold

for approximately 1 hour in two out of six birds but M1 metabolite concentrations remained above the human therapeutic threshold for 12–24 hours (Black et al. 2010). This underscores the importance of assaying for pharmacologically active metabolites in these studies. In American kestrels, tramadol at 5 mg/kg PO significantly increased thermal thresholds for 9 hours when compared with baseline thresholds, while 15 and 30 mg/kg PO resulted in fewer antinociceptive effects (Guzman et al. 2014b). In Muscovy ducks (*Cairina moschata domestica*), tramadol at 30 mg/kg PO was effective in improving gait in a temporary arthritis model and assessed by ground-reactive forces measured by a pressure-sensitive walkway system (Bailey et al. 2019). A pharmacokinetic study by the same investigators in the same species following administration of tramadol at 30 mg/kg PO, showed that it has an elimination half-life of 3.95 hours, with a maximum concentration of 780 ng/mL at 1.16 hours (Bailey et al. 2019). In this study, it was also demonstrated that Muscovy ducks readily produce the M1 metabolite and maintain it well above the concentrations that are known to be therapeutic for humans and other avian species. In African penguins (*Spheniscus demersus*) the pharmacokinetic parameters were determined following 10 mg/kg PO administration (Kilburn et al. 2014). The elimination half-life for tramadol was 7.3 hours, which is significantly longer than other species reported. Tramadol and M1 concentrations were determined and were consistent with therapeutic concentrations in humans for 12 hours for tramadol and 36 hours for M1. Based on plasma concentrations alone, the authors concluded that an oral dose of 10 mg/kg of tramadol once daily could be used in this species.

Tapentadol is an analgesic agent that acts as both a μ-opioid receptor agonist and a norepinephrine reuptake inhibitor. It is a common therapeutic agent in human medicine for management of acute and chronic pain and is beginning to be investigated for use in veterinary medicine. The pharmacokinetics of tapentadol were evaluated in Hispaniolan Amazon parrots following a single 30 mg/kg PO of a compounded 5 mg/mL tapentadol suspension (Duvall et al. 2021). Detectable plasma concentrations were identified in only two out of seven birds. The low oral bioavailability and short half-life of this drug in Hispaniolan Amazon parrots suggest that this drug would be of limited clinical use in this species, but further studies are recommended in other avian species to evaluate its analgesic potential.

Non-steroidal Anti-inflammatory Drugs

NSAIDs are used to relieve musculoskeletal and visceral pain, acute pain, and chronic pain such as in osteoarthritis. The pharmacological activity of NSAIDs has been reviewed elsewhere and the mechanism of action is similar when administered to birds (Bergh & Budsberg 2005; Papich 2008). A broad tissue distribution of cyclooxygenase (COX) has been demonstrated in chickens (Mathonnet et al. 2001). The relative expression of COX-1 and COX-2 enzymes varies between species and both enzymes are important in pain and inflammation. The application and dosages of NSAID formulations continues to be scientifically evaluated and clinically applied in birds. The intention of recently developed NSAIDs has been to spare COX-1 and emphasize COX-2 inhibition with the goal of providing analgesia and suppressing inflammation without inhibiting the physiologically important prostaglandins. The common NSAIDs used in avian medicine include meloxicam, carprofen, celecoxib, robenacoxib, and piroxicam, each with a distinct COX-1/COX-2 ratio and differing reports of effectiveness and toxicity in birds.

The most common adverse effects of NSAIDs include effects on the gastrointestinal system, renal system, and coagulation. NSAIDs have been implicated in humans and mammals with an increased risk of myocardial infarction and delays in bone healing (Dajani & Islam 2008; Gerstenfeld et al. 2003), but these effects have not been substantiated to date in birds. It is prudent to remember these adverse effects are often dose dependent and associated with chronic administration. The kidney uses both COX-1 and COX-2 for prostaglandin synthesis and injury occurs when renal prostaglandin synthesis is inhibited. Originally it was hypothesized that the adverse renal effects of NSAIDs were linked primarily to COX-1 inhibition but COX-2 metabolites have been implicated in maintenance of renal blood flow, mediation of renin release, and regulation of sodium excretion. Therefore, in conditions of relative intravascular volume depletion and/or renal hypoperfusion such as dehydration, hemorrhage, hemodynamic compromise, heart failure, and renal disease, interference with COX-2 activity can have significant deleterious effects on renal blood flow and glomerular filtration rate.

The pharmacokinetics of NSAIDs are typically measured from plasma samples but it is important to remember that tissue kinetics may differ significantly, with drugs that have short plasma half-lives being active in the tissue long after the drug has disappeared from the plasma. In mammals this has been evaluated using tissue cages, where it is possible to measure the effect and duration of the NSAID by quantitating the effect on prostaglandins in the tissue. With robenacoxib in cats for example, the mean residence time (MRT) following oral administration was 3.3 hours whereas the MRT in tissue was 24 hours (Pelligand et al. 2012). To the authors knowledge only a single report describes the use of this model in turkeys for evaluation of

sodium salicylate (Cramer et al. 2015) but the researchers did not include plasma concentrations.

Meloxicam is the most widely used anti-inflammatory medication today in avian practice. Meloxicam is a COX-2-selective NSAID that demonstrates COX-1 selectivity at higher doses (Baert & De Backer 2002a, 2003; Castineiras et al. 2021). Meloxicam is currently available in the United States as an oral tablet, oral suspension, and injectable formulation. Single-dose pharmacokinetic studies of meloxicam in chickens (Baert & De Backer 2002a; Souza et al. 2018, 2021), ostriches (*Struthio camelus*; Baert & De Backer 2002a), emus (*Dromaius novaehollandiae*; Baert & De Backer 2002b; Castineiras et al. 2020), mallard ducks (Baert & De Backer 2003), Bilgorajska geese (Sartini et al. 2020), brown pelicans (*Pelecanus occidentalis*; Horgan et al. 2020), turkeys (*Meleagris* spp.; Baert & De Backer 2003), Japanese quail (*Coturnix japonica*; Turk et al. 2021a), Chukar partridge (*Alectoris chukar*; Cetin et al. 2021), pigeons (Baert & De Backer 2003), zebra finches (Miller et al. 2019), ring-necked parakeets *(Psittacula krameria*; Wilson et al. 2004), Hispaniolan Amazon parrots (Molter et al. 2013), African grey parrots (Montesinos et al. 2011), cockatiels (*Nymphicus hollandicus*; Dhondt et al. 2017; Gasthuys et al. 2019), flamingos (*Phoeniconaias minor, Phoeconipterus ruber, Phoeconipterus ruber*; Boonstra et al. 2017; Lindemann et al. 2016; Zordan et al. 2016), African penguins (*Sphenicus demersus*; Morrison et al. 2018), red-tailed hawks and great-horned owls (Lacasse et al. 2013), and multiple vulture species (*Gyps africanus, Gyps coprotheres, Torgos tracheliotos*, and *Neophron pernopterus*; Naidoo et al. 2008) have been published.

Differences in dosage, bioavailability, clearance, and elimination half-lives most likely contribute to the clinical differences seen with the use of this NSAID. For example, the elimination half-life of meloxicam in chickens and pigeons is three times as long as that of ducks, ostriches, and turkeys (Baert & De Backer 2003). Meloxicam in Wyandotte hens had a greater area under the plasma concentration versus time curve, a smaller elimination rate constant, and longer terminal half-life, and the drug persisted longer in their egg yolks compared with white leghorn hens, suggesting the dosing interval of meloxicam administered PO may be every 24 hours as opposed to every 12 hours in white leghorn chickens. Following 1 mg/kg PO administration of meloxicam the elimination half-life and bioavailability of meloxicam in Hispaniolan Amazon parrots were 15.8 ± 8.6 hours and 49–75%, respectively (Molter et al. 2013). However, in African grey parrots following 1 mg/kg meloxicam PO the elimination half-life was twice that of Hispaniolan Amazon parrots, with significantly lower oral bioavailability (38.1% ± 3.6%) (Montesinos et al. 2017). In cockatiels, following 1 mg/kg meloxicam PO of the commercial formulation, it was found to have only 11% oral bioavailability and an elimination half-life of less than 1 hour (Dhondt et al. 2017). The highly variable bioavailability in avian species (Lacasse et al. 2013; Molter et al. 2013; Montesinos et al. 2011) is quite different to that in mammals where it is usually 85% or greater (Dhondt et al. 2017). A possible explanation could be variability in proventricular pH among species (Montesinos et al. 2017). In a multiple-dose pharmacokinetic study performed in African grey parrots evaluating three different dosages (1 mg/kg IM q24h (once a day), 1 mg/kg PO q24h, and 1.6 mg/kg PO q24h) plasma concentrations were maintained at values greater than effective analgesic concentrations described for other avian species and evidence of moderate drug accumulation was found with both IM and PO routes of administration (Montesinos et al. 2019). In white leghorn chickens, dosing of meloxicam 1 mg/kg PO q12h for 5 days resulted in the presence of meloxicam residues in eggs in the yolks and whites after 8 and 3 days, respectively (Souza et al. 2018) whereas Wyandotte chickens administered a single 1 mg/kg dose showed residues at 4 and 9 days, respectively (Souza et al. 2021). Based on these results, a 2-week withdrawal time should be adequate to avoid drug residues in eggs meant for consumption (Souza et al. 2018, 2021). Meloxicam was also identified in two out of three unfertilized eggs of captive bearded vultures after breeding failure, but the implication is unclear (Zorrilla et al. 2018). The large variability in pharmacokinetics between avian species is one of the main issues with analgesic therapy in birds, as cross-species allometric scaling is not reliable and therefore pharmacokinetic/pharmacodynamic analysis is required in every species (Baert & De Backer 2003).

A sustained-release formulation of meloxicam (Meloxicam SR, Wildlife Pharmaceuticals, Windsor, CO, USA) has been evaluated in two species: Hispaniolan Amazon parrots (Guzman et al. 2017a) and American flamingos (Sim & Cox 2018). Based on the results of these studies its use cannot be recommended due to huge pharmacokinetic variability (parrots) and lack of difference from standard meloxicam (flamingos).

There are very few studies evaluating the pharmacodynamics of meloxicam to date. In an experimental trial in lame chickens, meloxicam significantly increased the thermal threshold compared to saline (Hothersall et al. 2014). Administration of meloxicam at 0.5 or 2 mg/kg IM reduced clinical signs associated with experimental systemic inflammation induced by *E. coli* lipopolysaccharide in broiler chickens, but dexamethasone was ultimately preferred by the authors for its clinical effects of reducing the acute inflammation (Nakhaee et al. 2021).

Since higher doses of meloxicam can block COX-1 enzyme activity, this drug has the potential to induce the adverse effects of gastrointestinal, renal, and cardiac toxicity seen in mammals, yet reports of intoxication at doses used in avian practice are minimal. In a number of studies evaluating the adverse effects of meloxicam in budgerigars (*Melopsittacus undulates*, 0.1 mg/kg IM; Pereira & Werther 2007), African grey parrots (0.5 mg/kg IM; Montesinos et al. 2015), zebra finches (1–2 mg/kg PO; Miller et al. 2019), domestic pigeons (2 mg/kg IM; Desmarchelier et al. 2012b), Japanese quail (2 mg/kg IM; Sinclair et al. 2012), American kestrels (*Falco sparverius*, 2–20 mg/kg PO; Summa et al. 2017), and Hispaniolan Amazon parrots (1.6 mg/kg PO; Dijkstra et al. 2015), no significant renal, gastrointestinal, or hemostatic adverse effects were reported at doses in the therapeutic range. However, two out of nine American kestrels had gastric ulceration after a dose of 20 mg/kg (Summa et al. 2017). Plasma and urine N-acetyl-β-D-glucosaminidase activities were significantly increased in African grey parrots at 1.6 mg/kg meloxicam administered PO every 24 hours for 7 days (Montesinos et al. 2019). Elimination half-lives of meloxicam are highly variable, as indicated above, and those species with rapid elimination (Dhondt et al. 2017) are less likely to have adverse effects. Anecdotal reports of visceral gout and gastrointestinal ulceration in brown pelicans, using dosages commonly used in other species, prompted a pharmacokinetic study using a single dose of 0.2 mg/kg PO. The elimination half-life was 36 hours, the highest reported to date in any species, heightening suspicion that adverse effects, including renal toxicity, may be attributed to this (Horgan et al. 2020). The renal effects of NSAIDs have been of particular concern in the Asian vultures (*Gyps bengalensis*, *G. indicus*, and *G. tenuirostris*) (Naidoo et al. 2010; Oaks et al. 2004) but meloxicam may be the exception because of its short elimination half-life (<1 hour) (Swarup et al. 2007). However, recently meloxicam was detected in eggs of captive bearded vultures (*Gypaetus barbatus*) (Zorrilla et al. 2018). Despite meloxicam's large therapeutic range and relative safety compared with other NSAIDs, these new data demonstrate that dose extrapolation is not a suitable method for meloxicam dose determination in avian species. Species-specific pharmacokinetic, efficacy, and toxicity studies are necessary to determine appropriate dosages for different species.

The newer NSAID coxibs celecoxib, mavacoxib, and robenacoxib are COX-2 selective as opposed to meloxicam, which is COX-2 preferential, inhibiting both COX-1 and COX-2. Celecoxib in humans is used for acute pain, osteoarthritis, rheumatoid arthritis, and spondylitis. Its use in veterinary medicine is off-label in the United States: it is not approved for use in any veterinary species. Celecoxib 10 mg/kg PO every 24 hours has been used to reduce inflammation associated with avian ganglioneuritis (Hoppes et al. 2013). A recent study in cockatiels using this dose did not alter the clinical presentation, viral shedding, gross lesions, histopathology, or viral distribution in cockatiels experimentally inoculated with PaBV-2 (Escandon et al. 2019), but the birds were infected with a large viral load inducing severe disease, so it is difficult to determine whether this drug has any efficacy against natural inflammation induced by this disease. Mavacoxib administered orally has a long mean half-life of 15.5 days in dogs, allowing for monthly dosing after two loading doses administered 1 week apart (Lees et al. 2015). Plasma concentrations of 0.4 μg/mL mavacoxib were associated with efficacy in reducing osteoarthritis in dogs (Payne-Johnson et al. 2014).

The single-dose pharmacokinetics and oral bioavailability of celecoxib 10 mg/kg PO and mavacoxib 4 mg/kg PO were evaluated in the cockatiel (Dhondt et al. 2017). Mavacoxib was completely absorbed (bioavailability = 111%) but celecoxib only had a mean oral bioavailability of 56% (Dhondt et al. 2017). Bioavailability of the coxibs is often directly associated with feeding status; the presence of food has been shown to increase absorption of both NSAIDs (Cox et al. 2010). The cockatiels in this study were fed ad libitum. A further study in cockatiels with ad libitum feeding and additional gavage feedings during the study showed that changes in body temperature, mentation, and posture were less pronounced with a single dose of mavacoxib 4 mg/kg PO compared to celecoxib 10 mg/kg at the tested dosages (Gasthuys et al. 2019). This is likely associated with the higher oral bioavailability of mavacoxib in cockatiels compared to celecoxib and meloxicam. Plasma concentrations of 0.4 μg/mL mavacoxib, found to be effective in osteoarthritic dogs (Cox et al. 2011), were maintained for 1000 hours in the cockatiels in the aforementioned studies (Dhondt et al. 2017; Gasthuys et al. 2019) and Caribbean flamingos maintained plasma concentrations >0.4 μg/mL for 120 hours after a single dose of 6 mg/kg (Huckins et al. 2020). Elimination half-lives in cockatiels (135 hours) (Dhondt et al. 2017) and Caribbean flamingos (*Phoenicopterus ruber*) (74.5 hours) (Huckins et al. 2020) were not as long as in dogs but are still much longer than most NSAID elimination half-lives in birds and prompts additional studies to determine dosing regimens (Huckins et al. 2020).

No studies have been published to date on the use of robenacoxib, also a long-acting COX NSAID, but it is being used anecdotally at 2–10 mg/kg IM (Lamb 2019) weekly initially, then monthly in birds with clinical avian bornavirus (Rossi et al. 2018) and West Nile virus. Robenacoxib is available as tablets and in an injectable formulation currently in the United States

The oral bioavailability of carprofen was reported to be 61% in Japanese quail (Turk et al. 2021a). Carprofen given SC improved the locomotion of lame domestic fowl significantly in a dose-dependent manner (McGeowen et al. 1999) and lame birds self-selected food containing carprofen (Danbury et al. 2000). When carprofen was administered at 3–4 mg/kg in drinking water, 15% of birds died on day 10 of treatment so short-term (<7 days) therapy for lameness was recommended (Hadipour et al. 2011). Carprofen administered at 3 mg/kg IM q12h was insufficient to restore weight-bearing in induced arthritis in Hispaniolan Amazon parrots (Paul-Murphy et al. 2009b). The author (M.G.H.) has used this NSAID (1–4 mg/kg PO, SC, and IM q12–24h) short-term (<7 days) in many species. In pigeons, doses of 2, 5, and 10 mg/kg given IM once daily over 7 days resulted in significant increases in alanine aminotransferase and aspartate aminotransferase, and a mild decrease in total protein (primarily globulin) (Zollinger et al. 2011). Additionally, small intestinal vascular congestion was noted grossly and hepatic necrosis, renal congestion, and myodegeneration of the pectoral muscles were noted histologically. These effects were significantly associated with dosing (Zollinger et al. 2011). While not significant, hepatic lipidosis was also noted and the frequency increased with dose. The authors speculate this may be secondary to decreased food consumption noted in pigeons within the highest dosing group (Zollinger et al. 2011).

Even though it is believed that carprofen ingested by Gyps vultures does not pose a toxic risk like diclofenac, there are still concerns about its safety in these birds. A recent pharmacokinetic and toxicokinetic study in white-backed vultures (*Gyps africanus*) of 5 mg/kg administered IV, IM, and PO for the pharmacokinetic study and a subset of birds were administered the dosage found at injection sites in cattle (64 mg/kg) for the toxicology study. Carprofen was well tolerated at 5 mg/kg via all routes of administration, but oral bioavailability was only 42% (Naidoo et al. 2018). One vulture died in the toxicology, study with elevations of uric acid and potassium identified, like toxicity found with diclofenac and ketoprofen in Gyps vultures. The authors suggest that carprofen should not be used in domesticated ungulates in areas where carcasses are accessible or provided to vultures at supplementary feeding sites (Naidoo et al. 2018).

Ketoprofen is commonly used parenterally because of limited oral pharmacokinetic data and difficulty in accurately dosing in small species. In Japanese quail (*Coturnix japonica*) ketoprofen (2 mg/kg PO, IM, IV) showed very low oral (24%) and IM (54%) bioavailability and the shortest half-life reported for any species (Graham et al. 2005). Additional studies are needed to determine whether drug formulation or interspecies physiologic contrasts account for these differences. In mallard ducks ketoprofen (5 mg/kg IM) decreased blood thromboxane B_2 levels for approximately 12 hours (Machin et al. 2001).

Ketoprofen and meloxicam were detected in the eggs of captive-reared bearded vultures (Zorrilla et al. 2018). Two studies evaluating the effects of an extraordinarily high single dose (50 mg/kg IM) of ketoprofen, as a premedication to ketamine and midazolam in pigeons, found no significant clinical differences, biochemistry analytes, or histopathology between the groups (Hajizadeh et al. 2018a,b). Regardless of their findings, the extremely high dosing of this drug should be reviewed in multidose studies and with the utmost caution before considering it for clinical use.

Piroxicam is a nonselective NSAID used for its anti-inflammatory properties and its value as a chemopreventative and antitumor agent. It has a much higher potency against COX-1 than COX-2. In chickens, IM administration of 1–2 mg/kg of piroxicam twice daily for 4 days failed to result in gastrointestinal lesions consistent with toxicity (Awan et al. 2012). Piroxicam has been used in cranes for more than 20 years to treat a variety of conditions including trauma, inflammation, and postoperative pain with minimal observed side effects (Keiper et al. 2017). A pharmacokinetic study in brolga cranes (*Grus rubicunda*) evaluated two single doses of 0.5 and 1 mg/kg PO, finding that daily administration might be appropriate for this species based on plasma concentrations (Keiper et al. 2017).

Scavenging bird species such as vultures and eagles may be exposed to NSAIDs when they feed on livestock carcasses (Green et al. 2016; Sharma et al. 2014). The NSAID diclofenac played the major role in the catastrophic decline in vulture populations on the Indian subcontinent (Swan et al. 2006). Subsequently, other NSAIDs have also been identified as toxic to vultures. Ketoprofen and nimesulfide, a sulfonamide NSAID, caused visceral gout and death in vultures whereas meloxicam and tolfenamic acid (TA) were reported to be safe (Chandramohan et al. 2022; Cuthbert et al. 2016; Galligan et al. 2021, 2022; Naidoo et al. 2010; Nambirajan et al. 2021; Stokstad 2021).

Other NSAIDs must be identified to reduce the use of those toxic to vultures and other scavengers. TA is an NSAID belonging to the fenamates group (Lascelles et al. 2007). This NSAID inhibits both COX-1 and COX-2 receptor activity and exerts potent antitumor activity by both COX-dependent and -independent pathways (Corell 1994). TA was detected in 20% Eurasian griffon vulture (*Gyps fulvus*) nestling samples (Gómez-Ramírez et al. 2020), suggesting it is being used more frequently by veterinarians in the region. A study evaluated the safety of

TA in three *Gyps* species, all of which are susceptible to diclofenac poisoning. Two birds administered 3.5 mg/kg TA PO via gavage died with elevated uric acid levels and severe visceral gout, yet the remainder showed no adverse clinical or biochemical signs at the same or even higher dosages, suggesting the deaths may have been an anomaly due to the high dose used and the high ambient temperatures at the time of the experiment (Chandramohan et al. 2022). TA is likely to be safe to *Gyps* vultures at concentrations encountered by wild birds and could therefore be promoted as a safe alternative to toxic NSAIDs (Chandramohan et al. 2022).

To date only the pharmacokinetics of TA in chukar partridge (Cetin et al. 2021), Japanese quail (Turk et al. 2021a), and geese (*Anser cygnoides*)(Turk et al. 2021b) have been reported. The terminal elimination half-lives ($t_{1/2}\lambda_z$)of TA administered PO in chukar partridges, Japanese quail, and geese were 1.25, 1.95, and 2.31 hours, quite similar to meloxicam (Cetin et al. 2021; Turk et al. 2021b). These short $t_{1/2}\lambda_z$ are important in preventing drug accumulation and delaying toxic effects in repeated administrations in birds (Naidoo et al. 2008). Bioavailability after a 2 mg/kg dose was 88, 78, and 76% for the IM, SC, and oral routes, respectively in geese, and 57% via the oral route in Japanese quail, suggesting good absorption in these species.

Currently there are no specific dosing recommendations for TA in birds, but it is recommended at doses of 2–4 mg/kg in mammals and reptiles (Corum et al. 2019; Tekeli et al. 2020). While the few studies to date are promising, additional studies evaluating clinical efficacy, multidose pharmacokinetics, safety, and residue data of tolfenamic acid should be conducted before widespread use of TA in birds at mammalian doses.

Prostaglandin Receptor Antagonists

Grapiprant is a prostaglandin E2 (PGE_2) receptor antagonist approved for use in dogs in the United States. Grapiprant binds to the E-type prostanoid receptor 4, blocking the sensitization of sensory neurons and stimulation of inflammation, mediated by the PGE_2 receptor. It does not rely on inhibition of COX enzymes and preserves functions associated with COX enzyme pathways. Oral administration of grapiprant at 30 mg/kg to fasted red-tailed hawks achieved plasma concentrations approximately 100 times the canine therapeutic concentrations with no adverse effects identified. It is still unknown whether the dog concentrations are analgesic in birds or toxic in hawks after multidosing (Rodriguez et al. 2021). Grapiprant administered at the same dosage to the same red-tailed hawks with food had significantly lower plasma concentrations compared to when fasted, with delayed absorption and similar half-lives (M.G. Hawkins, pers. comm.). Due to the concern that target plasma concentrations may not be maintained if this dosage is administered every 24 hours versus every 12 hours, multidose modeling simulations showed that the concentrations troughs are still above the target plasma concentrations in dogs for analgesia (M.G. Hawkins, pers. comm.). Further studies to evaluate the pharmacokinetics and pharmacodynamics of multidose grapiprant with food in red-tailed hawks are underway.

Gabapentin

Gabapentin is an analog of the neurotransmitter gaba-aminobutyric acid that binds to voltage-gated calcium channels acting presynaptically to decrease the release of excitatory neurotransmitters, especially glutamate. In humans and animals, it is best used as an adjunct to other analgesics and seems to be most effective for neuropathic pain. Some formulations of gabapentin contain xylitol and these should not be used in birds until further safety evidence is available. The pharmacokinetics of gabapentin have been evaluated in several species. The oral bioavailability was found to be high (>80%) in one species (Hispaniolan Amazon parrots, *Amazona ventralis*) (Baine et al. 2015) and the peak plasma concentration occurs between 0.5 and 2.5 hours (Baine et al. 2015; Browning et al. 2018; Yaw et al. 2015). The terminal elimination half-life has been in the range of 3–5 hours and so gabapentin should be administered two or three times per day to maintain adequate plasma concentrations. In great horned owls (*Bubo virginianus*) following oral administration of 11 mg/kg PO, plasma gabapentin concentrations were maintained above 2 ug/mL for 9.6 hours (Yaw et al. 2015). In Caribbean flamingos (*Phoenicopterus ruber ruber*), gabapentin dosed at 25 mg/kg orally in most Caribbean flamingos maintained plasma concentrations above the therapeutic range established for humans for approximately 12 hours; however, dosages as high as 37 mg/kg orally every 12 hours may be needed in some individuals. Pregabalin is like gabapentin but its use in birds has not been described.

Amantadine

Amantadine is an antiviral medication that increases dopamine in the central nervous system and weakly inhibits the NMDA receptors that contribute to chronic pain (KuKanich 2013). Amantadine is synergistic with NSAIDs, opioids, and gabapentin/pregabalin. In humans,

amantadine has been shown to decrease opioid use in postoperative patients, decrease pain in postherpetic neuralgia, and aid in neuropathic pain (Abd Elmawgood et al. 2015; Bujak-Giżycka et al. 2012). Amantadine administered to dogs at 3–5 mg/kg orally every 24 hours with meloxicam showed significant improvement in management of osteoarthritis pain refractory to meloxicam alone (Lascelles et al. 2008). In orange-winged Amazon parrots, the single- and multiple-dose pharmacokinetic profile was evaluated following 10 mg/kg PO once and 5 mg/kg PO every 24 hours for 7 days (Berg et al. 2020). The heart rate, respiratory rate, behavior, and urofeces were monitored. Mean ± standard deviation maximum plasma concentration, time to maximum plasma concentration, and half-life were 1174 ± 186 ng/mL, 3.75 hours, and 23.2 hours, respectively, for the single-dose study and 1185 ± 270 ng/mL, 3.0 hours, and 21.5 hours, respectively, for the multiple-dose study at steady state. No obvious adverse effects were observed. Based on these results, once-daily administration of amantadine at 5 mg/kg orally in orange-winged Amazon parrots can maintain above-target plasma concentrations with weak accumulation. For long-term administration, especially for other species, it is recommended to check plasma concentrations over time. Further studies evaluating the safety and efficacy of amantadine in orange-winged Amazon parrots and other avian species is warranted. The use of amantadine in chickens, ducks, and turkeys is prohibited in the United States by the Federal Drug Administration.

Cannabidiol

Cannabidiol (CBD) oil is the primary nonpsychoactive cannabinoid derived from the cannabis plant (*Cannabis sativa*). The pharmacokinetics of a CBD oral formulation (50 mg/mL; Canna Companion, Mill Creek, WA, USA) have been evaluated in Hispaniolan Amazon parrots. The highly variable results and short half-life of the drug in Hispaniolan Amazon parrots, even at high doses, suggests that this formulation would have to be administered at least three or four times daily. Evaluation of other formulations and in other species is recommended to further characterize the analgesic potential of CBD in birds.

Balanced or Multimodal Analgesia

Combinations of drugs acting at different points in the nociceptive system are more effective and less toxic than either drug given alone. For example, opioids act centrally to limit nociceptive input whereas NSAIDS act peripherally to decrease inflammation, limiting the nociceptive information that enters the CNS. Synergy has been demonstrated in laboratory animals (Malmberg & Yaksh 1993) and is being tested in the clinical environment.

Appendix

Humidi-vent Mini Agibeck Product®, Hudson RCI, Temecula, CA, USA

0.9% saline, Baxter, Deerfield, IL, USA

Lactated Ringer's solution, Abbott Laboratories, N. Chicago, IL, USA

Normosol-R, CEVA Laboratories, Overland Park, KS, USA

Plasmalyte-A, Baxter, Deerfield, IL, USA

hetastarch 6%, Braun Medical Inc, Irvine, CA, USA

Hextend BioTime Inc., Emeryville, CA, USA

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16

Pigeons and Doves (Columbiformes)

Darryl Heard

Introduction

The order Columbiformes includes pigeons and doves. The typical columbiform has a short bill, small head, compact body, and short legs (Baptista et al. 1997). Several species are important for food production, while many are also displayed in zoos and kept as pets. Some are highly endangered (Baptista et al. 1997; del Hoyo et al. 1994). The rock dove or pigeon (*Columba livia*) is commonly used in avian research, including anesthesia. It is also valued for racing and is a ubiquitous urban inhabitant.

Anatomy and Physiology

Avian anatomy and physiology relevant to anesthesia are described in Chapter 15. Columbiform species range in size from the 30-g common ground dove (*Columbina passerina*) to the 2-kg crowned-pigeons of New Guinea (Baptista et al. 1997).

Physical Restraint

Columbiforms are relatively easy to handle and are nonthreatening. Pigeons can be gently held in the hand, incorporating the tail and legs in one grip. They can, however, launch themselves explosively into the air and escape. Food-production pigeon breeds may be obese and have hepatic lipidosis (fatty liver). In addition to causing dysfunction fatty livers are friable and may rupture, causing fatal hemorrhage during handling.

Vascular Access

Vascular access is as in other birds (Chapter 15) and includes the external jugular, basilic (ulnar) and medial tarsometatarsal or saphenous veins. The external jugular veins of pigeons are sometimes difficult to identify. Intraosseous catheters are placed in the ulna or tibiotarsus, avoiding the air-filled humerus or femur. Intraosseous catheters have been used for administration of propofol in pigeons (Guimarães et al. 2006; Lopez et al. 1994). In crowned and other large pigeons the medial saphenous vein is a useful site to administer parenteral anesthetics in physically restrained animals. A 23- or 25-gauge butterfly catheter can be preplaced and secured to facilitate drug administration.

Endotracheal Intubation

Endotracheal intubation is usually simple. Columbiforms, however, sometimes produce copious amounts of tracheal mucous. This may obstruct the tube or produce a "flapper valve" effect that allows air into the respiratory system with positive pressure ventilation, but not out. In these species the patient needs to be monitored carefully to prevent hyperinflation. Clear uncuffed endotracheal tubes are preferred to visualize any respiratory discharge and periodic extubation to assess for blockage may be necessary during prolonged procedures.

Preanesthetic Considerations

As with all patients, physical examination is indicated prior to anesthesia. Columbiformes possess large complex crops. Depending on the physiological status of the bird, fasting for 4 or more hours may reduce the amount of food in the crop, but not entirely. Fluids should also be removed in animals that are likely to drink excessively, but are not dehydrated.

As in other birds, assessment from a distance can reveal much information relevant to anesthetic management. For example, evaluation of respiration rate and effort, overall

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mentation, and evaluation of the stool for evidence of liver (biliverdinuria) and renal (polyuria) dysfunction. Increased respiratory effort and distress at rest can be evidence of significant dysfunction. Botman et al. (2016) showed awake pigeons covered with a blanket and held in a quiet environment for 15 minutes have a heart rate of 155 ± 28 beats per minute. The ability of a bird to breath through its nasal cavity is important to evaluate if a mask is being used for induction.

The body condition of the bird should be assessed. As mentioned previously, many domestic species bred for food production are obese and have substantial intracoelomic fat accumulation. This fat decreases air-sac volume and may contribute to lung compression in dorsally recumbent birds, as well as impaired air sac ventilation. Both effects may be additive to anesthetic-induced hypoventilation and explain the apparent increased anesthetic morbidity and mortality seen in these species. Similarly, breeding hens are more likely to have egg-yolk coelomitis, which can lead to fibrosis, fluid accumulation, and debilitating systemic infection and illness. A high fat to total body ratio may also be associated with abnormal drug distribution and accumulation, resulting in delayed induction and recovery.

Local and Regional Anesthesia

Local anesthetics can be used as in other avian species (Chapter 15). Imani and Hasani (2016) evaluated the effects of high dosages of subcutaneous lidocaine (4–100 mg/kg). They observed sedation at dosages beginning at 20 mg/kg, and paddling, wing stretching, muscle twitching, and seizures at very high dosages (70–100 mg/kg). These toxic dosages are similar to those in mammals, but the relatively small size of most columbiforms makes accurate calculation of injected volumes (≤10 mg/kg or 0.5 mL/kg of the 2% lidocaine) essential. It is assumed the dosage of bupivacaine is also similar (≤2.0 mg/kg).

Analgesia

Avian analgesia is covered in Chapter 15. Nonsteroidal anti-inflammatory drug (NSAID) pharmacokinetics and the therapeutic index are highly variable in birds, making safe drug selection difficult (Baert & Backer 2003; Palocz et al. 2016). Regardless of the drug and species, each analgesic regimen should be tailored to the individual and the type and severity of pain (Chapter 2). A multimodal approach may be necessary, especially for severe and chronic pain. Although pigeons appear to respond best to κ-opioid agonists (i.e., butorphanol 0.3–2.0 mg/kg bid to tid), there are a few papers indicating that μ-opioid agonists (morphine and fentanyl) are appropriate in other avian species and situations (Chapters 2 and 15).

Baert and Backer (2003) studied the pharmacokinetics of a single intravenous (IV) dose of sodium salicylate (25 mg/kg), meloxicam (0.5 mg/kg), and flunixin (1.1 mg/kg) in five bird species, including chickens, turkeys, and pigeons. Chickens had a half-life (5.5 hours) approximately 10-fold as long as the other species for flunixin. The half-life of chickens (3.2 hours) and pigeons (2.4 hours) was 3-fold as long as the other bird species for meloxicam, and for salicylic acid the half-life in pigeons (14.9 hours) was at least 3–5-fold longer than in the other bird species. Once again, this study emphasizes the variability in response to NSAIDs in birds and the potential for toxicity.

In a similar study, Palocz et al. (2016) evaluated the toxic effect of administered diclofenac (5 and 50 mg/kg) and acetyl-salicylic acid (50 mg/kg) administered orally for 3 days in broiler chickens, domestic pigeons, budgerigars, and common quails. They also evaluated the effect of water deprivation on toxicity. Both doses of diclofenac caused harmful effects (renal failure and gout) in all species, with the high dose causing death in all species. Pigeons, however, appeared least sensitive to the drug. The water-deprivation significantly accelerated the mortality of chickens. The acetyl-salicylic acid was clinically well tolerated in all examined species.

Furthermore, Hussain et al. (2008) investigated the toxico-pathological effects of diclofenac sodium (0, 0.25, 2.5, 10, and 20 mg/kg orally for 7 days) in broiler chicks (15 days old), pigeons (3 months old), and Japanese quail (4 weeks old). Dose-dependent clinical signs in all included depression, somnolence, decreased body weight, and mortality. Severity of clinical disease was most severe in broiler chicks, followed by pigeons and Japanese quail. Broiler chicks and pigeons developed visceral gout at the higher dosages (10 and 20 mg/kg), but not Japanese quail. The kidneys and liver were enlarged in all and the kidneys showed acute renal necrosis. The livers had fatty change and necrosis of hepatocytes.

Meloxicam (0.5 mg/kg intramuscular [IM]) was ineffective in minimizing postoperative orthopedic pain in pigeons (Desmarchelier et al. 2012). A higher dosage (2.0 mg/kg IM), however, provided quantifiable analgesia that appeared safe in experimental conditions (Desmarchelier et al. 2012).

Chen et al. (2023) studied the pharmacokinetics of meloxicam (1 mg/kg IV, IM, PO) in pigeons. Based on the analgesic threshold (3.5 μg/mL) in parrots, they recommended a higher dose (e.g., 2 mg/kg) or shorter dosing interval (e.g., every 6 hours) for treating pain in pigeons. Coutant et al. (2023) described the successful use of an

implantable osmotic pump, filled with 0.2 mL of 40 mg/mL injectable meloxicam, in maintaining clinically significant blood levels for 12 hours to 6 days. In pigeons, carprofen (2–10 mg/kg IM once daily for 7 days) was associated with increased aspartate aminotransferase and alanine aminotransferase enzyme concentrations, gross lesions in muscle injection sites and liver, and histologic lesions in liver and muscle (Zollinger et al. 2011).

Tramadol appears useful for managing postoperative as well as chronic pain associated with degenerative joint disease. This drug is metabolized to an active metabolite, O-desmethyltramadol (Black et al. 2010). Although relatively high dosages (≥5–10 mg/kg once to twice a day PO) are recommended in birds based on some pharmacokinetic studies (Black et al. 2010; Souza et al. 2009, 2011, 2012) and a pain response study in Hispaniolan parrots (Guzman et al. 2012), this author has seen good responses in some birds with degenerative joint disease at lower dosages (1–5 mg/kg once to twice a day PO). Further research is necessary to define the blood levels associated with analgesia in pigeons and other birds, rather than using human levels. The main observed side effects are anorexia, ataxia and dysphoria, and vomiting. These effects may be seen at high dosages or after repetitive dosing. There also appears to be some individual variation in response, possibly due to variable metabolism to the active form.

Induction and Maintenance Protocols

Some sedative and parenteral anesthetic dosages are summarized in Table 16.1.

Sedation

All birds are relatively resistant to the effects of alpha-2 adrenergic agonists. In pigeons, xylazine (16 mg/kg IM) or detomidine (1.4 mg/kg IM) produced only minor to moderate sedation adequate for handling and sample collection (Durrani 2008, 2009). Similarly, in pigeons medetomidine (0.08–2.0 mg/kg IM) produced inadequate sedation for handling and minor diagnostic procedures accompanied by moderate bradypnea and bradycardia (Pollock et al. 2001; Sandmeier 2000). At the lower end of the dosage range medetomidine only produced ataxia to sternal recumbency with retention of the righting reflex (Pollock et al. 2001). In chickens, and presumably other birds, xylazine inhibits ventricular activity (Park & Park 1988). The duration of this effect is dose-dependent and reversible with either yohimbine or 4-aminopyridine.

Intranasal pipette administration of xylazine (30 mg/kg), diazepam (6 mg/kg), or midazolam (6 mg/kg) provided fast reliable sedation in pigeons (Moghadam et al. 2009). Unlike the benzodiazepines, however, xylazine failed to produce adequate sedation for dorsal recumbency and sedation was prolonged. The onset of action of midazolam was more rapid than that of diazepam. A similar study in pigeons (Hornak et al. 2015) showed midazolam (5 mg/kg) intranasally (IN) provided inadequate sedation for restraint in dorsal recumbency. The addition of dexmedetomidine (0.08 mg/kg), however, provided effective immobilization from 20 to 30 minutes after administration (Hornak et al. 2015). Atipamezole reversed sedation.

Parenteral Anesthesia

Ketamine and ketamine combinations have either been evaluated or used clinically in columbiforms (Table 16.1). The adverse effects are the same as in other avian species. Ketamine alone is not recommended because of increased salivation, muscle rigidity, and rough, sometimes prolonged, recoveries associated with wing flapping and struggling. The addition of a benzodiazepine (i.e., diazepam or midazolam) provides improved muscle relaxation and sedation, but not analgesia (Abbas et al. 2018). The addition of an alpha-2 adrenergic agonist (i.e., xylazine, detomidine, or medetomidine) is also associated with improved muscle relaxation, as well as surgical analgesia. These agonists are, however, more likely to produce cardiopulmonary depression, hypothermia, and prolonged recovery. Atipamezole, administered IM when birds first show signs of recovery, can be used to reverse medetomidine, detomidine, and xylazine. Butorphanol added to the ketamine combinations further enhances surgical analgesia, but will also further depress cardiopulmonary function (Atalan et al. 2002).

The short-acting anesthetic propofol has been evaluated in pigeons (Fitzgerald & Cooper 1990; Guimarães et al. 2006; Mehmannavaz et al. 2015). Propofol (14 mg/kg IV) produced smooth rapid induction and good muscle relaxation (Fitzgerald & Cooper 1990). The duration of effect was 2–7 minutes and was associated with marked respiratory depression. A very narrow safety margin was observed when ventilation was not assisted. Mehmannavaz et al. (2015) showed propofol (14 mg/kg bolus, then constant rate infusion 1.33 mg/kg/min using the ulna vein) induced rougher and more variable inductions compared to isoflurane, with longer recoveries.

The addition of alfaxalone (4 mg/kg IM) improved the quality of mask induction with isoflurane in oxygen (Lim et al. 2023). The physiological, including adverse, effects of alfaxalone are similar to those of propofol. When given intravenously, rapid administration and/or high dosages can result in marked hypoventilation/apnea, as well as

Table 16.1 Published reports of some parenteral sedatives and anesthetic drugs in pigeons (mg/kg).

Ketamine	Xylazine	Dexmedetomidine	Medetomidine	Detomidine	Diazepam	Midazolam	Butorphanol	Comments	Reference
						5.0 IN		Inadequate immobilization for restraint in dorsal recumbency.	Hornak et al. (2015)
		0.08 IN				5.0 IN		Effective degree of immobilization from 20 to 30 minutes after administration, at which time birds tolerated postural changes without resistance. Atipamezole antagonized both side effects and sedation, but complete recovery had not occurred within 10 minutes after its application.	Hornak et al. (2015)
						4.0 IM	2.0 IM	Mild to moderate sedation with sternal recumbency. Reversal with flumazenil 0.05 mg/kg IM. Concentrated midazolam (50 mg/mL) allowed for smaller injection volumes compared to regular midazolam (5 mg/mL).	Martel et al. (2021)
60 IM								Light sedation and anesthesia/analgesia. Hyperthermia and rough recovery. Not recommended for use alone.	Durrani et al. (2008)
				1.4 IM				Light sedation and anesthesia/analgesia. Bradypnea, bradycardia, and hypothermia. Safe for handling and least painful procedures.	Durrani et al. (2008)
60 IM				1.4 IM				Rapid onset of action (~2 minutes). Prolonged deep anesthesia and recovery with bradypnea, bradycardia, and hypothermia. Can be used for major surgical procedures.	Durrani et al. (2008)
100 IM			0.2 IM				0.2 IM	Ketamine given 15 minutes after Medetomidine/Butorphanol. Medetomidine reversed with atipamezole 60 minutes after K. Effective anesthesia for ~90% of pigeons. Bradypnea, bradycardia, arrhythmias, and hypothermia.	Atalan et al. (2002)
120 IM			0.2 IM					K 10 minutes after M. Deep anesthesia for 15–60 minutes associated with initial tachypnea then bradypnea, profound bradycardia, and progressive hyporthermia. Prolongation of P–R and R–R intervals on ECG.	Uzun et al. (2003)

30 IM		0.125 IM			M reversed with atipamezole 0.065 IM at first sign of recovery. Deeper anesthesia and analgesia than Detomidine-Ketamine. Recovery rapid and smooth. Clinically, level of anesthesia unreliable and associated with wing flapping.	Lumeij & Deenik (2003)
60 IM			2 IM		Prolonged recovery.	Lumeij & Deenik (2003)
10 IM			0.2 IM		Sedation and muscle relaxation without loss of consciousness.	Azizpour & Hassani (2012)
75–150 IM					Extensor rigidity, salivation, dose-dependent hypoxemia, respiratory acidemia, and hypercapnia.	Neal et al. (1981)
	16 IM				Light sedation/anesthesia. Safe for handling and less painful procedures.	Durrani et al. (2009)
60 IM					Light sedation/anesthesia and rough recovery. Not recommended.	Durrani et al. (2009)
30 IM	8 IM				Rapid onset (2 minutes). Deep anesthesia/ analgesia with prolonged recovery. Suitable for painful procedures ≤90 minutes.	Durrani et al. (2009)
		0.08–0.20 IM			Ataxia to sternal recumbency, but righting response retained.	Pollock et al. (2001)
5 IM		0.08 IM			Variable effects; mild to moderate sedation.	Pollock et al. (2001)
		0.08 IM		0.5 IM	Variable effects; mild to moderate sedation.	Pollock et al. (2001)

IM, intramuscular; M, Medetomidine; K, Ketamine.

hypotension. In other bird species excitement and poor muscle relaxation have been observed.

Intubation and ventilation, preferably with oxygen, are recommended when parenteral anesthetics are used for surgery and prolonged anesthesia. Administration of balanced electrolyte solutions either IV or IO will also ameliorate some of their hypotensive effects.

Inhalation Anesthesia

Isoflurane and sevoflurane are the most commonly used inhalant anesthetics in clinical practice. Their physiological effects and potencies in columbiforms are the same or slightly higher than in other avian orders (Botman et al. 2016; Korbel 1998; Legler et al. 2019). Isoflurane anesthetized pigeons were more likely to have bradyarrythmias than when awake (Legler et al. 2019). Although sevoflurane is associated with a more rapid induction and recovery (Korbel 1998), it does not appear to be clinically significant in birds.

As described previously, many domestic species have large stores of intracoelomic fat that impair ventilation, potentially prolonging inhalant anesthetic equilibration and recovery. In isoflurane anesthetized pigeons, controlled ventilation delivered by a pressure-limited device was not associated with clinically important adverse cardiopulmonary changes but may be associated with respiratory alkalemia and cardiovascular depression when air-sac integrity has been disrupted (Touzot-Jourde et al. 2005).

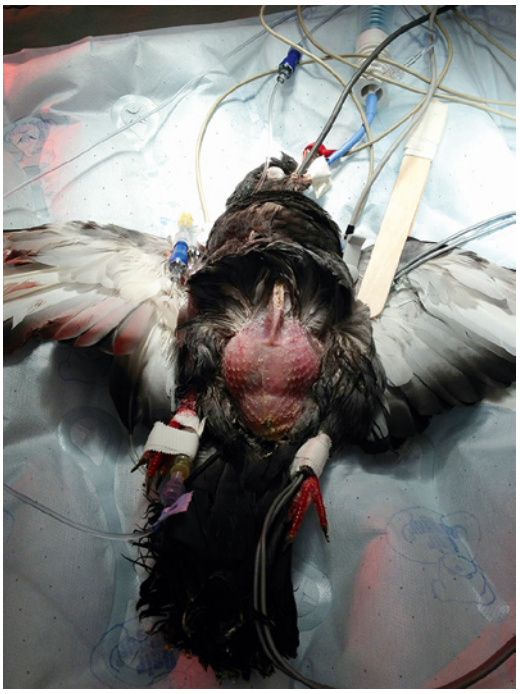


Figure 16.1 An anesthetized domestic pigeon (*Columba livia domestica*) prepared for a surgical celiotomy (photo courtesy of Dr Amy Alexander). Note the bird is intubated and connected to a nonrebreathing system (Bain). There are catheters in the ulnar and medial metatarsal veins for fluid and continuous rate infusion. For monitoring there is an esophageal thermometer, a side stream end-tidal CO_2 monitor, a pulse oximeter probe on the patagium, and a Doppler probe on the ulnar and metatarsal arteries.

Monitoring

Monitoring is the same as in other birds (Chapter 15), and similar to mammals (Chapter 3). End-tidalET carbon dioxide concentration, an indirect measure of arterial partial pressure of carbon dioxide ($PaCO_2$), is inaccurate in pigeons and probably other avian species (Touzot-Jourde et al. 2005). This is particularly so during celioscopy, when the air sacs are perforated (Touzot-Jourde et al. 2005). Nevertheless, the present author has found this to be a useful monitoring tool for assessing respiration and pulmonary blood flow.

It is essential in avian anesthesia to have a dedicated anesthetist responsible for constant monitoring since there is a very narrow window for resuscitation. Redundancy in monitoring is also important as a way to cover when a sensor is displaced (Fig. 16.1).

Field Immobilization (Wild Capture)

Physical trapping and capture techniques are well described by Bub et al. (1996). As mentioned previously, the main problems associated with wild columbiforme is self-trauma and hyperthermia, with perhaps associated capture myopathy. Inhalation anesthesia using a precision vaporizer, when available, is preferred for induction because it is rapid and likely to minimize struggling. Intranasal midazolam (1–2 mg/kg) may achieve rapid sedation and decrease struggling and stress-induced injury.

Alpha-chlorolose has been used for sedation and capture of doves (Martin 1967). It is administered orally, has a prolonged effect, and can be associated with mortality. When used for the capture of birds that may later be killed for food, local rules and regulations must first be reviewed.

Recommended Anesthetic Regimens

Premedication with midazolam (1–2 mg/kg IM, IN) usually provides adequate sedation for handling. The addition of butorphanol (2 mg/kg IM, IN) will provide more profound sedation, as will alfaxalone (2–4 mg/kg IM) or ketamine (3–5 mg/kg IM).

Columbiforms are usually induced with a mask and nonbreathing system to provide either isoflurane or

sevoflurane in oxygen. Once sufficiently relaxed the bird is intubated with a uncuffed, preferably clear, endotracheal tube and maintained with an inhalant anesthetic. Since inhalant anesthetics do not inhibit nocioception, a multimodal analgesic plan should be used for painful procedures. This can include butorphanol (0.5–2.0 mg/kg IM every 2–4 hours), meloxicam 1–2 mg/kg, low-dose ketamine (3–5 mg/kg IM, IV), and local anesthesia with lidocaine (≤10 mg/kg). Constant-rate infusions of ketamine, butorphanol, or meloxicam may also be appropriate for severe pain.

Alternatively, columbiforms can be induced with either propofol (5–15 mg/kg IV) or alfaxalone (5–15 mg/kg IM, subcutaneous, IV). When given IV either drug should be given slowly to reduce the adverse cardiopulmonary effects, which include hypoventilation and possible apnea, as well as hypotension and decreased cardiac contractility. Once induced, the pigeons should be intubated or maintained with an inhalant in oxygen or constant rate infusion. Respiratory (assisted ventilation) and circulatory support (IV fluids) should be provided. Analgesia should also be provided as discussed above.

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17

Chickens, Quail, Turkeys, Pheasants, Peafowl, and Other Galliformes

Darryl Heard

Introduction

The order Galliformes contains the megapodes, guans, chachalacas, currasows, pheasants, grouse, junglefowl (domestic chicken), turkeys, quail, and peafowl. Most galliforms are robust ground-dwelling birds, but are able to fly. Several species are important for food production. For example, the domestic chicken, derived from the jungle fowl, is used for both meat and egg production. Many are also displayed in zoos and kept as pets. Some are highly endangered (Baptista et al. 1997; del Hoyo et al. 1994). Chickens are commonly used for avian anesthesia research due to their ready availability. Furthermore, domestic turkeys are used in cardiovascular research, particularly related to cardiomyopathy (Simpson et al. 2017) and hypertension.

Anatomy and Physiology

Avian anatomy and physiology relevant to anesthesia are described in Chapter 15. One of the largest galliformes is the wild turkey (*Meleagris gallopavo*), weighing up to 8–10 kg. Some currasows and guans have markedly elongated, flattened tracheas relative to body size (Fitch 1999). This is thought to be an evolutionary adaptation to exaggerate the apparent size of a vocalizing bird, but seems to make them more prone to tracheal injury.

Physical Restraint

Galliformes are relatively easy to handle. The main threat to the human restrainer is the large spurs present in some species. Megapodes, as the name suggests, have large powerful legs relative to their body size. Galliforms will often sit still in the presence of a perceived threat. When given the opportunity, however, they use their powerful leg and flight muscles to explosively propel themselves into the air. In the process many will shed feathers (fright molt) to prevent a predator or human grabbing hold. The feather loss can be extensive and aesthetically unpleasant, especially for zoo display animals and private pets.

Rapid acceleration into the air can also propel the bird into a ceiling, cage top, or wire, causing severe trauma to the animal. Loss of skin on the skull can be extensive and potentially life-threatening. To reduce injury in aviaries a false soft ceiling can be constructed to allow for absorption of the impact force. Similarly, when temporarily housing these birds they should be kept in a quiet, dark environment.

Many galliformes are also excellent runners and can readily escape a human pursuer. Consequently, it is important to handle them in an enclosed escape-proof enclosure or room and have appropriate nets available. Camouflaged plumage may also make it difficult to detect escapees in vegetation.

Many food-production species are obese and may have hepatic lipidosis (fatty liver). In addition to dysfunction, fatty livers are friable, predisposing to spontaneous rupture and fatal hemorrhage. Short periods of struggling may also lead to hyperthermia, which will be exacerbated with obesity and in birds adapted to a cold environment (e.g., grouse and ptarmigan). To avoid hyperthermia and struggling in zoo pheasants and other excitable galliforms, this author prefers anesthesia for even routine physical examination.

Vascular Access

Vascular access is as in other birds (Chapter 15) and includes the external jugular, the basilic, and the medial tarsometatarsal or saphenous vein. Intraosseous catheters used for administration of intravenous parenteral anesthetics (e.g., propofol, alfaxalone, ketamine) are placed in

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the ulna (Valverde et al. 1993) or tibiotarsus (Yayla et al. 2014, 2015). In large galliformes the medial saphenous vein is a useful site to administer parenteral anesthetics in physically restrained animals. This author uses either a 23- or 25-gauge butterfly catheter or a preplaced and secured over-the-needle catheter in this vessel. Removal of the wings of the butterfly catheter counter intuitively facilitates its placement and securement with tape.

Endotracheal Intubation

Endotracheal intubation is usually simple. Galliforms, however, can sometimes produce copious amounts of tracheal mucous. This may obstruct the tube or produce a "flapper valve" effect that allows air into the respiratory system with positive pressure ventilation, but not out. In these species the patient needs to be monitored carefully to prevent hyperinflation. Clear endotracheal tubes are preferred to visualize any respiratory discharge, and periodic extubation to assess for blockage may be necessary during prolonged procedures.

As discussed above, the convoluted tracheal anatomy of some currasows and guans may cause problems if secretions increase in response to intubation or the bird aspirates gastric reflux under anesthesia. Some clinicians prefer not to intubate these species because of the potential for tracheal obstruction or stenosis postoperatively (Evans et al. 2009). This, unfortunately, precludes supportive ventilation. If fluid accumulation is suspected (i.e., increased respiratory noise) it must be removed with suction. A long suction tube is placed as far down the trachea through the endotracheal tube and aspiration performed as the tube is pulled out. If this fails to relieve the problem then either endoscopy or radiographic evaluation must be performed. If the obstruction cannot be immediately corrected an air-sac cannula will need to be placed for recovery (Fig. 17.1) (Chapter 15).

Preanesthetic Considerations

As with all patients, physical examination is indicated prior to anesthesia. This may, however, be difficult in some galliforms because of stress and struggling as described above. Prolonged struggling may lead to hyperthermia, as well as potential myopathy (Spraker et al. 1987). Species adapted to cold (e.g., grouse) or high montane (e.g., some species of pheasant and tragopan) environments are more likely to develop these problems. Much information can also be gained from direct observation of the bird without handling, for example respiratory rate and effort, attitude,



Figure 17.1 A rooster with respiratory disease recovering in a temperature-controlled incubator with a clear front for ease of viewing. Note the dark color of the combs and wattles secondary to hypoxemia. Respiration is being monitored using a side-stream capnograph attached to an air-sac cannula. Oxygen is also being administered into the incubator.

evaluation of the stool for biliverdinuria (liver disease)/polyuria (possible renal disease), and color of the wattles etc. The latter can change from the normal bright red to blue/purple (hypoxemia/shock/heart disease) to pale (anemia).

Galliforms possess large complex crops. Depending on the physiological status and size of the bird, fasting for 4 or more hours may reduce the amount of food in the crop, but will not guarantee passive reflux under anesthesia. Fluids can also be removed during this period in birds that are likely to drink excessively, but are not dehydrated. Careful positioning of the head and neck relative to the crop and stomach further reduces the potential for reflux. Gauze can also be placed just caudal to the glottis to soak up and physically reduce reflux. Tape should be secured to the gauze to facilitate removal and act as a reminder to remove it at the end of the procedure.

The body condition of the bird should be assessed. As mentioned previously, many domestic species bred for food production are obese and have substantial intracoelomic fat accumulation. This fat decreases the air-sac volume and may contribute to lung compression in dorsally recumbent birds, as well as impaired air-sac ventilation. Both effects may be additive to anesthetic-induced hypoventilation and explain the apparent increased anesthetic morbidity and mortality seen in these species/breeds. Similarly, birds bred for egg production are more likely to have egg-yolk coelomitis, which can lead to fibrosis, fluid accumulation, and debilitating systemic infection and illness. A high fat to total body ratio may also be

associated with abnormal drug distribution and accumulation, resulting in delayed induction and recovery.

Local and Regional Anesthesia

Local anesthetics can be used as in other avian species (Chapter 15). Care must be taken to ensure accurate calculation and administration to prevent intoxication. Chickens (and likely other birds) do not appear any more sensitive to local anesthetics than most mammals. In isoflurane-anesthetized broiler chickens a bolus of lidocaine (6 mg/kg intravenous [IV]) produced no adverse cardiovascular effects (Brandao et al. 2015). In the same chicken breed, also anesthetized with isoflurane, bupivacaine (1.96 mg/kg IV) was associated with a 50% probability of clinically relevant decreases in mean arterial pressure and heart rate (DiGeronimo et al. 2017). However, these effects were unlikely at a lower dosage (1.33 mg/kg IV).

Brachial plexus blockade has been used experimentally in chickens with variable success (Cardozo et al. 2009; Figueiredo et al. 2008). Figueiredo et al. (2008) dissected chicken cadavers to determine anatomical landmarks for correct catheter placement. They then sedated adult female chickens (midazolam 1 mg/kg, butorphanol 1 mg/kg intramuscular [IM]) and after 15 minutes restrained the birds in lateral recumbency with their heads covered. The wing to be blocked was abducted at a 90° angle to the thorax and the apex of the axilla (proximal condyle of the humerus, proximal region of the coracoid and scapula) was palpated. A 20-SWG 50-mm catheter electrode (Braun Melsungen AG, Melsungen, Germany), teflon-coated except at the tip, was attached to a peripheral nerve stimulator (2–5 Hz, 0.12 mA, S48 stimulator; Grass, Warwick, RI, USA). The catheter extension was filled and connected to a 3-mL syringe containing either lidocaine (20 mg/mL, 1 mL/kg) with epinephrine or bupivacaine (5 mg/mL, 1 mL/kg). The catheter was inserted at a 45° angle to the skin just below the apex of the axilla. It was advanced through the pectoralis muscle and fascia toward the chest wall into the region around the first rib. The appropriate muscle response was confirmed when there was muscle contraction and flexion of the wing. Proximity to the brachial plexus was assessed as when the strongest abduction of the humerus and flexion of the wing occurred. After localization of the brachial plexus by the nerve stimulator the local anesthetic solution was injected in 0.5-mL aliquots into the plexus sheath over 60 seconds. Onset of sensory denervation was 3–5 minutes, and duration of blockade was 60–90 minutes. The researchers, however, observed a relatively high failure rate of 33% with this technique. Cardozo et al. (2009) had more success using ropivacaine (0.75%, 1 mL/kg). The onset and duration of effect were approximately 15 and 115 minutes, respectively.

Khamisabadi et al. (2021) describe a technique for spinal anesthesia in 8-week-old broiler chickens using either lidocaine (2 mg/kg) or bupivacaine (0.5 mg/kg). After aseptic preparation, a 23-gauge spinal needle was inserted into the synsacrococcygeal space of the chickens with correct needle placement confirmed by a sudden loss of resistance. The onset and duration of effect for bupivacaine were approximately 3 and 55 minutes, respectively. Lidocaine had a faster onset (1–2 minutes) and shorter duration of effect (18 minutes).

Analgesia

Avian analgesia is covered in Chapters 2 and 15. When working with domestic birds that are classified as food animals it is important to understand the laws regarding the use of anesthetic and analgesic drugs in those species. It may not be up to you as a veterinarian to decide when and what drugs you can use.

Nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and tramadol have been used and studied in several galliform species. In birds NSAID pharmacokinetics and therapeutic index are highly variable, making safe drug selection difficult (Baert & Backer 2003). Of the presently available NSAIDs, this author prefers using meloxicam (0.2–0.5 mg/kg once a day to twice a day, per os or orally). Regardless of the drug and species, each analgesic regimen should be tailored to the individual and the type and severity of pain (Chapter 2). A multimodal approach may be necessary, especially for severe and chronic pain. Furthermore, any analgesic plan should be tailored to the individual regardless of whether for anesthesia or a chronic disease process. This includes modification depending on response.

Baert and Backer (2003) studied the pharmacokinetics of a single IV dose of sodium salicylate (25 mg/kg), meloxicam (0.5 mg/kg), and flunixin (1.1 mg/kg) in five bird species, including chickens and turkeys. Chickens had a half-life (5.5 hours) approximately 10-fold as long as the other species for flunixin. The half-lives of chickens (3.2 hours) and pigeons (2.4 hours) were 3-fold as long as the other bird species for meloxicam, and for salicylic acid the half-life in pigeons (14.9 hours) was at least 3–5-fold longer than in the other bird species. Once again, this study emphasizes the variability in response to NSAIDs in birds and the potential for toxicity. Meloxicam (5 mg/kg subcutaneous) and carprofen (25 mg/kg) improved gait function in a group of mildly lame broiler chickens (Caplen et al. 2013). However, the effects and safety of repetitive dosing were not evaluated.

Hussain et al. (2008) investigated the toxico-pathological effects of diclofenac sodium (0, 0.25, 2.5, 10, and 20 mg/kg PO for 7 days) in broiler chicks (15 days old), pigeons (3 months old), and Japanese quail (4 weeks old). Dose-dependent clinical signs in all included depression, somnolence, decreased body weight, and mortality. Severity of clinical disease was most severe in broiler chicks, followed by pigeons and Japanese quail. Broiler chicks and pigeons developed visceral gout at the higher dosages (10 and 20 mg/kg), but not Japanese quail. The kidneys and liver were enlarged in all, the kidneys showed acute renal necrosis, and the livers had fatty change and necrosis of hepatocytes.

Although many bird species appear to respond best to κ-opioid agonists (i.e., butorphanol 0.3–2.0 mg/kg twice a day to thrice a day), there are a few papers indicating μ-opioid agonists (e.g., morphine, hydromorphone, and fentanyl) are efficacious in some galliforms (Chapters 2 and 15; Concannon et al. 1995; Evrard & Balthazart 2002).

In Japanese quail (*Cortunix japonica*), morphine at relatively high dosages (10 and 20 mg/kg IM) significantly altered response latency and threshold in the hot water and foot pressure quantitative nocioception tests (Evrard & Balthazart 2002). These effects were blocked by naloxone. Although morphine (2 mg/kg IV) achieved blood levels associated with analgesia in broiler chickens, clearance was much higher than in mammals (Singh et al. 2010). This dosage would have to be given IV every 2 hours or as a continuous infusion to maintain adequate blood levels. In chickens, both the μ-opioid receptor agonist morphine and the κ agonist U50488H decreased isoflurane MAC in a dose-dependent (1–3 mg/kg IV) manner without significant effects on heart rate and blood pressure (Concannon et al. 1995). In hens, methadone (6 mg/kg IM) decreased isoflurane minimum anesthetic concentration (MAC) or dose (MAD) by 30% within 15 minutes of administration, but was also associated with mild respiratory acidemia, bradyarrythmias, and hypertension (Escobar et al. 2016). Similarly, IV boluses of fentanyl (10 and 30 μg/kg) reduced isoflurane MAC (6.2% and 13.2%, respectively) in isoflurane-anesthetized chickens (da Rocha et al. 2017). Interestingly these dosages were not associated with clinically significant cardiopulmonary effects.

Tramadol may be useful for managing postoperative pain as well as chronic pain associated with degenerative joint disease. This drug is metabolized to an active metabolite, O-desmethyltramadol (Black et al. 2010). Although relatively high dosages (≥5–10 mg/kg once to twice a day PO) are being recommended in birds based on some pharmacokinetic studies (Black et al. 2010; Souza et al. 2009, 2011, 2012) and a pain response study in Hispaniolan parrots (Guzman & Souza 2012), this author has seen good responses in some birds with degenerative joint disease at lower dosages (1–5 mg/kg once to twice a day PO). Further research is necessary to define blood levels associated with analgesia in birds, rather than using human levels. The main observed side effects are anorexia, ataxia and dysphoria, and vomiting. These effects may be seen at high dosages or after repetitive dosing. There also appears to be some individual variation in response, possibly due to variable metabolism to the active form. A combination of tramadol (5–10 mg/kg IM) and ketamine (10–15 mg/kg IM) with infiltration of 2% lidocaine at the surgical site has been recommended for minor surgical procedures in spontaneously breathing layer chickens (Oghenemega & Oguntoye 2015). In another study in chicks, however, the addition of ketorolac to ketamine appeared to provide better analgesia and anesthetic induction than tramadol (Mousa & Al-Zubaidy 2019).

Continuous infusion of lidocaine (3–6 mg/kg IV bolus followed by 3–6 mg/kg/h) has been evaluated in anesthetized chickens for its potential analgesic as well as inhalant anesthetic sparing effects (Escobar et al. 2023). Unfortunately, this study failed to show any effect on isoflurane MAC, suggesting no analgesic or anesthetic sparing effects.

Induction and Maintenance Protocols

Published sedative and parenteral anesthetic dosages for a variety of domestic galliforms are summarized in Table 17.1.

Sedation

Midazolam

The safest and most useful sedative in galliforms is midazolam (1–2 mg/kg IM or IV). Although not an analgesic, it does produce sufficient restraint to place an intravenous catheter or facilitate mask induction with an inhalant anesthetic. It can be reversed with an equal volume of intramuscular flumazenil (0.1 mg/mL). The addition of butorphanol (0.5–2.0 mg/kg IM, IV) or alfaxalone will provide more profound sedation and some analgesia (Knutson et al. 2022).

Alpha-2 Adrenergic Agonists

All birds are relatively resistant to the effects of alpha-2 adrenergic agonists. In chickens, and presumably other birds, xylazine inhibits ventricular activity (Park & Park 1988). The duration of this effect is dose-dependent and reversible with either yohimbine or 4-aminopyridine. In rock partridges (*Alectoris graeca*), xylazine (10 mg/kg IM), medetomidine (0.15 mg/kg IM), detomidine (0.3 mg/kg IM), or diazepam (6 mg/kg IM) produced variable sedation adequate to allow

Table 17.1 A summary of some published parenteral anesthetic regimens used in domestic Galliformes (dosages in mg/kg).

Species	Ketamine	Xylazine	Medetomidine	Detomidine	Diazepam	Midazolam	Butorphanol	Comments	Reference
Chicken, rooster	25 IM	3 IM			4 IM			Xylazine given 15 minutes before other drugs. Adequate anesthesia for typhylectomy, but associated with hypothermia, cardiopulmonary depression, and prolonged recovery.	Mostachio et al. (2008)
Chicken, white leghorn cockerel	10 IV	2 IV						Drugs combined in a single injection. Induction and recovery ~2 and 70 minutes, respectively. Adequate anesthesia for typhylectomy, bradycardia, and bradypnea.	Maiti et al. (2006)
Chicken, white leghorn cockerel	75 IM				2.5 IV			Ketamine given 5 minutes after diazepam. Induction and recovery ~9 and 80 minutes, respectively. Adequate anesthesia for typhylectomy. Hypothermia.	Maiti et al. (2006)
Chicken, white leghorn cockerel	50 IV					2 IM		Ketamine given 5 minutes after midazolam. Induction and recovery ~18 and 100 minutes, respectively. Adequate anesthesia for typhylectomy.	Maiti et al. (2006)
Chicken, layer	15 IM							~30 minutes between loss of righting to sternal recumbency. Adequate anesthesia for typhylectomy.	Eyarefe & Oguntoye (2012)
Chicken, layer	15 IM							Combined with lidocaine 4 subcutaneous infiltrated along midline incision. Duration of recumbency ~100 minutes. Mild bradycardia, bradypena and hypothermia relative to Ketamine alone.	Eyarefe & Oguntoye (2012)
Chicken, cockerel					0.5 IM			Facilitated nonpainful physical restraint.	Mahmud et al. (2014)
Chicken, cockerel	20 IM							Poor relaxation, poor quality recoveries.	Mahmud et al. (2014)
Chicken, cockerel	10 IM				2.0 IM			Some analgesia, good immobilization, poor quality recoveries.	Mahmud et al. (2014)
Ring-necked pheasant	150 IM 80 IM 80 IM	 3.0 IM	 0.20 IM 		9.0 IM			All birds premedicated then administered Ketamine at 5 minutes. Excellent anesthesia with all combinations. Shorter duration with Medetomidine/Ketamine and greater cardiopulmonary depression with Xylazine/Ketamine. All associated with hypothermia.	Kaya et al. (2019)
Guinea fowl	15 IM	2.5 IM						No apparent analgesia in response to clamping of skin and toes.	Ajadi et al. (2009)

(*Continued*)

Table 17.1 (Continued)

Species	Ketamine	Xylazine	Medetomidine	Detomidine	Diazepam	Midazolam	Butorphanol	Comments	Reference
Guinea fowl	15 IM	2.5 IM				0.3 IM		Duration of analgesia 37 ± 24 minutes. Midazolam prolonged recumbency, but was associated with some regurgitation and bradypnea.	Ajadi et al. (2009)
Guinea fowl	25 IM	1.0 IM						Rapid onset and good surgical anesthesia. Yohimbine 1.0 IV 40 minutes after Xylazine/ Ketamine administration shortened recovery.	Teare (1987)
Quail, *Cortunix* sp.	50 IM, IO	8.0 IM, IO						Faster induction and duration of effect shorter with IO, and cardiopulmonary depression greater.	Kamilloglu et al. (2014)
Quail, *Cortunix* sp.	20 IM, IO			1.0 IM, IO				Rapid induction with IO, but similar duration of effect with IM and IO. Hypothermia with both groups.	Yayla et al. (2015)
Quail, *Cortunix* sp.	30 IM	9.0 IM						Sedation, light anesthesia, and surgical analgesia achieved with Xylazine, Ketamine, and Ketamine/Xylazine, respectively. As expected, Ketamine alone was associated with a rough recovery.	Durrani et al. (2014)
	60 IM								
		18 IM							

IM, intramuscular; IO, intraosseous; IV, intravenous.

handling and for radiography (Uzun et al. 2006). Duration of effect and time to recovery were prolonged, especially for diazepam and detomidine. The greatest sedation was observed with xylazine, but as would be expected it produced profound respiratory depression. All drugs were associated with decreased cloacal temperatures over time.

Parenteral Anesthesia

Intubation and ventilation, preferably with oxygen, are recommended when parenteral anesthetics are used alone for surgery and prolonged anesthesia. Administration of balanced electrolyte solutions either IV or intraosseous (IO) will also ameliorate some of their hypotensive effects.

Ketamine

Ketamine and ketamine combinations have either been evaluated or used clinically in galliforms (Table 17.1). The adverse effects are the same as in other avian and mammalian species. Ketamine alone is not recommended because of increased salivation, muscle rigidity, and rough, sometimes prolonged, recoveries associated with wing flapping and struggling. The addition of a benzodiazepine (i.e., diazepam or midazolam) provides improved muscle relaxation and sedation, but not analgesia. The addition of an alpha-2 adrenergic agonist (i.e., xylazine, detomidine, or medetomidine) is also associated with improved muscle relaxation, as well as surgical analgesia. These agonists are, however, more likely to produce cardiopulmonary depression, hypothermia, and prolonged recovery. Atipamezole, administered IM when birds first show signs of recovery, can be used to reverse medetomidine, detomidine, and xylazine.

In guinea fowl, yohimbine (1.0 mg/kg IV) shortened recovery from a combination of xylazine (1.0 mg/kg IM) and ketamine (25 mg/kg IM) (Teare 1987). Yohimbine, however, is no longer commercially available and can replaced by atipamezole (1 mg IM/20 mg xylazine). Butorphanol (and perhaps morphine, hydromorphone, or fentanyl) added to the ketamine combinations enhances surgical analgesia, but will also further depress cardiopulmonary function.

Propofol

Propofol administration using the medial saphenous vein facilitates induction of large birds. In turkeys, propofol (5 mg/kg IV) administered over 20 seconds produced a rapid induction, but was associated with a short period of apnea, then bradypnea, hypercarbia, hypoxemia, and hypotension (Schumacher et al. 1997). Anesthesia was successfully maintained with a constant rate infusion of 0.5 mg/kg/min. Recovery was rapid and smooth once the infusion was discontinued. Propofol does not produce analgesia, and must be used with other drugs for painful surgical procedures.

In chickens, propofol (4.5–9.7 mg/kg IV), followed by a constant rate infusion (0.5–1.5 mg/kg/min) for 20 minutes, produced rapid induction and general anesthesia (Lukasik et al. 1997). As in other species, sometimes marked cardiopulmonary depression was observed. Single or multiple runs of premature ventricular complexes were also observed in many birds. One bird required lidocaine (0.5 mg/kg IV) for ventricular tachycardia. Propofol at three times the induction dosage was fatal in all birds, indicating it has a low therapeutic index (Lukasik et al. 1997).

Alfaxalone

Alfaxalone has also been used for IV induction, as well as combined with other sedatives and anesthetics as part of an IM premedication regimen (Knutson et al. 2022). Unfortunately, the present concentration of alfaxalone limits its administration to smaller birds or sedative dosages to avoid the IM injection of inhumane volumes.

The required dosages and adverse physiological effects of alfaxalone are remarkably similar to those of propofol (hypoventilation/apnea, hypotension), but there are some differences. Alfaxalone administered intravenously (especially rapidly and at high dosages) is often associated with hyperactivity and struggling during induction and recovery. Two hens administered 5 mg/kg alfaxalone IV 20 minutes after premedication displayed signs of excitement including rigid limbs and dorsiflexion of the head and neck (White & Martinez-Taboada 2019). Muscle relaxation was achieved after administration of a further 5 mg/kg in one bird. In a controlled study in chickens, the lowest IV alfaxalone doses required for anesthetic induction and endotracheal intubation in unpremedicated and premedicated chickens were 7.5 and 4 mg/kg, respectively (Mastakov et al. 2021). The duration of anesthesia for all dose rates within the study ranged from 51 seconds to 4 minutes and 45 seconds. Premedication generally improved the quality of induction and recovery, but significantly increased the time required for the chickens to stand after being anesthetized and to return to normal behaviors. Most chickens exhibited varying degrees of hyperactivity on anesthetic induction and recovery.

In chickens, the effects of midazolam (2.5 mg/kg) combined with either alfaxalone (15 mg/kg IM) or butorphanol (3 mg/kg IM) were compared in a crossover study (Knutson et al. 2022). The midazolam/alfaxalone combination resulted in faster onset of sedative effects, longer duration of recumbency, higher peak sedation, and improved success of radiographic positioning compared with

butorphanol/midazolam. All birds were reversed with flumazenil (0.05 mg/kg IM) at 30 minutes after the original injections.

The sedative effects of alfaxalone (15 mg/kg IM) combined with either ketamine (5 mg/kg IM) or midazolam (1 mg/kg IM) were similarly compared in chickens (Chang et al. 2022). Alfaxalone in combination with either ketamine or midazolam induced loss of righting reflex in 78% and 56% of the birds, respectively. The quality of induction was also poor after administration of ketamine/midazolam.

In Indian peafowl alfaxalone (10 mg/kg IM) provided only moderate sedation (Hasse et al. 2022). At a higher dosage (20 mg/kg IM) all birds experienced adverse effects, including seizure-like episodes and hypersensitivity to stimuli. Recovery was also prolonged. Alfaxalone alone is not recommended alone in this species and possible other galliforms (Hasse et al. 2022).

Muscle Relaxants

Although not an anesthetic or analgesic, the nondepolarizing, short-acting muscle relaxant atracurium besylate (0.15–0.45 mg/kg IV) can be used as an adjunct to inhalation anesthesia (Nicholson & Ilkiw 1992). Muscle relaxation is monitored with a nerve stimulator and reversed with edrophonium (0.5 mg/kg IV). In chickens, the effective dosage of atracurium to result in 95% twitch depression in 50% of birds was 0.25 mg/kg, whereas the dosage to result in 95% twitch depression in 95% of birds was 0.46 mg/kg (Nicholson & Ilkiw 1992). The duration of effect at 0.25 mg/kg was approximately 35 minutes and at the highest dosage (0.45 mg/kg) was 50 minutes. The cardiopulmonary effects of atracurium and edrophonium were clinically insignificant.

Inhalation Anesthesia

Isoflurane and sevoflurane are the most commonly used inhalant anesthetics in clinical practice. Their physiological effects and potencies in galliformes are the same as in other avian orders (Deori et al. 2017; Midon et al. 2021; Naganobu & Hagio 2000; Naganobu et al. 2000) (Chapter 15). Although sevoflurane is associated with a more rapid induction and recovery, it is not a clinically significant difference compared to isoflurane. As described previously, many domestic species have large stores of intracoelomic fat that impair ventilation, potentially prolonging inhalant anesthetic equilibration and recovery. Compared with halothane or pentobarbital, isoflurane anesthesia resulted in a significantly lower threshold for electrical fibrillation of the chicken heart (Greenlees et al. 1990).

Monitoring

Monitoring is the same as in other birds (Chapter 15) and similar to mammals (Chapter 3). It is important to have a dedicated anesthetist for any avian anesthesia since physiological changes can occur rapidly and the window of time for successful resuscitation is small. Furthermore, it is valuable to have redundancy in monitoring. For example, using both a Doppler flow monitor as well as an ECG and/or esophageal monitors. The bispectral index has been successfully used and validated to monitor brain electrical activity and the level of unconsciousness in chickens during isoflurane anesthesia (Martin-Jurado et al. 2008).

End-tidal carbon dioxide concentration ($ETCO_2$), an indirect measure of arterial partial pressure of carbon dioxide ($PaCO_2$), is inaccurate in pigeons and probably other avian species (Touzot-Jourde et al. 2005). This is particularly so during celioscopy, when the air sacs are perforated (Touzot-Jourde et al. 2005). Similarly, in chickens $ETCO_2$ was not accurate in predicting $PaCO_2$ values in birds ventilated using air-sac cannulation (Paré et al. 2013). Despite these concerns, the present author finds this monitoring modality most useful for assessing respiration as well as blood flow through the lungs (Fig. 17.1).

As in all birds, hypothermia is a major issue during avian anesthesia and can contribute to morbidity/mortality as well as a prolonged recovery if not assessed and managed. Minimally the cloacal temperature should be continuously monitored, but an esophageal thermometer is preferred for assessment of core body temperature.

Recovery

The main issues in recovery are return to spontaneous respiration, hypothermia, hypotension, hypoglycemia, struggling, and analgesia. Once the procedure is ended the bird should be transported to a warmed incubator and placed in sternal recumbency, with the head and neck elevated, for recovery (Fig. 17.1). All reversal drugs should be administered intramuscularly at this time. The endotracheal tube is maintained in place until the bird is able to hold its head in a normal position, is breathing spontaneously, and struggles/coughs to remove the tube. The cloacal temperature should be monitored and the bird kept in the incubator until it returns to a normal range. If a medial metatarsal (saphenous) catheter is in place it can be maintained into recovery if necessary.

Recommended Anesthetic Protocols

Most galliforms are readily restrained and induced with an inhalant anesthetic (isoflurane or sevoflurane) administered by mask. As previously discussed, they subsequently should be intubated and provided with supplemental ventilation for even relatively short procedures. Hypoventilation will be even more problematic in obese domestic poultry. Inhalant anesthetics do produce unconsciousness, but are not analgesic. Consequently, for painful procedures appropriate analgesics should be added to the protocol.

Midazolam (2 mg/kg IM) can be used to facilitate handling. Although the author has not used this technique in galliforms, midazolam can also be given slowly intranasally (IN) for more rapid absorption. Midazolam (5 mg/mL) can be reversed with an equal volume of flumazenil (0.1 mg/mL). The addition of butorphanol (0.5–2.0 mg/kg IM, IN) will provide more profound chemical restraint, but greater cardiopulmonary depression. A combination of midazolam (2 mg/kg IM), butorphanol (0.5–2.0 mg/kg IM), and low-dose ketamine (3 mg/kg IM) can facilitate restraint to correct nonsurgical egg binding in poultry.

For large galliforms (e.g., turkeys, roosters) induction with either propofol or alfaxalone may be used for induction by IV administration in the catheterized medial metatarsal vein. Either drug should be administered by slow injection to effect to reduce adverse cardiopulmonary effects. Although birds can be maintained solely with either drug, they should still be intubated and ventilated. Alternatively, birds can be maintained using an inhalant anesthetic in oxygen. Once again, suitable analgesia should be provided.

For painful procedures a multimodal approach to analgesia is recommended, for example premedication with meloxicam (0.2–0.5 mg/kg IM), an opioid (morphine 2 mg/kg IM or hydromorphone 3–6 mg/kg IM), and low-dose ketamine (2–3 mg/kg IM). Ketamine and opiids can also be continuously infused during the procedure for added analgesia. Use local anesthetics (lidocaine <10 mg/kg) at the surgical incision site when applicable. Spinal anesthesia may also help when appropriate (Khamisabadi et al. 2021). This approach is in addition to the above-described induction and maintenance techniques. Tramadol (5–10 mg/kg PO twice a day) can be tried postoperatively, but it is controversial whether it has any effect for postoperative pain in birds.

Field Immobilization (Wild Capture)

Physical trapping and capture techniques are well described by Bub et al. (1996). As mentioned previously, the main problems associated with wild galliforms are self-trauma, "fright" molting, and hyperthermia with associated capture myopathy (Spraker et al. 1987). Inhalation anesthesia using a precision vaporizer, when available, is preferred for induction because it is rapid and likely to minimize struggling. Intranasal midazolam (1–2 mg/kg) may achieve rapid sedation and decrease struggling and stress-induced injury.

Alpha-chlorolose has been used for sedation and capture of wild turkeys (Bergman et al. 2007). It is administered orally, has a prolonged effect, and can be associated with mortality. When used for capture of birds that may later be killed for food, local rules and regulations must first be reviewed.

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18

Raptors

Michelle Willette, Patrick Redig, Dana Franzen-Klein, and Julia Ponder

Introduction

Raptors or birds of prey are an assemblage of avian species representing convergent evolution from diverse lineages, as opposed to distinct taxonomic relationships among major orders. All are completely carnivorous birds, acquiring their food by active hunting and/or scavenging. The major orders of raptors are the Strigiformes (owls), Falconiformes (falcons), Accipitriformes (hawks, eagles), and vultures. Two major vulture groups exist, the so-called Old-World vultures (order Falconiformes) and the New-World vultures (order Cathartiformes). There are approximately 280 species in various orders world-wide. Ravens (Passeriformes – Corvidae) and shrikes (Passeriformes: Laniidae) are sometimes included among the raptors due to similarity in life-history habits and a strong tendency to carnivory. McClure et al. (2020) proposed a definition of raptors combining phylogeny with morphology and ecology as species within orders that evolved from raptorial land birds (Telluraves) in which most species maintained raptorial lifestyles. Raptors would therefore include all species within Accipitriformes, Cathartiformes, Falconiformes, and Strigiformes and include seriemas (Cariamiformes).

Average or representative weights for raptors range from the diminutive elf (*Micrathene whitneyi*) and saw-whet owls (*Aegolius acadicus*) (40–85 g) to the large eagles of the Amazon and Philippine rainforest (harpy eagle [*Harpia harpyja*] 5–9 kg M/F; Philippine eagle [*Spilornis holospilus*] 4–6 kg M/F) and the condors (California [*Gymnogyps californianus*] and Andean [*Vultur gryphus*] 9–12 kg, respectively). In all species, except the New World vultures and ravens, reverse sexual dimorphism is expressed, with females ranging from 10% to 30% larger than the males. With few exceptions, plumage characteristics are not dimorphic and there is substantial overlap in weights between males and females, hence sexual determination is not a definitive process except at the extremes of the size ranges.

Anatomy and Physiology

All raptors possess strong hooked beaks that are capable of inflicting mild to serious damage to handlers and can also damage anesthesia equipment such as masks and hoses if not properly restrained. Additionally, except for vultures, all have very strong grasping feet armed with sharp, curved talons rendering the need for proper restraint is paramount. The mouth of nearly all is large and wide, and the glottis is clearly visible at the base of the tongue.

Across species of raptors, the anatomy of the respiratory system does not vary appreciably except in size, and it exhibits the basic avian anatomy and physiology of lungs and air sacs as found in other avian groups (Chapter 15) (Heard 1997; Ludders 1998). As with other avian species, it is important to remember that the tracheal rings are complete and cuffed intubation tubes should not be used.

Procedures involving anesthesia in raptors are regularly conducted in dorsal, lateral, and sternal recumbency without marked overt differences in ventilation or manner of managing the anesthetic episode. Studies involving airsac volumes by computed tomography of isoflurane anesthetized red-tailed hawks (*Buteo jamaicensis*) demonstrated subjects had the greatest lung and air-sac volumes in sternal recumbency compared to lateral or dorsal positioning (Malka et al. 2009). There were no changes in ventilatory rate as a function of position and other respiratory variables were not evaluated. Dorsal recumbency has long been regarded as reducing ventilatory function owing to increased effort to raise the sternum and pressure from

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viscera against the abdominal airsacs. However, a study by Hawkins et al. (2013) utilizing red-tailed hawks suggests that dorsal recumbency did not compromise ventilation or impair oxygen transport relative to right lateral recumbency. Regardless, sternal recumbency is often recommended for long anesthetic procedures when feasible (Redig & Rousch 1978).

The digestive tract of raptors is typical of carnivorous birds, with some variations. Falcons, hawks, eagles, and vultures have a crop, a varying saccular or expandable portion of the esophagus that stores food. Owls do not possess a true crop, rather the mid-cervical esophagus is freely expansible and functions as a site of temporary food storage. All have a proventriculus (glandular stomach) positioned as a bell-shaped structure on the anterior aspect of the ventriculus. The latter is the site of chemical digestion and pellet formation. Pellets are formed from nondigestible food residues that are egested at the completion of the digestion cycle. The intestinal tract is relatively short and has rapid transit times. Owls have ceca whilst Falconiformes do not. The functional significance of ceca is poorly understood. When the gastrointestinal tract is full of food or contains a yet to be egested pellet, there can be considerable enteric expansion and concomitant reduction in airspace in the abdominal airsacs. A 12–24-hour fast is generally recommended prior to anesthesia in all but the smallest raptors, where a small amount of "clean meat" (devoid of bones, feathers, or fur) may be fed up to a couple of hours before anesthesia without complication.

Handling, Control, and Restraint

Many raptors are maintained in captivity, some in very close association with humans, as in the sport of falconry, or trained and bonded to handlers for use in educational or ambassador programs; this bonding necessitates different approaches to handling for restraint than for their wild counterparts. Most raptors are armed "front and back", and even relatively tame, docile birds will often strike with the beak or talons when being restrained; caution and protection are strongly advised in all situations. Proper restraint ultimately requires control of the wings and legs (Fig. 18.1a); covering the latter with a towel or a properly fitting hood after the bird is restrained decreases visual stimulation, which can decrease stress and the tendency for the bird to struggle (Doss & Mans 2016).

The overall goals of handling are to maintain the safety of the handler, clinician, and patient, to provide proper positioning for medical procedures, to protect feathers from bending and breakage, and to minimize stress. The major hazards to clinician and handler safety include talon wounds, beak wounds, and wing slapping, especially from eagles. The latter have been known to cause facial injuries in handlers and/or break their glasses. Personal protective gear, consisting of gloves of appropriate thickness and gauntlet length, and safety glasses, is recommended. Additionally, the use of a welder's leather cape that protects the arms and shoulders from bite wounds is recommended when handling eagles.

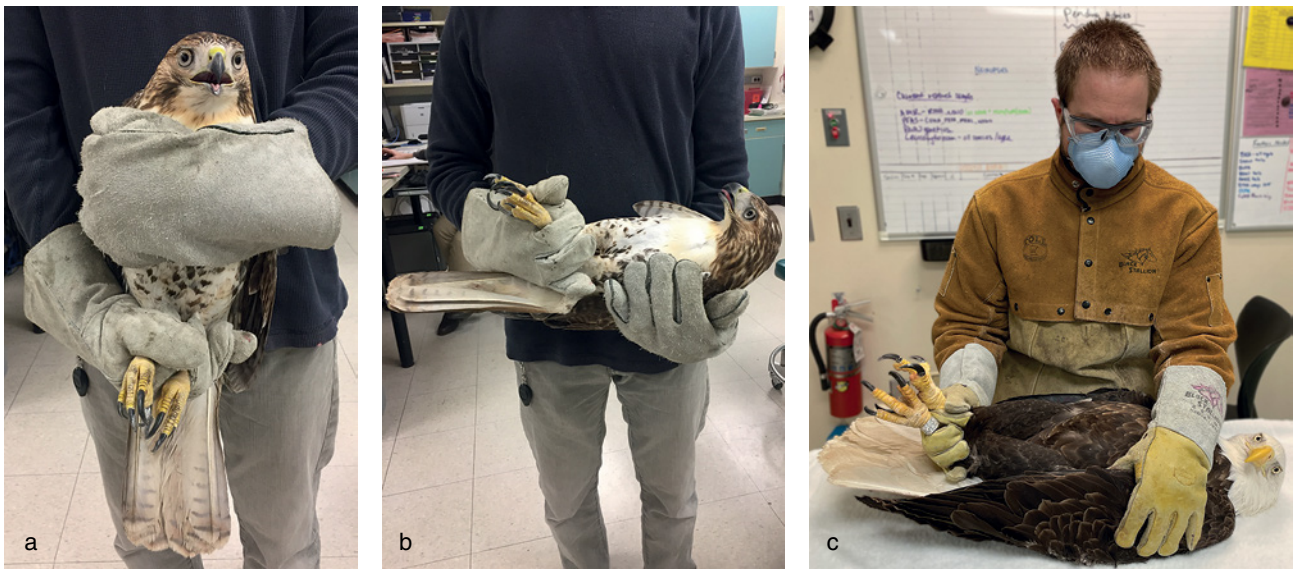


Figure 18.1 Safely restrained raptor (red-tailed hawk), vertically (a) and horizontally (b), prior to the application of a head covering. (c) Safely restrained large raptor (bald eagle) on the examination table. Notice the protective gear worn by the handler, including leather welder's vest, gauntleted gloves, and safety glasses. Note: Some individuals and species (bald eagles) may be calmer without their head covered.

To protect the bird and to avoid struggling and unintended injuries, it is important to establish good communication between the handler and clinician so that who has control over the wings and legs of the bird at any given time is never in doubt. Use only slow, smooth continuous movements, and cover the head of the patient with a hood or a towel to block out visual stimuli.

Capture of Untrained, Wild Birds

For wild birds being handled for rehabilitation or untrained display birds, "capture" is essentially the first component of the restraint procedure. The goal is capture with a minimum of risk to the handler and patient, achieving firm control on a strong, struggling patient and, concurrently, minimizing stress or emotional trauma to the bird. Capture can be accomplished in any number of ways depending on the demeanor of the bird and skill of the handler. Effective means include a dip net, covering the birds with a large towel, or approaching the perched bird in the dark, using a light source that is quickly clicked off and on to provide the handler with a brief window of light to observe where the bird is and allow approach. Some species, such as great horned owls (*Bubo virginianus*), will sit on a perch giving a vivid threat display, but, in most cases, not make any attempt to escape or attack; these can be grasped quite easily by the legs. Regardless of how the bird is approached, the objective is to bring one's hands near the legs, one on either side. As the hands are moved slowly closer, there will come a point where the bird's personal space has been invaded (usually within about 3–5 in. of the legs) and, instead of looking directly at the person approaching them, they will divert their gaze momentarily in the direction they intend to flee. In that moment, a quick grasping of each leg (at the level of the tarsometatarsus or tibiotarsus) and lifting the bird off its perch will accomplish the capture portion. At that point, both legs are grasped in the dominant hand with the index finger between the legs (at the level of the tarsometatarsi) and the other hand is used to fold the wings into the body. The bird is subsequently laid flat on a table and the head is covered. Some species, such as bald eagles, may be calmer without their head covered (Fig. 18.1b).

It should be noted that restraining an awake/unsedated bird in dorsal recumbency could incite a stress/fear response known as tonic immobility (TI). TI is a response, well conserved across vertebrate species, to predation or other inescapable danger. Described centuries ago, TI is often noted in prey species (thanatosis or death-feigning) but has been reported in raptors, including turkey vultures (*Cathartes aura*), red kites (*Milvus milvus*), and recently black vultures (*Coragyps atratus*), which was confirmed through bispectral index which corresponded to a fully awake bird (Spina & Silveira 2019). TI is characterized by catatonia and unresponsiveness to external stimuli and perhaps analgesia. The analgesic effects of TI are not uniform across species and in birds (chickens and pigeons) it is not clear whether TI results in analgesia or hyperalgesia (Baker et al. 2019).

These capture methods work up to a point with most raptors up to about 5–6 kg, which includes most species – the average handler can readily overcome the bird's muscle strength. The very large eagles (Harpy and Philippine), along with the large vultures, demand greater skill and respect when being captured. The eagles have very large and powerful legs that require the handler to have considerable strength and attention to detail to overcome their efforts to struggle free.

Vultures, both Old and New World, will defend themselves during capture by regurgitating. The material ejected is malodorous and difficult to remove from clothing.

Capture of Trained Raptors

For trained birds in which a bond of trust has been established, restraint is best accomplished without the drama of a capture episode (Speer et al. 2018). Though strictly manual methods are mostly used, chemical sedation can positively impact the process (see below). For manual restraint, if the subject is perched on a handler's gloved fist, it can be slowly approached (use of darkness is again helpful, but less necessary) from the front and the legs gently grasped by one hand with an index finger in between them. Control of the wings is gained as the bird is gently lifted off the fist and placed on a table and the head covered. Alternatively, the bird may be grasped over the wings from behind and firmly, but gently lifted off the fist and laid on a table. Many falconry birds will have a hood on their head, and this renders each of these methods that much easier. Another useful and relatively stress-free method for restraint of a hooded falcon is to place an oversized anesthesia face mask over the head of the bird and flow isoflurane for a few minutes until the bird is unstable, gently catching them when they fall backwards off the perch and continue with induction.

Many of the issues of restraint of trained birds may be avoided by using small volumes of chemical restraint agents injected with a very small (27-gauge) needle into the pectoral muscle or given via the mouth or nares without antecedent manual restraint. An injected mixture of ketamine and dexmedetomidine (previously medetomidine) has been shown to be highly effective (Molero et al. 2007) and safe in large falcons and others. This approach induced ataxia and general loss of response

in 3–4 minutes that readily allowed further induction with low concentrations of isoflurane (2% induction and 1% maintenance). On cessation of isoflurane and intramuscular (IM) administration of the antagonist atipamezole (0.15 mg/kg), a smooth, uneventful recovery occurred within 10 minutes. The metabolism of ketamine while the bird was under isoflurane allowed recovery without the uncontrolled wing-flapping and other movements associated with recovery from ketamine anesthesia. Other injectable agents and combinations have been used in a similar manner (Table 18.1). This approach works best with low-volume drugs/combinations.

Ancillary Aspects of Anesthesia in Raptors

Intubation and Air-sac Cannulation

Intubation is not undertaken for short procedures (20–30 minutes) in stable patients and undertaken with care in raptors weighing less than approximately 150 g, especially sharp-shinned hawks (*Accipiter striatus*). In these smaller birds, the inside diameter of the tube that would fit inside the trachea becomes too small and too prone to blockage by mucus. Appropriately sized tubes should be available, however, to provide a means for rapid intubation and ventilation should the bird become apneic.

Intubation of raptors is a straightforward procedure and recommended to provide a means of ventilatory support for any procedures that exceed 20–30 minutes or in unstable or unfasted patients. Mask administration is generally adequate for procedures of shorter duration, but it is recommended to have appropriately sized intubation tubes readily available should apnea occur. An uncuffed tracheal tube that slides easily into the trachea is selected; it is inserted only sufficiently to prevent the tip from slipping easily out of the trachea. Pieces of white adhesive tape are used to affix the tube to the beak or the head to prevent it being dislodged (Fig. 18.2). Intubation should be conducted only in birds that have been taken to a plane of surgical anesthesia via mask induction; attempts to intubate an awake bird are extremely stressful and should not be attempted. In some birds, insertion of the endotracheal tube will induce a period of apnea. This can be pre-empted by topically applying a small volume of 2% lidocaine to the rim of the glottis a few minutes prior to tube insertion.

Raptors are also amenable to air-sac cannulation and this is a very useful modality for relieving dyspnea associated with upper airway obstruction or for administering gas anesthesia in instances where the presence of an endotracheal tube would interfere with manipulations about the head and mouth. Caudal thoracic airsac cannulation takes advantage of the normal physiologic direction of airflow from caudal to cranial to enter the lungs for gas exchange. Depending on the reason for cannulation, two scenarios for tube size are considered. Where relief of dyspnea from upper airway blockage is the goal, a tube should be selected that is similar in size or slightly larger than the trachea itself to provide a low-resistance pathway for air movement during spontaneous breathing (Fig. 18.3a). Where the cannula is intended for anesthesia administration, a smaller diameter tube that is more flexible (8–12 French red rubber tube or silicon) and of sufficient length (50–100 cm) to allow attachment of the anesthetic machine tubing at some distance from the patient is desirable (Fig. 18.3b).

Insertion of the air-sac cannula is relatively simple and can be accomplished following mask induction. The tube is inserted on either the right or left side. The site is prepared for surgical approach and a stab incision made in the last intercostal space midway between the attachment point of the ribs on the vertebral column and the intercostal joint (Fig. 18.4a) then extended slightly by blunt dissection with a hemostat. The tube is inserted between the ribs, arriving in the posterior thoracic air sac. Successful placement of the tube can be assessed by holding a small feather over the open end of the tube or by looking for condensation from expired air on the wall of a clear breathing tube. Once proper placement has been determined, adhesive tape "wings" are applied to the tube at the level of exit through the skin and sutured to the body wall with two small sutures (Fig. 18.4b). Breathing tubes may be left in place for several days to allow time for management and relief of the source of dyspnea. As with tracheal intubation, the tube is inserted only sufficiently to prevent slipping out of the body wall to prevent the tube from being blocked by internal organs.

Positive Pressure Ventilation

Intermittent positive pressure ventilation (PPV) is essential for ventilator support during extended anesthetic periods (>30 minutes). Despite leakage from the loose-fitting nature of the intubation tube, manual ventilation can be achieved by compression of a rebreathing bag attached to the open anesthesia circuit or by an ambu bag. Because of leakage as well as little risk of overinflation given the compliance of the air sacs and coelomic wall, pressures and volumes used for ventilation can be judged by watching the excursions of the sternum in the dorsally recumbent bird or elevations of the base of the tail in the ventrally recumbent bird. The rate of ventilation for the nonspontaneously breathing raptor is generally 6–12 respiratory cycles per minute. Provision of intermittent PPV in the spontaneously breathing, anesthetized bird during a prolonged anesthetic episode is important; a rate of 2 cycles per

Table 18.1 Reported dosages of more commonly used injectable anesthetics in raptors.

Agent	Red-tailed Hawk	Bald Eagle	Golden Eagle	Great Horned Owl	Falcons	Others	Comments	Reference
Alfaxalone						Multiple species	2–4 mg/kg IV	Ramsey (2011)
						Common buzzards (*Buteo buteo*)	Alfaxalone (10 mg/kg IV) produced good to excellent anesthesia in buzzards; heart rate, rhythm, and hemodynamic values remained stable	Kiliç (2021)
Ketamine						Multiple species	Dosed at 5–20 mg/kg, variable results, difficult recoveries	Samour et al. (1984)
Ketamine/diazepam	x			x	x	Eagles and vultures	3–8 mg/kg (K) + 0.5–1 mg/kg (D) IM	Heidenreich (1997)
						Multiple species	10–30 mg/kg (K) + 1.5 mg/kg (D) IV	Redig and Duke (1976)
Ketamine/ medetomidine*					x	Raptors	Ketamine (2–5 mg/kg IM) + medetomidine (25–100 µg/kg, lower dose IV, higher rate IM); reverse with atipamezole (65 µg/kg IM)	Ramsey (2011)
						Raptors	2–4 mg/kg (K) + 25–75 µg/kg (M) IV	Jalanka (1991)
						Multiple species	3–5 mg/kg (K) + 50–100 µg/kg (M) IM	Molero et al. (2007)
							Administered as preanesthetic to isoflurane in Saker falcons, reversed with atipamezole after isoflurane anesthesia	Lawton (2008)
							Dosage schedule: 3 mg/kg–60 µg/kg–0.15 mg/kg ketamine–medetomidine–atipamezole	
							5–30 mg/kg (K) + 150–350 µg/kg (M) IM	
Ketamine/xylazine						*Bubo* ssp.	10–15 mg/kg (K) + 2 mg/kg (X) IM	Carpenter & Marion (2005)
						Multiple species	For owls, response variable in *Bubo* spp.[1]	Redig (1998)
							Dosage recommendations reflecting species variations in response using a 5:1 combination of ketamine and xylazine; largely superseded by ketamine/medetomidine procedures	
Ketamine/xylazine/ yohimbine	x						Yohimbine administered 20 minutes after induction with a 2:1 combination of ketamine and xylazine yielded a dose-related reversal response and smooth recovery; xylazine superseded as above	Degernes et al. (1988)
Propofol	x			x		Multiple species	Induction and CRI rates assessed in hawks and owls (4.48 mg/kg and 0.48 mg/kg/min for hawks, and 3.36 mg/kg and 0.56 mg/kg/min for owls); hypoventilation, prolonged and variable recovery, moderate-to-severe excitation observed	Hawkins et al. (2003)
							1.33 mg/kg IV	Huckabee (2000)

(*Continued*)

Table 18.1 (Continued)

Agent	Red-tailed Hawk	Bald Eagle	Golden Eagle	Great Horned Owl	Falcons	Others	Comments	Reference
Tramadol/ketamine/xylazine Ketamine/benzodiazepines						Common buzzards (*Buteo buteo*)	By adding tramadol IM to ketamine-benzodiazepines or ketamine-xylazine anesthetic protocols, response duration to thermal sense increased up to 3 hours after recovery Tramadol did not have any significant effects on anesthesia times or ECG	Raisi et al. (2019)
Tiletamine/zolazepam (telazol)				x		Screech owls (*Otus asio*)	Telazol at 5–10 mg/kg provided satisfactory chemical restraint for at least 30 minutes in the two species of owls but was not satisfactory in red-tailed hawks at any dose	Kreeger et al. (1993)
Xylazine/yohimbine						Multiple species	Multiple species, 8–10 mg/kg IM and 2–8 mg/kg IV; generally inconsistent results and unfavorable levels of sedation; reversed with yohimbine (0.2 mg/kg)	Freed and Baker (1989)
Fentanyl/lidocaine Brachial plexus block					x		A combination of fentanyl:lidocaine (50 μg/kg:5 mg/kg) was effective for brachial plexus nerve block; required use of a nerve locator	d'Ovidio et al. (2011)
Lidocaine/bupivacaine brachial plexus block				X			A combination of 0.02 mL of 0.125% lidocaine and 0.125% bupivacaine was infused intraoperatively into the perineural sheaths of brachial plexus nerves prior to transection (scapulohumeral amputation)	Latney et al. (2018)

CRI, continuous rate infusion; ECG, electrocardiogram; IM, intramuscular; IV, intravenous; K, ketamine; m, medetomidine.
[1] Authors' experience.
* Medetomidine is no longer commercially available at the time of writing and has been replaced by dexmedetomidine.

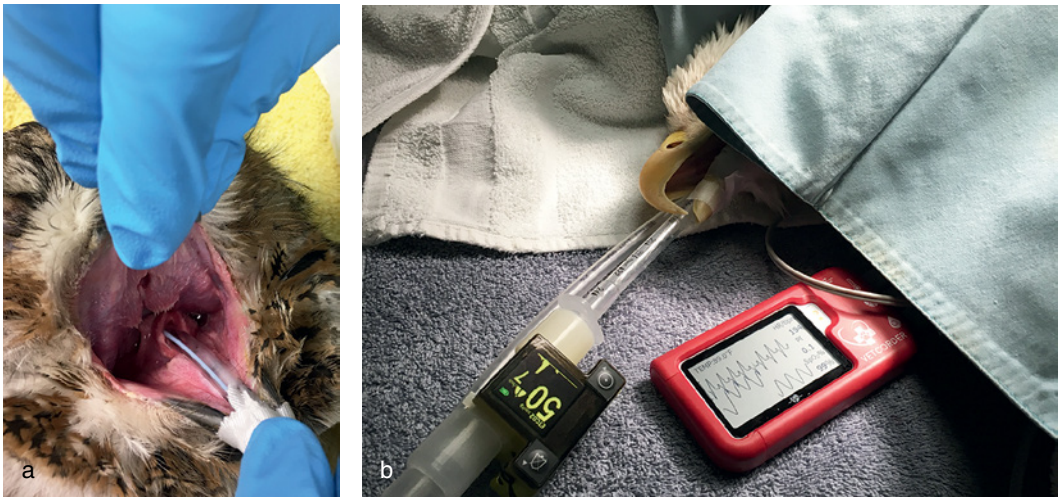


Figure 18.2 Insertion of an intubation tube in an owl (a) and an intubated bald eagle (b). Note the capnograph ($EtCO_2$, respiration rate, and real-time $EtCO_2$ waveform) and Vetcorder (SpO_2 sensor, two-lead electrocardiogram, and temperature cable).

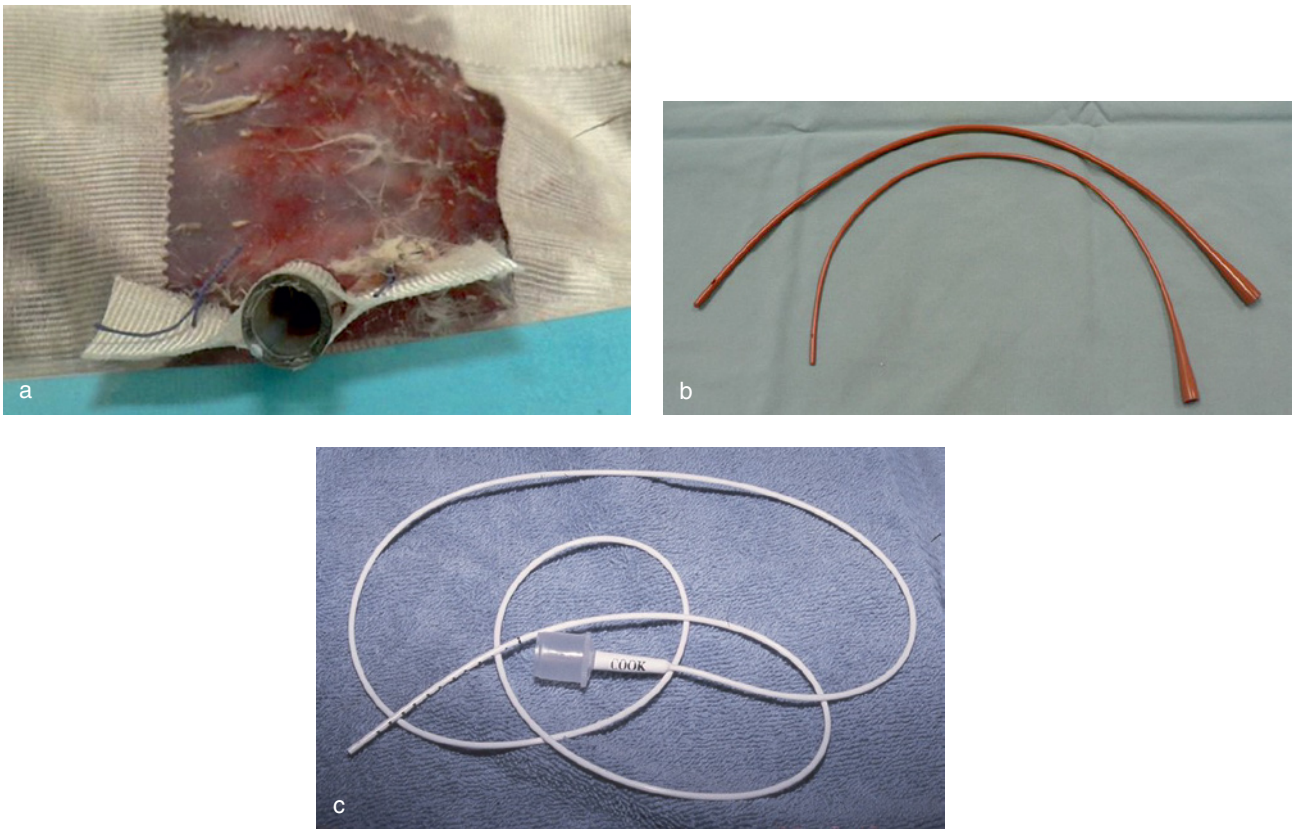


Figure 18.3 (a) Large-diameter air-sac cannula in place for use as a breathing tube. Small-diameter (8–12 Fr, 2.7–4.0 mm) air-sac cannula made from a red rubber tube (b) and a commercially available dedicated air-sac cannula tube (c) for use in administering gas anesthesia. Note the added length to provide maneuverability without dislodging the tube from its insertion site (see Fig. 19.4c).

minute (2 breaths/cycle) is sufficient to maintain blood gases in a suitable range (Aguilar et al. 1995) for extended time periods. Two breaths are needed to complete the respiratory cycle in an avian species instead of one as in mammals, therefore each cycle of PPV should consist of two breathes instead of one. Mechanical ventilators have been used to great effect by some clinicians (Hawkins & Pascoe 2007), though the incomplete seal around the uncuffed endotracheal tube can make implementation challenging.

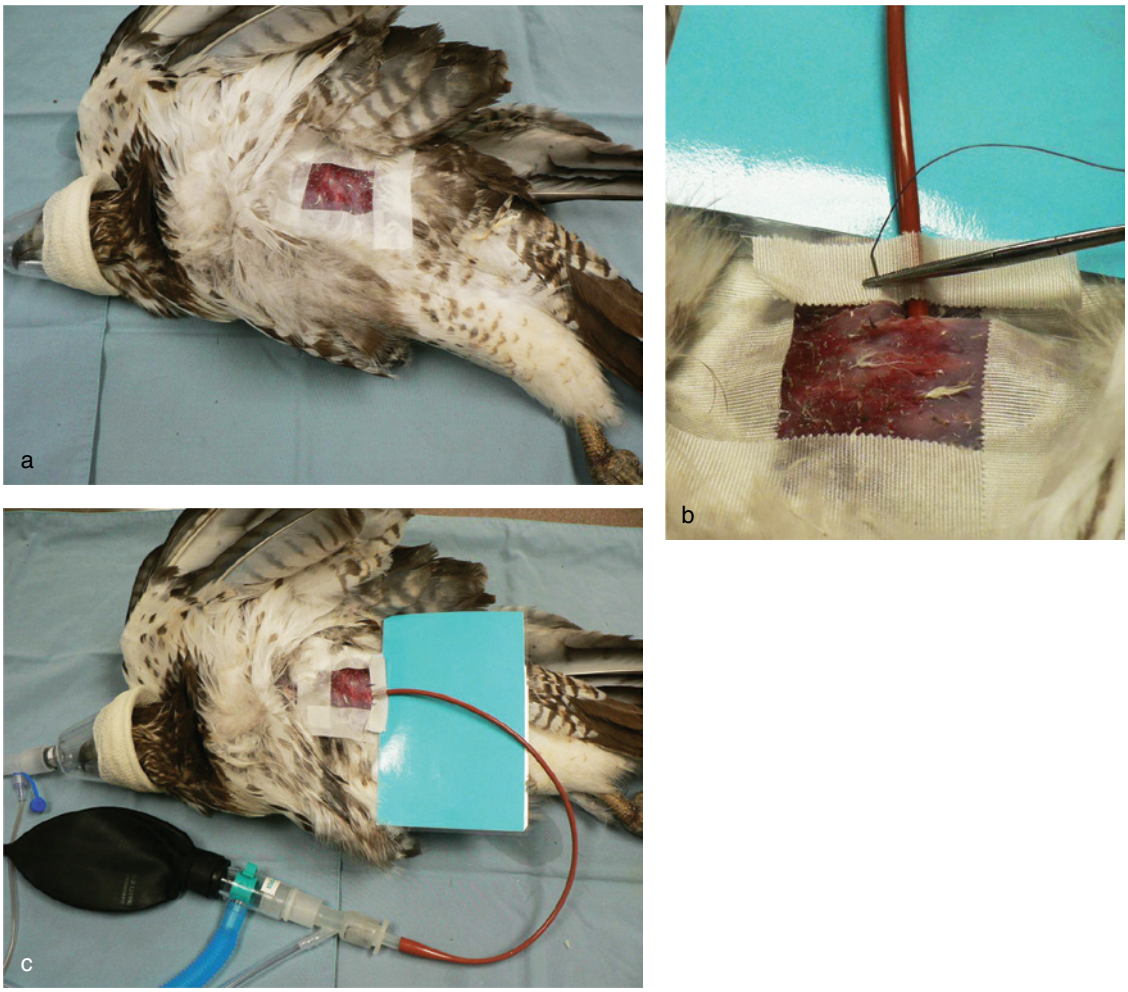


Figure 18.4 (a) Positioning of the patient and preparation of the insertion site in the last intercostal space for an air-sac cannula. (b) Anchoring the air-sac cannula in place by suturing tape wings to the body wall. (c) Air-sac cannula installed and attached to anesthesia administration tubing.

Vascular Access

The sites for vascular access in general include the right jugular (in some cases, the left is sufficiently large to permit needle or catheter insertion), the basilic vein on the ventral aspect of the humerus, the cutaneous ulnar vein where it crosses the ventral aspect of the elbow, and the medial metatarsal vein, just proximal to the hock joint. The latter is somewhat variable. In addition, in raptors weighing less than 100 g, the cutaneous ulnar vein may be too small to access, except in falcons, where even in the case of kestrels and merlins (*Falco columbarius*), it is sufficiently large to allow venipuncture.

An intraosseous catheter is a practical alternative in small or vasoconstricted patients. Sites include the proximal tibiotarsus and distal ulna. The distal ulna should not be utilized in Cathartiformes or other species with a pneumatized ulna (Coutant et al. 2018). Delivery of medications is considered to have a similar onset of action and peak blood levels as intravenous administration (Aguilar 1993).

Injectable Drugs for Sedation and Anesthesia

Inhalant anesthetic agents are the workhorse of avian anesthesia and presently are highly recommended over injectable agents. There is a historical (Cooper 1974; Cooper & Frank 1974; Redig & Duke 1976) as well as increasing contemporary interest in the role of injectable agents as stand-alone, short-term, reversible anesthetic agents, both as sparing agents for isoflurane and other inhalant agents, and for sedation and analgesia (Lee & Lennox 2016; Hawkins & Griffenhagen 2022). This is especially true of newer injectable agents.

Analgesia is an important consideration when utilizing gas anesthesia as gaseous agents do not provide any analgesia. Pain management is best accomplished through a multimodal approach where combinations of injectable drugs to address various pain pathways are used, thereby allowing lower concentrations of gas anesthetic and more effective pain management.

The recognized disadvantages of injectable agents are the interspecies variation and the general lack of research on a species-by-species basis to establish optimal dosing schedules and knowledge about pharmacological effects, not only for raptors, but for most avian species (Chapter 16). Some injectable drugs commonly used for minor procedures or as a preanesthetic for gas agents are discussed below. Prior to the use of any injectable agents, the patient should be weighed to the nearest 10 g and the dose calculated accordingly.

Sedative Agents and Protocols

Benzodiazepines such as diazepam (0.2–0.5 mg/kg IM) and midazolam (0.1–0.5 mg/kg IM) have been used successfully for short nonpainful procedures or preanesthetic sedation. These drugs have sedative and antianxiety effects, as well as providing good muscle relaxation. However, they provide no analgesia. Reports in psittacines suggest the use of midazolam directly instilled in the nares for sedation (2 mg/kg; Mans et al. 2011) or intramuscularly in combination with butorphanol (midazolam 0.25–0.5 mg/kg:butorphanol 1–3 mg/kg; Lennox 2011). Reversal of midazolam with flumazenil (0.05 mg/kg) is a further enhancement to its use. Altundag et al. (2021) administered midazolam intranasally to common buzzards (*Buteo buteo*) dosed at 2 mg/kg, which resulted in mild to moderate sedation in approximately 7 minutes. It was antagonized intranasally with flumazenil dosed at 0.05 mg/kg intranasally; reversal occurred in ~14 minutes. Limited experiences at the Raptor Center using intranasal midazolam with bald eagles (*Haliaeetus leucocephalus*) and a few other species showed inconsistent results relative to IM injections.

Adrenergic agonists such as xylazine (Freed & Baker 1989), medetomidine (Lawton 2008), and dexmedetomidine (Santangelo et al. 2009) may be used for general sedation or as a preanesthetic to inhalant anesthesia. They have the advantages of requiring very small volumes and of being reversible with yohimbine or atipamezole. Lawton (2008) recommends the usage of medetomidine dosed at 60–85 μg/kg. Reported dosage ranges for the more potent dexmedetomidine ranged from 25 μg/kg in common buzzards to 75 μg/kg in common kestrels (*Falco tinunculus*) (Santangelo et al. 2009). As adrenergic agonists, these agents may have some effect in countering the hypotensive conditions associated with isoflurane anesthesia (Goelz et al. 1990; Aguilar et al. 1995; Schellbacher et al. 2011). Their use as immobilizing agents for anything other than minor surgical procedures is not recommended. These may have utility for conducting procedures in the field such as a means of low stress restraint for transmitter attachment or blood collection (see below for use with opioids for analgesia).

These drugs are adequate for short procedures or can be utilized as a preanesthetic for inhalant anesthesia, where they have a significant minimum anesthetic concentration (MAC)-sparing and analgesic effects. Their use can cause notable bradycardia and respiratory depression. Xylazine has been used as a short-term sedative, but it is regarded as unreliable (though still useful with caution) due to its cardio-respiratory effects and the possibility of hyperexcitability (Freed & Baker 1989; Lawton 2008).

Short-term Anesthesia with Injectable Agents

Ketamine, a dissociative anesthetic, produces dose-related unconsciousness and analgesia, but with highly variable species-specific results and recoveries characterized by uncontrolled movements (Samour et al. 1984). Dosing varies between 10 and 200 mg/kg according to the bird's size (the larger the bird, the smaller the per kilogram dose used, but there is much species variability). We regard the upper end of this dosage range as excessively high and dangerous by a factor of 10. This drug should never be used alone. Despite indications of use in older literature (Redig & Duke 1976), ketamine can be safely used only up to a dose of 20 mg/kg in raptors; lower doses are recommended, and these can be achieved by combining it with an adrenergic agonist.

Combinations of ketamine and alpha-2 adrenergic agonists (e.g., xylazine, medetomidine, dexmedetomidine) or benzodiazepines (diazepam, midazolam) have utility in anesthesia of raptors. A mixture of ketamine and diazepam was one of the original protocols utilized in raptors but was found to be inferior to subsequent combinations of agents (Redig & Duke 1976; Kreeger et al. 1993; Heidenreich 1997). A combination of ketamine and xylazine (5:1 ratio) was extensively used at one time with varying degrees of success and marked species dependency as to results (Redig 1998). A combination of ketamine and xylazine in a 2:1 ratio was shown to be reversible with yohimbine and suggested to have utility for short procedures owing to the rapid metabolism of the ketamine (Degernes et al. 1988).

Further study on xylazine alone as a sedative by Freed and Baker (1989) in a variety of raptors showed generally poor sedation, but good reversibility with yohimbine. For the most part, all uses of xylazine have been superseded by medetomidine or dexmedetomidine (Ramsey 2011).

Butorphanol (1–3 mg/kg IM every 4–6 hours) is a commonly used injectable opioid analgesic in avian species. Used as a preoperative medication or a constant rate infusion (CRI) intra-operatively, butorphanol is inhalant sparing in some avian species (Riggs et al. 2008). It is typically dosed at 1 mg/kg preanesthesia, but doses as low as 0.3 mg/kg are effective as a preanesthetic agent; owing to its short half-life (1–2 hours) it may be repeated for long procedures (Hawkins & Pascoe 2007). The analgesic properties in raptors species appear lower than in other avian groups.

Based on current research, pure μ agonists appear to provide better analgesic effects in raptor species than κ agonists (Guzman et al, 2013, 2014a, 2018; Ceulemans et al. 2014). While the authors still utilize butorphanol with or without midazolam for sedation (Graham & Heatley 2007), buprenorphine is utilized for analgesia at a dose of 0.1 mg/kg IM except for accipiter species, where the dose is decreased to 0.05 mg/kg IM. Hydromorphone (0.1, 0.3, and 0.6 mg/kg IM) significantly increased the thermal nociception threshold for American kestrels (*Falco sparverius*) for 3–6 hours; appreciable sedation was detected in four birds when administered 0.6 mg of hydromorphone/kg (Guzman et al. 2013).

Tramadol is a synthetic analogue of codeine. It is a centrally acting μ agonist, and it has also been shown to bind weakly to κ and δ opioid receptors. By inhibiting the re-uptake of both norepinephrine and serotonin, tramadol activates the descending pain inhibitory system, therefore decreasing the sensation of pain. The pharmacokinetics of oral and/or intravenous administration of tramadol as well as its thermal antinociceptive effects have been looked at in several avian species, including bald eagles, red-tailed hawks, and American kestrels (Souza et al. 2009, 2011; Guzman 2014b). There are few reports using tramadol to produce balanced anesthesia in birds. Raisi et al. (2019) added tramadol IM (4 mg/kg) to ketamine–benzodiazepines or ketamine–xylazine anesthetic protocols in common buzzards. In this study, response duration to thermal sense increased up to 3 hours after recovery. Tramadol did not have any significant effects on anesthesia times or electrocardiograms (ECGs).

Another opioid, fentanyl, has been demonstrated to reduce the MAC for isoflurane in red-tailed hawks (Pavez et al. 2011). In Italy, wild birds were premedicated with midazolam (1–2 mg/kg, size dependent), induced with isoflurane, and partially maintained with an intravenous infusion of midazolam:fentanyl (1 mg/kg/h:30 μg/kg/h). This allowed for a lower maintenance percentage of isoflurane and the recovery was good or excellent (Paesano et al. 2015).

Propofol, a nonbarbiturate anesthetic, has been used as a bolus (1.33 mg/kg IV, titrate to effect) for induction and/or used as a CRI for maintenance of anesthesia; note propofol has no analgesic properties. Propofol provides a rapid induction, but some species are reported to have extended recoveries and excessive excitement. A study in red-tailed hawks and great horned owls (Hawkins et al. 2003) utilizing propofol for induction by direct intravenous injection at 1 mg/kg/min followed by maintenance with CRI at predetermined doses (0.48 mg/kg/min for red-tailed hawks and 0.56 mg/kg/min for great horned owls) induced a light plane of anesthesia accompanied by transient central nervous system signs during recovery. Respiratory depression and apnea were noted, necessitating the recommendation that ventilatory support be provided in all phases of its use. The authors concluded this agent was of limited utility in these raptor species.

Alfaxalone (reformulated with cyclodextrin) is a neuroactive steroid anesthetic agent commonly used in companion and exotic animal patients, with various effective routes of administration. There are multiple recent articles regarding its use in avian species. Like propofol, alfaxalone has a rapid onset of action, provides satisfactory muscle relaxation, and is not associated with accumulation after repeat dosing; like propofol, it also has no analgesic properties.

Kiliç (2021) administered alfaxalone IV (catheter) to common buzzards at a dose of 10 mg/kg during a 1-minute period followed by repeated bolus injections of 2–4 mg/kg of alfaxalone for up to 30 minutes (only when birds showed signs of awakening). Heart rate, respiratory rate, cloacal temperature, electrolytes, and blood gas values were monitored. This study indicated that alfaxalone produced good to excellent anesthesia in buzzards, characterized by rapid induction of anesthesia, excellent muscle relaxation, unresponsiveness to noxious stimuli, and smooth, uneventful recovery from anesthesia. Hypoventilation and apnea were uncommon at clinically relevant doses but became the most important adverse effects when larger doses were administered rapidly intravenously.

Local and Regional Anesthesia (Nerve Blocks)

Perioperative regional anesthesia using nerve blocks has received scant attention and initial attempts involving blind injection of local anesthetics (lidocaine/bupivicaine)

have yielded variable results in achieving a brachial plexus nerve block (Brenner et al. 2010; Figueiredo et al. 2008). A significant improvement in efficacy has been reported by incorporating fentanyl with lidocaine (fentanyl 50 μg/kg:lidocaine l5 mg/kg) and injecting it with the aid of a nerve locator. This approach was successful in providing analgesia and an isoflurane sparing effect in the repair of a humeral fracture in a peregrine falcon (*Falco peregrinus*) (d'Ovidio et al 2011). Latney et al. (2018) used a brachial plexus block for a scapulohumeral amputation in a 7-year-old peregrine falcon with a chronic malunion fracture of the left humerus secondary to self-trauma which occurred after left metacarpal and radio-ulnar amputations. A combination of 0.02 mL of 0.125% lidocaine and 0.125% bupivacaine was infused intraoperatively into the perineural sheaths of brachial plexus nerves prior to transection (scapulohumeral amputation). Part of a case series, none of the patients exhibited postoperative pain as evidenced by immediate return to function, immediate recovery of normal behavioral repertoires, and absence of pain on palpation of the surgical site and pectoral musculature. Extensive follow-up for all cases revealed no disease recurrence or surgical complications. While these appear to be valuable approaches to improving overall anesthesia for orthopedic procedures, clearly more work needs to be done to establish effective procedures across a variety of species and situations.

Inhalant Anesthesia

The halogenated hydrocarbons (isoflurane, sevoflurane, desflurane) have been used successfully in a wide variety of raptors (Table 18.2) and have long since replaced halothane or methoxyflurane. Each has its own characteristics of solubility in blood that affect the way they are used. Isoflurane is the most utilitarian, providing a suitably short induction time accompanied by little excitation, a sufficient down time after mask removal to allow some short procedures, and a rapid recovery. It has been in use for raptors since the 1980s (Clutton 1986). Isoflurane has been shown to be arrhythmogenic in bald eagles (Aguilar et al. 1995). In addition, a Doppler echocardiography-based study showed that isoflurane in addition to reducing heart rate also reduced blood flow velocity, but there was disconcordant species variability in these measures (Straub et al. 2003). In contrast, sevoflurane and desflurane, while having shorter induction times and lesser cardiac and ventilatory impacts (Joyner et al. 2008), had very much more rapid recovery times, making it nearly impossible to conduct any examination or minor procedures with the mask removed before the bird began to recover (Granone et al. 2012). One study of sevoflurane in crested caracaras (*Carcara plancus*) showed that while it caused mild reduction in various cardiopulmonary parameters, it was not arrhythmogenic (Escobar et al. 2009).

A study comparing isoflurane to sevoflurane was conducted in bald eagles (Joyner et al. 2008). Sevoflurane produced more rapid induction and recovery than isoflurane, caused a lower increase in blood pressure, heart rate, and temperature over time, and had a slightly lesser occurrence of cardiac arrhythmias, although they were seen with both agents. Sevoflurane had higher MAC values than isoflurane and was less likely to induce hypotension.

Preanesthetic Preparation

The goal of preanesthetic evaluation and preparation is to minimize the risk of anesthesia. While not always possible in emergency situations, taking the time to evaluate and prepare the patient can reduce the risk of an adverse event during anesthesia.

Fasting recommendations vary from none in small birds (use clean meat) with high metabolic rates to 12–24 hours in larger raptors (e.g., >500 g). If fasting is not an option, removing crop contents will reduce the risk of regurgitation and aspiration during recovery.

In addition to fasting, it is helpful to allow birds to acclimate in a quiet environment prior to anesthesia. This will allow for a decreased stress level and may reveal clinical symptoms previously hidden.

For raptors undergoing anesthesia for surgical procedures, fluids are routinely administered preoperatively during surgical preparation. Crystalloids (saline, lactated Ringers) up to 50 mL/kg are given subcutaneously in the inguinal area and/or intravenously. For long surgical procedures or in critical patients, it is recommended to insert an indwelling venous or intraosseous catheter shortly after induction and provide a slow drip of an intravenous solution (10 mL/kg/h for the first 2 hours, then reduced to 5 mL/kg/h for routine maintenance). This also provides ready access to an injection port in the event antibradycardic (atropine) or emergency drugs need to be administered.

Crystalloids are generally sufficient to maintain vascular volume in the face of inhalant agent-induced vasodilatation (Steffey & Mama 2007). Colloids, however, may be indicated in providing prolonged vascular support if there is a need to enhance colloidal osmotic pressure and arterial blood pressure, for instance in hypoproteinemic patients.

An in-line bubbler vessel, to provide humidification, can be used to counteract insensible loss of fluids associated with the administration of 100% oxygen (Fig. 18.5).

Table 18.2 Inhalant anesthetics in raptors.

Agent	Red-tailed Hawk	Bald Eagle	Golden Eagle	Great Horned Owl	Falcons	Other	Comment	Reference
Isoflurane			x				Among first reported uses of isoflurane in raptors – In 2:1 nitrous oxide:oxygen gas – difficulties with apnea, hypothermia, and inadequate immobilization at a vaporizer setting of 1–1.5%	Clutton (1986)
Various inhalants						Broad applications	General review of literature on use of inhalants	Fitzgerald and Blais (1993)
Isoflurane		x					Reported incidence of arrhythmias	Aguilar et al. (1995)
Isoflurane						Poultry	Very good safety in high-risk avian patients with heart diseases or trauma	Olkowski and Classen (1998)
Isoflurane						Multiple species	Procedural methods for administering and monitoring isoflurane with observations on species variations in response	Redig (1998)
Ketamine/ medetomidine/ isoflurane					x		Anesthesia of falcons with a combination of ketamine–medetomidine and isoflurane	Molero et al. (2007)
Isoflurane						Common buzzard (*Buteo buteo*)	Doppler-derived responses to isoflurane indicating alterations in blood flow velocity	Straub et al. (2003)
Isoflurane/sevoflurane		x					Showed decrease occurrence of arrhythmias with sevoflurane in bald eagles	Joyner et al. (2008)
Sevoflurane						Caracara (*Caracara plancus*)	Moderate cardiovascular and respiratory depression	Escobar et al. (2009)
Isoflurane/fentanyl	x						Fentanyl administration resulted in reductions in isoflurane Minimum Anesthetic Concentration without impact on blood gases or cardiovascular functions	Pavez et al. (2011)
Isoflurane/ sevoflurane/desflurane	x						Compared three agents for induction, recovery parameters	Granone et al. (2012)
Isoflurane/sevoflurane						Crested serpent eagle (*Spilornis cheela*)	Sevoflurane and Isoflurane anesthesia resulted in minor respiratory effects; both anesthetics are suitable agents	Chan et al. (2013)
Fentanyl/midazolam/ isoflurane						Multiple avian species	Premedicated with midazolam (1–2 mg/kg, size dependent); induced with isoflurane; partially maintained with midazolam:fentanyl (1 mg/kg/h:30 μg/kg/h) infusion (Continuous intravenous infusion). Allowed for lower maintenance percentage of isoflurane; recovery was good or excellent.	Paesano et al. (2015)
Isoflurane						Cinereous vulture (*Aegypius monachus*)	Increasing isoflurane concentrations during spontaneous ventilation led to dose-dependent increases in HR and End-tidal carbon dioxide concentration, with minimal changes in RR, decreased arterial Blood Pressure, and respiratory acidosis	Seok et al. (2017)



Figure 18.5 In-line bubbler bottle for humidification of transport and anesthetic gases.

Pain Management and Inhalation Agent Sparing

Analgesia in birds is also discussed in Chapter 16. Inhalation agents are regarded as having generally inadequate analgesia properties and therefore additional pain control is desirable. Utilization of concurrent analgesics also reduces the amount of isoflurane necessary for a procedure. The authors currently use buprenorphine IM (0.1 mg/kg, except for accipiter species which are dosed at 0.05 mg/kg) with or without midazolam IM (1 mg/kg). This combination can result in a brief period of apnea and/or shallow breathing. Typical surgical candidates (e.g., fracture patients) will have been placed on oral meloxicam, gabapentin, and/or oral tramadol prior to surgical preparation.

Atropine is avoided as a premedication as it does not effectively dry up oral and pharyngeal secretions, tending instead to make them more viscous (Fitzgerald & Blais 1993).

Dyspnea

Even when severe or arising from severe airsac disease (e.g., aspergillosis), dyspnea is not usually regarded as a contraindication to inhalant anesthesia. Between the state of unconsciousness, analgesia, and the 100% oxygen stream in which the gas is administered, dyspnea is almost always immediately lessened or relieved, allowing relatively normal anesthesia to proceed. If possible, the cause of the dyspnea can be evaluated and sometimes alleviated (e.g., foreign body in the trachea).

Administration of Inhalant Agents

Induction

The administration of sedative and preanesthetic agents prior to induction with the gaseous agent is recommended, ideally with the bird being unrestrained in a dark and quiet location while the sedatives take effect. However, this is not always desirable or practical and must be weighed against any additional pain and distress resulting from multiple manual restraints (Ramsey 2011). An advantage of the highly efficient avian respiratory system is that it is very easy to rapidly induce anesthesia through a face mask.

Anesthesia is typically induced with 4–5% isoflurane (or sevoflurane at 5–8%) in oxygen (1–2 L/min, depending on the size of the patient) using a face mask and a nonrebreathing (Ayres T-piece or Bain) system. As soon as the bird begins to relax and the involuntary nictating membrane response slows, the vaporizer setting should be reduced to 2–3% and adjusted as necessary to maintain the desired plane of anesthesia. For procedures lasting longer than 20–30 minutes, birds should be intubated as described above and, in any case, intubation tubes should be available for emergencies. As many birds will keep their eyelids partially open during anesthesia, it is recommended to install ophthalmic ointment to prevent corneal drying.

Owls respond well to induction at lower concentrations of isoflurane. Use of higher levels results in a too-rapid induction that increases the difficulty for equilibrating at a surgical plane without going into a dangerously deep level. Accipiters (especially sharp-shinned and sparrow hawks [*Falco sparverius*], goshawks [*Accipiter gentilis*], and Cooper's hawks [*Accipiter cooperii*] to a lesser extent) and merlins also benefit from a similar low-dose approach to induction.

Maintenance

Most raptors can be maintained at 1.5–2.5% isoflurane or 2–4% sevoflurane (lower concentrations if premedicated with analgesics or sedatives) with an oxygen flow rate of 1–2 L/min. Golden eagles (*Aquila chrysaetos*) and gyrfalcons (*Falco rusticolus*) require higher maintenance concentrations of isoflurane, usually at 3.5% or 4%. Anesthetic agents depress ventilation to a greater extent in

birds than in mammals (Edling et al. 2001) and therefore hypoventilation should be presumed in all anesthetized birds. Intermittent PPV (2–4 cycles per minute) (Aguilar et al. 1995) manually administered is recommended to support the anesthetized patient. Since the avian patient can rapidly change depth during anesthesia, the patient should be constantly monitored by a person dedicated to this role. Key variables to monitor are respiratory rate and character (slow, even cycles being the desired condition), heart rate and rhythm, physical reflexes (especially corneal reflex), temperature, and blood pressure. Importantly, corneal and palpebral reflexes are slowed, but not eliminated during anesthetic episodes.

Monitoring

The following variables are routinely used for monitoring inhalation anesthesia: respiratory rate and character, end-tidal CO_2, pulse oximetry, nictating membrane response, heart rate, ECG, and muscle relaxation (neck or limb). In addition, monitoring body temperature through an esophageal or cloacal thermometer is important to guard against both hyper- and hypothermia. In the intubated bird, end-tidal capnography using a side-stream sampling system (Fig. 18.2) is very effective for routine monitoring of ventilation (Edling et al. 2001; Desmarchelier et al. 2007). In such applications, ventilation is managed to keep end-tidal CO_2 between 35 and 45 mmHg, effectively avoiding respiratory acidemia from inadequate ventilation, but not leading to respiratory alkalemia (Desmarchelier et al. 2007).

Respiratory Rate and Ventilation

Since changes in respiratory rate typically precede cardiac changes, respiration is probably the single most important factor to monitor. Respiratory patterns should be deep, even, and at a moderate rate, typically 12–20 breaths per minute. This rate, however, is highly variable depending on the size of the bird, with larger patients having slower respiratory rates. The character and pattern over the duration of the episode are more important than the absolute rate.

It has been held in the past that because of their lack of alveoli, birds do not have a functional residual volume of air in their lungs to buffer changes in arterial partial pressures of oxygen and carbon dioxide (PaO_2 and $PaCO_2$) (McLelland 1989; Edling et al. 2001) and gas exchange does not occur unless there is movement of air through the air capillaries; this would suggest apnea could be immediately serious. Experience, however, has shown this not to be the case, and it has been argued (Hawkins & Pascoe 2007) that birds contain a large reservoir of air in the air sacs and, when maintained on a 100% O_2 supply, there is sufficient movement of gas across short diffusion distances to maintain O_2 levels for a short period of time. This observation is consistent with our experience in the anesthesia of thousands of raptors, and while not dismissing the risks of apnea, nonetheless it moderates the reaction to it. Conversely, if apnea occurs in a bird breathing room air (e.g., if anesthetized with an injectable agent), apnea would be a considerably more serious issue requiring aggressive response. Potential causes of apnea include placement of an endotracheal tube, poor ventilation, dive response (trigeminal nerve response), hypothermia, and respiratory depression secondary to anesthetic drugs. The most important monitoring system for avian anesthesia is an alert technician who recognizes changes in respiratory patterns, evaluates the underlying causes, and corrects them. Should apnea occur, anesthetic gases should be turned off, the delivery system purged, oxygen flow re-established, and the patient manually ventilated. Oftentimes, manipulation or insertion (if not previously intubated) of the endotracheal tube or stimulation of the tongue or the abdomen caudal to the sternum will re-initiate spontaneous breathing. If such stimulation is not effective, attach an ambu bag or other means of delivering air into the endotracheal tube (by mouth if necessary) and ventilate at 10–12 cycles per minute until respiration is restored. Gas delivery will need to be resumed at this point or the bird is likely to begin showing signs of recovery.

Heart Rate and Rhythm

In addition to a stethoscope (direct or esophageal), a Doppler monitor or electrocardiograph machine can be used to monitor heart rate and rhythm (Fig. 18.2). Rates vary inversely with the size of the bird. Small raptors will have rates >200 beats per minute (bpm) and generally too rapid to count. Mid-size birds (200–600 g) will maintain heart rates between 180 and 250 bpm, while eagles will have heart rates of 80–150 bpm. Maintenance of an even, steady rhythm in the range of an acceptable rate for a given species is more important than an absolute number. Cardiac complications can be minimized by proper fluid therapy, oxygenation, ventilation, and appropriate anesthetic depth. Decreased heart rate should prompt a reduction of anesthetic gas concentration, evaluation and treatment of hypotension, and review of the patient's surgical situation (pain, tissue trauma, positioning). Atropine administered intratracheally, intramuscularly, or via vascular access is an effective treatment for anesthetic-related bradycardia. Hypotension is countered

by crystalloid or colloid fluid administration. Cardiac arrest is typically preceded by apnea, but on rare occasions it can occur without warning and largely for unknown reasons; underlying pathology is seldom found. Unfortunately, cardiac arrest is typically not successfully reversed.

Arrhythmias, primarily A-V blocks, have been reported to occur in a high percentage of bald eagles anesthetized with isoflurane (Aguilar et al. 1995; Joyner et al. 2008). However, it is not accompanied by cardiac arrest or other complications. Their causes are not apparent. As a practical matter, in our application in thousands of anesthetic episodes of anesthesia in eagles, they do not appear to present undue risk of morbidity or mortality.

Reflexes

Anesthetic depth can be evaluated by standard reflexes such as palpebral, corneal, and pedal withdrawal, with corneal reflex being the most useful. For nonpainful procedures, a light plane of anesthesia will correlate with loss of voluntary motion, but the presence of all three monitored reflexes. At a surgical plane of anesthesia, the palpebral and withdrawal reflexes will be absent, and the corneal reflex will be present, but slow. Complete absence of a corneal reflex indicates a very deep state of anesthesia and is avoided.

Temperature

Monitoring and maintaining body temperature is critical in an anesthetized raptor. Small raptors may quickly lose body heat because of impaired thermoregulation due to their small body mass relative to surface area. Large species and northern owl species that have a very heavy insulating down feather coats may become hyperthermic. In addition to impaired thermoregulation, the use of room temperature fluids, alcohol during surgical preparation, cool anesthetic gases, and removal of feathers for the surgical approach can contribute to hypothermia. Monitoring body temperature can be done with an esophageal thermometer or a cloacal probe. Heat loss can be mitigated by providing a heat source such as a forced-air warming system (Bair-hugger®) or a circulating warm water blanket, or a conventional heating pad maintained on a low setting and usually turned off after a procedure has begun. The use of clear plastic surgical drapes may be beneficial in small birds as they provide both insulation for the patient as well as visualization of the patient. However, they are good insulators and will result in hyperthermia in larger raptors. Hyperthermia can be prevented or reversed by placing ice packs alongside the body of the patient.

Vascular

Blood pressure assessment may be useful (Lloyd et al. 2007). When used with an appropriately sized blood pressure cuff, a Doppler unit may provide both heart rate and blood pressure information (Hawkins & Pascoe 2007). While useful for heart rate, the high variability in blood pressure results diminishes the usefulness of this method for routine monitoring (Zehnder et al. 2009). Alternatively, monitoring the strength of the pulse on a peripheral artery and the capillary refill time can be used as acceptable surrogates for blood pressure monitoring.

Pulse oximetry technology has advanced in recent years, and there are devices and models that are adapted for use in avian and exotic animal patients (Vetcorder). Pulse oximetry values can be obtained on the digits or patagial web of most raptor patients (Fig. 18.6). For the patagium, part the feathers with a small amount of alcohol to allow for visualization and appropriate contact of the device, and apply the pulse oximeter directly over a small vessel (Lierz & Korbel 2012).

Recovery

Recovery is a critical phase of the anesthetic episode. Recovery is generally rapid once the gas anesthetic is removed, occurring gradually over several minutes (Joyner et al. 2008). The vaporizer should be turned off and the endotracheal tube briefly disconnected while the system is purged, then reattached so the bird can be maintained on oxygen during the recovery process and be prepared for assisted mechanical ventilation in the event of apnea. A brief excitatory phase will be experienced as the anesthetic plane lightens, which may be accompanied by regurgitation. Extubation is done when the bird begins to make head movements. At the time of extubation and periodically during recovery, the oral cavity should be checked for signs of regurgitation or airway obstruction and any offending material removed with cotton-tipped applicators. It is critical not to impair the respiratory movements of the keel, as well as to be able to continue to monitor respiration. Gentle physical stimulation by moving the wings and legs can increase the rate/depth of respiration and help awaken the bird.

Once the bird can hold its head and protect its airway, it should be placed on a doughnut ring made from a towel and laid in a warm, dark, quiet environment to complete its recovery. Most birds are fully recovered in 30 minutes from inhalation anesthetic. Administration of intra-operative analgesics and/or sedatives will typically cause the bird to sleep quietly for an extended time when left alone after recovery from the inhalant gases.



Figure 18.6 (a) Pulse oximetry clip on a red-tailed hawk patagium. (b) Pulse oximetry clip on a great horned owl digit.

Anesthetic Administration Through an Air-sac Cannula

Gas flow rates need to be reduced relative to those that would be used for maintenance of a bird with either a face mask or an open system (0.5–1 L/min) (Fitzgerald & Blais 1993) or 2 to 3 times minute volume (Hawkins & Pascoe 2007) to prevent alkalemia from overventilation. Isoflurane and sevoflurane vaporizers have been shown to deliver anesthetics with acceptable precision and accuracy at flow rates as low as 0.05 L/min (50 mL/min) and some flow meters will allow accurate assessment of flow rate at levels as low as 0.05 L/min (Ambrisko & Klide 2006). Use of an inline bubbler system humidifies the carrier gas and the stream of bubbles allows a further assessment of flow rate. At this point, no guidelines exist for optimizing flow rates. As a practical matter, flow rates between 250 and 500 mL/min are used; if there is a need to reduce ventilation, lower flow rates or a smaller diameter cannula size is used to reduce the rate of gas presentation into the air sac. Respiration movements cease entirely and monitoring is done by assessment of heart rate and corneal reflexes. Future refinements on this methodology should include pulse oximetry, capnographic monitoring of exhaled gases, and optimization of gas flows. A bird maintained with an air-sac cannula will typically start to exhibit respiratory movements within less than a minute of the removal of the tube.

Special Considerations

Special attention needs to be applied when administering anesthetics to accipiter species of raptors (goshawks, Cooper's hawks, sparrowhawks, and sharp-shinned hawks). Consider reducing the dose of any injectable agents and inducing with lower levels of gaseous agents. A higher level of attention is paid to hydration status, pain reduction, and use of inhalant gas-sparing agents during anesthetic episodes. Accipiter species are prone to sudden cardiac arrest, especially during recovery. The causes are not apparent (catecholamine-mediated?), but it appears to be associated with the return of consciousness and visual awareness of their surroundings.

Additional use of pain management as an adjunct to isoflurane anesthesia maybe required for owls and golden eagles, and for most raptors when surgical procedures are being conducted on their feet (e.g., bumblefoot treatment).

Anesthetic Risk

It has been published that anesthesia in birds is associated with a higher mortality rate (3.95% for parrots, 1.76% for other avian species) as compared to domestic mammals (cats 0.24%, dogs 0.17%) and humans (0.02–0.005%), although the literature is limited (Brodbelt et al. 2008;

Carter & Story 2013). The published studies are retrospective, with the definition of anesthetic-related deaths varying from death while under anesthesia to death within 48 hours (or more) of an anesthetic event.

A study utilizing isoflurane with over 6500 anesthetic events with chickens and turkeys, many with high-risk conditions (heart disease, trauma), resulted in no complications (Oklowski 1998). In contrast, a retrospective study by Seamon et al. (2017) involved birds presented to a veterinary referral hospital. Of 352 birds, 3.4% of the birds died during anesthesia, 4.3% died in intensive care after anesthesia, and 6.3% were euthanized after anesthesia. None of the variables studied (sex, wild/captive/pet, and preanesthetic health status) were significantly associated with survival versus nonsurvival.

Two other papers demonstrated that preanesthetic health status was significantly correlated with mortality during or post anesthetic. Dobbs (2021) reviewed avian anesthesia mortality and the associated risk factors over a 5-year period in a United Kingdom zoological collection. A total of 135 individuals across 37 species (including five species of owls but no other raptors) were manually restrained and induced with isoflurane via facemask (no premedication) for a total of 206 events. The anesthesia related mortality rate was 3.88%. Abnormal health status (15 times higher risk than birds classified as healthy) and longer anesthetic procedures were associated with a significantly increased risk of anesthesia-related death.

Utilizing American Society of Anesthesiologists grades 1–5 to classify health status prior to anesthesia, Hollwarth et al. (2022) reviewed 1820 anesthetic records from 168 avian species over 3 years and showed that while both healthy and unhealthy birds had a higher mortality rate than dogs and cats, the unhealthy birds had 11.5 times (ASA 3), 40 times (ASA 4), and 185 times (ASA 5) higher odds of suffering a mortality event than healthy birds (ASA 1 and 2).

Given the diversity of bird species, the variety of circumstances requiring general anesthesia, and the range of anesthetic agents and approaches, broad studies may be of limited value. In addition, the ability to compare anesthetic risk with publications on mammalian anesthetic risk is risks is fraught with inconsistencies, including that most procedures performed on birds requiring general anesthesia are not elective and are performed on unhealthy patients, particularly in referral hospitals. Unpublished data from the Raptor Center reflects the importance of species as a variable in raptors; Cooper's hawks have an anesthetic risk in a similar range to parrots, twice as high as merlins and 3–4 times higher than red-tailed hawks, great horned owls, and bald eagles. The Raptor Center admits over a thousand raptor patients annually, generally unhealthy. Almost all of them receive isoflurane general anesthesia at least once; many of them receive multiple anesthetic events over many weeks or months. It is the authors' impression that raptor mortality events are very low and repeated anesthetic events in the same individual do not present increased risk.

Summary

Best practices for raptor anesthesia are built on the foundation of a relatively few species-specific scientific studies, extrapolation of knowledge from other species, and incorporation of a wealth of evidence-based practice. As a group, raptors with a wide variety of health conditions are frequently anesthetized for physical examinations, medical treatments, and surgery. Outside of a few species-specific differences – a hallmark of avian medicine – raptor anesthesia is fundamentally a subset of avian anesthesia. Attention to basic principles, including performing a thorough physical examination to determine health status in advance, correcting as many pre-existing conditions as possible, careful monitoring of the patient during the anesthetic event, and minimizing the anesthetic duration, is the basis for maximizing successful outcomes.

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19

Ratites

Jessica Siegal-Willott

Introduction

Ratites belong to the avian orders Struthioniformes (ostriches), Casuariformes (emus and cassowaries), Rheiformes (rheas), and Apterygiformes (kiwis) (Smith 2003). Depending on the classification system, Tinaniformes (tinamous) may also be included.

Taxonomy and Biology

Ostriches (*Struthio camelus*) are the largest living birds (Table 19.1). There are several recognized subspecies confined to Africa and portions of the Middle East. Ostriches are sexually dimorphic; males are generally larger and have distinctive black feathers and wing plumes.

The common rhea (*Rhea americana*) and Darwin's or lesser rhea (*Rhea pterocnemia*) are endemic to the grasslands of South America. The emu (*Dromaius novaehollandiae*) is confined to Australia. Emus are second in size to the ostrich, with the females slightly larger than males. There are three cassowary species, the double-wattled (*Casuarius casuarius*), single wattled (*Casuarius unappendiculatus*), and the dwarf (*Casuarius bennetti*), all native to the Australasian rainforests. The three species of kiwi are confined to New Zealand: the great spotted (*Apteryx haastii*), the little spotted (*A. owenii*), and the brown (*A. australis*). Tinamous are small, flighted ground-dwelling birds from the forests of South America. There are 47 recognized species and they are either classified as or are considered the closest avian relatives to the ratites described above.

Anatomy and Physiology

The term "ratite" refers to the flat raft-like sternum lacking a keel bone for attachment of the large flight muscles. All have elongated necks and relatively long, muscular legs, but little pectoral muscle development. All possess elongated toenails for aggression or defense, and are strong and rapid runners. Ostrich toenails are blunted, whereas those of other ratites are sharp. Rheas can abruptly change direction when running, and both rheas and cassowaries are powerful swimmers.

As with other birds, ratites lack a diaphragm. They possess much-reduced air sacs compared to flighted birds. Respiration requires movement of the sternum down and forward, with the ribs expanding outwards. This is inhibited when weight, such as from a person straddling the bird, is applied from above. Death of birds thus restrained has been attributed to hypoxemia. Only the femur is pneumatized in ostriches and emus (Fowler 1996).

The normal respiratory rate of an adult ostrich is 6–12 breaths per minute, but may increase up to 40–60 breaths per minute during periods of hyperthermia. Normal body temperature (38–40°C) is maintained during thermal stress using evaporative cooling from the trachea, air sacs, and pharynx (Fowler 1996). The ratite glottis is simple with a large opening, an adaptation proposed to facilitate inhalation of air during strenuous exercise (Fig. 19.1). The trachea is composed of complete cartilaginous rings.

Ratites possess a renal-portal system, similar to other birds. Although theoretically it might enhance excretion of renally eliminated drugs, in ostriches administered xylazine/tiletamine/zolazepam there was no significant difference between injection in the thigh or muscles at the base of the wings in onset, duration or recovery (Carvalho et al. 2006). The physiologic role of the renal-portal system is poorly understood; care is used when potentially nephrotoxic drugs or those primarily eliminated by the kidneys (i.e., ketamine) are administered into the thigh musculature or medial metatarsal vein.

The ostrich is the largest living bird, with some males weighing as much as 160 kg (Table 19.1). Both male and female emus possess a ventral midline tracheal sac, approximately 10–15 cm cranial to the thoracic inlet.

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Table 19.1 Reported weight and height ranges for ratites and tinamous.

Species	Height (m)	Weight (kg)
Ostrich	2.1–3.0	≤160**
Emu	1.5–1.9	30–55*
Cassowarys		
Double wattled	1.3–1.7	♂ 29–34
Single wattled	1.5–1.8	♀ ≤58
Dwarf	1.0–1.1	NR
		17.6–25
Rheas		
Greater	1.2–1.7	20–25**
Darwin's	1.0–1.1	10–25**
Kiwis	0.35–0.55	0.67–4*
Tinamous	NR	0.04–2.3*

NR, not reported. *Females larger than males; **males larger than females.

The kiwi nares are located close to the beak tip; this location is thought to facilitate the scent location of food amongst forest leaf litter. The kiwi egg is the largest proportionately of any living bird. Prior to oviposition it occupies a large proportion of the coelomic cavity, with a consequent reduction in air sac space. Further compromise to respiration due to pulmonary compression will occur if the animal is turned on its back. Kiwis also have lower body temperature (36.6–40.3°C) and metabolic rate than most other birds (Smith 2003).

Physical Restraint

Young ratites (chicks and small juveniles weighing ≤6 kg) are manually restrained by supporting under the body and allowing the legs to either hang or be folded. Birds weighing 6–15 kg are restrained with a hand around the abdomen, leaving the legs free. Care is taken during catching or handling to prevent damage to the legs. Chicks can also be wrapped in a towel for restraint or travel.

Juveniles and adult ratites require experienced handlers for restraint. These birds are large and strong, and possess large claws on the toes that can be used for defense. Emus and cassowaries in particular have large nails on the medial digit. Male ostriches are especially dangerous during the breeding season. Ratites jump, kick, and slash in a forward direction, and thus are approached from behind or the side to minimize risk of injury to the handler. Emus can also kick sideways, and rheas can kick in any direction. Gloves and protective clothing are often useful in preventing trauma from the distal limbs during restraint. Assuming a flat (prone) position on the ground will prevent trauma from kicking if escape from the bird is not possible.

Physical restraint of adult ratites by experienced handlers involves straddling the bird, with its legs in front of the holder. The wings should be grasped at the level of the humerus; the bird may also be restrained by a hand over the breastplate. Emus and cassowaries should not be restrained at the humerus, as the wings are reduced in size and may fracture. Emus accustomed to handling, and gently restrained from behind, may allow collection of blood



Figure 19.1 The glottis of most ratites, as in this rhea (a) and intubated cassowary (b), is large and readily visible at the base of the tongue.

or injection of anesthetics into the right jugular vein. The bird will, however, respond violently if the upper neck or head is grabbed.

Alternatively, in ostriches the head may be grasped and quickly lowered below the level of the body. This prevents the ratite from kicking above its head level, minimizing the risks to the handler. This method of restraint is often used to place a hood, and possibly injection of medications.

Padded chutes, boards, alleyways, and stanchions are useful in the movement, separation, and isolation of individual animals for restraint and anesthetic procedures. Dim lighting (emus, rheas, cassowaries, ostriches) and/or hooding (ostriches only) to decrease visual stimuli are useful for restraint. Hoods should cover the eyes without occluding the nostrils and extend approximately a third of the distance down the neck (Cornick-Seahorn 1996) (Fig. 19.2). Hooks are not recommended for catching or restraint as they may result in lacerations of the neck and/or trachea, and possibly death of the bird if not used appropriately (Raines 1998). In some situations, however, this is the only way to catch the head for hood placement. Proper construction and application of hooks are described by Fowler (1995).

Emus present special challenges. Their skin is thin and easily lacerated. The head and long neck are vulnerable to injury because of the lack of significant muscle or soft tissue covering. The trachea is also easily collapsed. These birds are readily stressed, with subsequent respiratory or circulatory collapse, exertional rhabdomyolysis, self-trauma, and hyperthermia. Lastly, emus are capable of jumping high distances (≤2 m) and will attempt escape. Juvenile emus are more tractable, requiring only an experienced handler. One hand is placed between the legs and on to the sternum, leaving the other hand free to immbolize the head and neck (Mouser 1996).

Cassowaries are aggressive, requiring sedation or anesthesia for most handling procedures; hooding or covering the eyes is not adequate for safe restraint. During the very short period of sexual receptivity, captive females may be approached and allow examination and blood collection.

If possible, physical restraint occurs in secure areas, with solid, nonslip surfaces, free of large, deep-water sources, obstacles that may injure the bird or handler (hooks, nails, ledges, holes, wire, machinery, etc.), and at a suitable ambient temperature. Capture enclosures are designed to minimize risks to the patient and handlers, with easily accessible exit routes. Padded equine recovery stalls, with lights that can be dimmed, are excellent areas for restraint, induction, and recovery. Heavy foam pads, when used as shields, protect handlers and are used to compress birds in a confined space for intramuscular (IM) or intravenous (IV) injections. These pads are cleaned and disinfected between uses. Wooden shields are also useful to protect handlers when approaching lightly anesthetized animals (Fig. 19.3).



Figure 19.2 A hood reduces excitement and struggling in ostriches; it is not recommended in other ratites.



Figure 19.3 Wooden shields are used to protect handlers when approaching partially anesthetized ratites.

Vascular Access

Intravenous injections and phlebotomy are performed using either the right jugular (14–22-gauge), brachial, or medial metatarsal vein. The medial metatarsal vein (Fig. 19.4) is not accessible in the awake adult. In emus and cassowaries the basilic (ulnar) vein is small (although still able to be catheterized) as a result of vestigial wing development (Fig. 19.5). The wings are also prone to fracture during manual restraint (Cornick-Seahorn 1996).

IV fluids are administered to anesthetized ratites at 5–10 mL/kg/h. Fluids commonly used include lactated Ringer's solution, Ringer's solution, and 0.9% sodium chloride. Fluid supplementation with dextrose may be warranted in young and/or debilitated birds. If IV access is not possible, intraosseous (IO) catheters may be placed in juvenile birds. The ulna and tibiotarsus are commonly used for IO access.

Endotracheal Intubation

Noncuffed endotracheal (ET) tubes are used to prevent pressure necrosis of the tracheal mucosa, although some authors prefer cuffed tubes to minimize the risk of aspiration and ensure effective mechanical ventilation. The glottis is large and easily visualized for insertion of the ET tube (Fig. 19.1). Light bandaging around the neck of emus prevents air from distending the subcutaneous air sac during positive pressure ventilation.



Figure 19.4 The medial metatarsal vein can be catheterized for fluid administration in anesthetized cassowaries and other ratites.



Figure 19.5 The wings of emus, cassowaries, and other ratites are small and can be fractured if used to restrain an animal. The basilic (ulnar) vein on the medial surface of the wing can be used for blood collection in sedated or anesthetized animals, and for catheterization for fluid administration under anesthesia.

The head and neck are positioned to prevent kinking of the ET tube and to minimize risk of regurgitation and aspiration. Tube internal diameter varies with bird size, ranging from 4 to 18 mm. Intubation and positive pressure ventilation are recommended for all prolonged (≥10 minutes) or surgical procedures. Ventilatory support aims to achieve a tidal volume of 10–20 mL/kg, respiratory rate of 6–12 breaths per minute, and a peak inspiratory pressure of 10–15 cm water (Cornick-Seahorn 1996; Fowler 1996).

Analgesia

Use of analgesics is based on experience in other avian species (see also Chapters 2 and 15). Limited work has been done to establish dosage ranges in ratites. Fentanyl and butorphanol have been used as adjuncts to general anesthesia for pain control (Cornick-Seahorn 1996).

Chemical Restraint and Anesthesia

The drugs used for chemical restraint in ratites are summarized in Table 19.2. IM administration is routine; the cranial and caudal thigh muscles and lumbosacral area (in

Table 19.2 Anesthetic agents used in adult ratites.

Agent	Ostrich	Emu	Rhea	Cassowary	Comments	Reference
Sedation						
Azaperone	0.5–2					Jensen (1990)
	0.55					Gilsleider (1998)
Acepromazine	0.25					Ciboto et al. (2006)
Detomidine	1.5					Jensen (1990)
Diazepam	0.05			1 q18h		Tully et al. (1996a)
	0.3–0.5				For recovery	Smith (2003); Cornick-Seahorn (1996)
						Cornick-Seahorn (1996)
	0.1–0.2[a]					Ramsey (1991)
						Gilsleider (1998)
	0.1–0.3[a]					Lin et al. (1997)
	0.3[a]					Cornick-Seahorn (1996)
	0.33[a,b]					Fowler (1995)
	0.5–1					
		5[a,e]	5[a,e]			
	5[e] PO					
Medetomidine	0.1					Van Heerden & Kefren (1991)
	0.26–0.31				Light sedation	
					Heavy Sedation	Westcott & Reid (2002)
	0.38–0.54					
						Westcott & Reid (2002)
Medetomidine/ ketamine				0.09–0.13/3.4–4.3[b]	Heavy sedation	Citino (pers. comm.)
Medetomidine, medetomidine/ midazolam				0.12–0.13	First dart	Citino (pers. comm.)
				0.04/0.2[b]	Second dart combo	
Midazolam	0.15[d]					Cornick & Jensen (1992)
	0.15[a,b]					Lin et al. (1997)
Telazol/ diazepam		3.3/0.13 [b]				Tully et al. (1996a)
Xylazine	0.2–2					Gilsleider (1998)
	0.4–0.9					Cornick & Jensen (1992)
	0.5–1					Fowler (1995)
	1					Ciboto et al. (2006)
	4					Al-Sobayil et al. (2009)
Xylazine/ butorphanol			2.26–2.75/ 0.12–0.2			Lin et al. (1997)
Immobilization						
Carfentanil	3.3[e]					Fowler (1995)
Carfentanil/ ketamine	3/200[e]					Fowler (1995)
Carfentanil/ midazolam/ ketamine				0.04–0.06/0.1–0.2/2.5–4.9[g]	Stormy induction possible	Citino (pers. comm.)
Etorphine	1.5–6[e,h]					Fowler (1995)

(*Continued*)

Table 19.2 (Continued)

Agent	Ostrich	Emu	Rhea	Cassowary	Comments	Reference
Etorphine/ acepromazine	2.5–3/50[b,e]				Variable	Stoskopf et al. (1982)
	3.6/15[b,e]				Excitement Moderate sedation	Samour et al. (1990)
Etorphine/ acepromazine/ xylazine	6/25/200[e]					Samour et al. (1990)
Etorphine/ ketamine				0.1/6.5 5(ket amine)[c]	Reverse etorphine with diprenorphine Long, smooth recoveries	Ensley et al. (1984)
	2–6[e]/150–200[e]			7–12[e]/100–300[e]		Stoskopf et al. (1982)
Etorphine/ medetomidine	8–9/4–8[e,h]					
Medetomidine/ ketamine	0.08/2[b]				Bradycardia	Langan et al. (2000)
	0.05–0.15/3–7					Fowler (1995)
Metomidate/ azaperone	20/6.6[b] 10/3.3[b]				Apnea; respiratory side effects; salivationregurgitation at higher dose	Van Heerden & Kefren (1991)
Telazol	5–20[b]					Van Heerden & Kefren (1991)
Xylazine	1–2.2					Jensen (1992); Fowler (1995)
Ketamine			12.5			Smith (2005)
Thiafentanil/ medetomidine		0.175/0.09				Cushing & McClean (2010)
Induction						
Alphaxalone/ alphadolone	2.41–4.8[a]					Cullen et al. (1995)
Carfentanil	0.03[d]				Poor induction; apnea	Honnas (1991)
	0.3					Cornick & Jensen (1992)
Diazepam/ telazol	0.1/4.4					Cornick-Seahorn (1995)
Diazepam/ ketamine		0.5/8[a]				Tully et al. (1996b)
	0.22/4.4[a,d]					Honnas (1991)
	0.2–0.3[a]/2–10[a]					Gilsleider (1998)
	0.1/8					Fowler (1995)
	0.24/4.75[a]					Burba (1996)
	0.25[a]/5[a]					Ciboto et al. (2006)
	0.22[a]/4.4[a]				Bradycardia, hypercapnia, poor induction	Cornick & Jensen (1992)
Isoflurane	5%	5%	5%		Juveniles (<6 months)	
Ketamine	8[a]				Given 20 minutes post xylazine	Al-Sobayil et al. (2009)

Table 19.2 (Continued)

Agent	Ostrich	Emu	Rhea	Cassowary	Comments	Reference
Ketamine/ xylazine/ guaifenesin		15/3/0.1% K/0.05% X/5% G			Induce with K/X; maintain on K/X/G IV at 2–4 mL/ kg/h	Cornick-Seahorn (1996)
Propofol	3[b]				Apnea may occur	Langan et al. (2000)
	0.2 mg/kg/min[f]					Langan et al. (2000)
	10[a]					Pye (2007)
	4[a]					Ciboto et al. (2006)
Telazol	3.7[a]					Honnas (1991)
	3[a]					Ciboto et al. (2006)
	3.7[a]				Poor/rough recovery; apnea	Cornick & Jensen (1992)
	2.3–4.9[a]	2.3–4.9[a]	2.3–4.9[a]		After sedation with diazepam	Lin et al. (1997)
	4.35					Tully et al. (1996a)
	5					Gilsleider (1998)
Xylazine/ alphaxalone/ alphadolone	1.13–1.85/ 1.66–3.53[a]					Cullen et al. (1995)
Xylazine/ butorphanol/ telazol	1.06–2.03/ 0.10–0.14/ 2.3–4.0[a]	1.06–2.03/ 0.10–0.14/ 3.4–4.9[a]	2.12–2.75/ 0.12–0.55/ 3.0–5.8[a]		Higher doses needed in rheas	Lin et al. (1997)
Xylazine/ carfentanil	0.5/0.015[a]					Honnas et al. (1991)
	0.5/0.15[a,d]				Apnea	Cornick & Jensen (1992)
	150 mg[e]/3 mg[e]				Reverse with yohimbine / naltrexone	Raath (1992)
Xylazine/ diazepam/ ketamine	0.44/0.15/2.8[d]					Honnas et al. (1991)
	0.44/0.15[a]/2.8[a]				Poor induction	Cornick & Jensen (1992)
Xylazine/ diazepam/ ketamine						
Xylazine/ ketamine	0.45/25					Matthews et al. (1991)
	2.2/2.2–3.3					Fowler (1995)
	0.5–1/2–10[a]					Gilsleider (1998)
Xylazine/ ketamine/ alphaxalone-alphadolone	1/5/12–17.1[a,b]				Supplemental A-A needed for prolonged procedures	Gandini et al. (1986)
Analgesia						
Butorphanol	0.02					Cornick-Seahorn et al. (1995, 1996)
	0.02–0.05[a]					
	0.5–1					Pye (2007)

(*Continued*)

Table 19.2 (Continued)

Agent	Ostrich	Emu	Rhea	Cassowary	Comments	Reference
Ketoprofen	1–2					Pye (2007)
Reversals						
Atipamezole	5–20[a,e]	0.2[a]				Ostrowski & Ancrenaz (1995)
						Cushing & McClean (2010)
Diprenorphine	2× etorphine dose (mg)			2× etorphine dose (mg)		Stoskopf et al. (1982)
Naltrexone	90–125 mg:1 mg carfentanil					Raath et al. (1992)
		50× thiafentanil dose (mg)				Cushing & McClean (2010)
Yohimbine	0.11					Lin et al. (1997)
Emergency drugs						
Atropine	0.035					Fowler et al. (1987)
Doxapram	5[a]					Ostrowski & Ancrenaz (1995)
Epinephrine	0.02–0.2[a]					Cornick-Seahorn (1996)
Glycopyrrolate	0.011[a]					Cornick & Jensen (1992)
Lidocaine	1–2[a]				For ventricular arrythmias	Cornick-Seahorn (1996)

A-A, Alfaxalone-Alfadalone; K, ketamine; X, xylazine; G, guaifenesin; PO, per os.
[a] Intravenous administration.
[b] Juvenile animal.
[c] Supplemental drug needed on mg/kg basis.
[d] Supplemental isoflurane needed for intubation.
[e] Total mg per bird.
[f] Constant rate infusion of propofol used to maintain a light plane of anesthesia in juvenile ostrich.
[g] Supplemental ketamine needed for transportation.
[h] Free ranging.
Doses are based on mg/kg basis. All agents administered intramuscularly (IM) unless stated otherwise.

nonobese birds) are used, since the pectoral muscles are not developed (Fig. 19.6). Injections into larger, more proximal thigh musculature may be more effective than those at more distal locations (Cushing & McClean 2010). The role of the renal-portal system in drug elimination following administration into caudal musculature has not been fully elucidated. IV drug administration offers the most rapid method of immobilization; in intractable animals, IM sedation may be required prior to IV access.

Fasting times vary based on age and size of the bird, with little to no fasting in those <6 months old to prevent hypoglycemia. Adult ratites are fasted for 12–24 hours prior to induction (Cornick-Seahorn 1996; Lin et al. 1997).

Chemical immobilization is conducted in safe, secure areas with escape routes available for all personnel



Figure 19.6 Intramuscular injections are administered into the upper thigh. This is done with either remote or hand injection.

involved. Successful chemical immobilization varies with age and species, as well as the experience level of the handlers and anesthetist(s).

Premedications

Anticholinergics are not commonly used, as they increase the viscosity of respiratory secretions, potentially leading to airway obstruction (Gilsleider 1998). Bradycardia is not commonly encountered during ratite anesthesia. In ostriches, anticholinergic therapy is indicated if heart rate falls below 30–35 beats per minute (bpm) (Cornick & Jensen 1992). However, anticholinergic therapy is not consistently effective in treating bradycardia (Cornick & Jensen 1992). Many instances of bradycardia are likely due to hypertension and therefore refractory to anticholinergics.

Tranquilization and sedation have been achieved using acepromazine, azaperone, diazepam, midazolam, xylazine, detomidine, ketamine, and medetomidine, allowing for blood collection, minor procedures, and facilitation of induction of anesthesia (Table 19.2). These medications are usually administered IM; oral diazepam has been used successfully to sedate ostriches and cassowaries (Fowler 1995; Kapustin, pers. comm.).

Xylazine is commonly used, either alone or in combination with ketamine. Caution is warranted when using this alpha-2 agonist because it has significant cardiorespiratory depressant effect. Onset of action is usually within 10 minutes and may provide up to 30 minutes of sedation (Gilsleider 1998). High doses of xylazine IM allowed for IV ketamine induction 20 minutes later in adult ostriches (Al-Sobayil et al. 2009). Low-dose medetomidine allowed for safe approach and limited handling in adult captive and free-ranging cassowaries, and was fully reversed with atipamezole administration (Westcott & Reid 2002). Higher doses produced heavy sedation adequate for full examination (Westcott & Reid 2002). Juvenile (<1 year) cassowaries were heavily sedated using medetomidine/ketamine combination; the degree of sedation was somewhat variable, and supplemental medetomidine/ketamine was occasionally necessary for some procedures (Citino, pers. comm.). Medetomidine IM, followed by medetomidine/midazolam IM in these same cassowaries produced mild sedation adequate for crate-loading (Citino, pers. comm.).

Acepromazine is useful for muscle relaxation, but is contraindicated in debilitated animals and is not a preferred method of tranquilization. Safer drugs for healthy and ill birds include diazepam and midazolam. Azaperone is useful for transport of animals because it provides little muscle relaxation, but adequate tranquilization for up to 24 hours (Cornick-Seahorn 1996; Gilsleider 1998).

Immobilization

Opioid Combinations

Carfentanil and etorphine have been used with limited and variable success. Carfentanil produces rapid recumbency, but has been associated with excitatory activity (frenzied running, circling, walking backwards) (Cornick & Jensen 1992; Citino, pers. comm.). In severe cases this excitatory phase results in exertional rhabdomyolysis or trauma. When using potent opioids in cassowaries, the animals may remain standing and/or will unpredictably arouse sufficiently to cause injury to handlers (Heard, pers. comm.). Etorphine has been used in combination with acepromazine, acepromazine and xylazine, ketamine, and medetomidine. In each case satisfactory muscle relaxation and sedation were achieved, and use of medetomidine allowed for complete immobilization. In ostriches etorphine combined with medetomidine produced recumbency in <10 minutes in most cases (Ostrowski & Ancrenaz 1995). Risks with these combinations include regurgitation, aspiration, myopathy, and death (Cornick-Seahorn 1996).

In juvenile ostriches (<1 year) etorphine/acepromazine had no or variable effect, from mild sedation to profound immobilization. Etorphine/ketamine showed similar, but more reliable immobilization and recovery when administered to adult ostriches (Stoskopf et al. 1982). Some of the variability may have been due to dart failure. Manual restraint was used to assist the adults into sternal recumbency following adequate tranquilization. In contrast, lower dosages of etorphine/acepromazine administered via blow dart produced moderate sedation for 10–20 minutes in juvenile birds, with some ataxia and excitement during the initial immobilization (Samour et al. 1990). In adult ostriches higher dosages of etorphine/acepromazine, in combination with xylazine, improved sedation and allowed manual restraint for diagnostic procedures. Initial effects were similar to those noted above (Samour et al. 1990). Ostriches appear resistant to high etorphine dosages (Stoskopf et al. 1982; Samour et al. 1990). Given the unpredictable effects of etorphine/acepromazine combinations, alternative immobilizing and induction agents should be considered first.

In adult cassowaries etorphine (≤10 mg) did not produce immobilization (Stoskopf et al. 1982). However, a combination of etorphine/ketamine produced immobilization within 25 minutes in most birds, but was associated with long, rough recoveries (Stoskopf et al. 1982). A similar etorphine/ketamine combination (6/400 mg) was used to successfully induce a cassowary for surgical removal of a mass (Ensley et al. 1984). This combination produced recumbency within 5 minutes, but supplemental ketamine

was necessary for safe handling and administration of general anesthesia (Table 19.2). Adult cassowaries have been immobilized with a carfentanil/midazolam/ketamine combination. Animals were recumbent within 10 minutes, and occasionally exhibited an excitatory phase. Supplemental ketamine was given in some instances to allow for safe transport (Citino, pers. comm.). Heard (pers. comm.) has had good success using tiletamine/zolazepam (2 mg/kg) combined with concentrated (20 mg/mL) medetomidine (300 μg/kg) and midazolam (0.2 mg/kg). Induction and recovery can still involve struggling and ataxia, and are best done in a confined space such as a smooth-walled transport box. The animal may need to be trained to enter the box for induction.

In adult emus thiafentanil/medetomidine administration via Pneudart produced recumbency within 10 minutes in most cases; supplemental ketamine was necessary in three cases. Risks with this combination included respiratory acidosis and bradypnea, treated with IV atipamezole and supplemental orotracheal oxygen administration. Recovery following reversal and midazolam administration was rapid and smooth (Cushing & McClean 2010).

Other Combinations

In ostrich chicks undergoing four different anesthetic combinations, only metomidate/azaperone IM produced satisfactory anesthesia and analgesia with relatively few side effects (Van Heerden & Kefren 1991). In the same chicks, tiletamine/zolazepam, metomidate, and metomidate/azaperone IM produced successful immobilization; an adult ostrich given a similar dose of tiletamine/zolazepam exhibited violent kicking and self-trauma, and insufficient immobilization (Van Heerden & Kefren 1991). The immobilization times were dosage dependent and most combinations did not fully eliminate voluntary movements. Medetomidine alone (0.1 mg/kg) did not produce immobilization (Van Heerden & Kefren 1991). In contrast, juvenile ostriches (9–11 months old) were successfully immobilized with a medetomidine/ketamine (0.08/2 mg/kg) combination, although recumbency was not achieved in all cases (Langan et al. 2000). Tiletamine/zolazepam in combination with diazepam has also been used to immobilize a juvenile emu (Tully et al. 1996a), and ketamine alone has been used to immobilize an adult rhea, although quality of immobilization was not reported (Smith et al. 2005).

Induction

In young (≤6 months) and easily restrained animals (including kiwis and tinamous) induction may be accomplished using isoflurane alone; large subadult to adult birds require parenteral anesthetics. Inhalant induction is accomplished by starting at a high concentration (such as 5%), then decreasing to maintenance levels. This technique allows for rapid and smooth induction, and is the preferred method for ratites.

A variety of parenteral anesthetics alone or in combination (e.g., xylazine, ketamine, carfentanil, tiletamine/zolazepam, etc.) (Table 19.2) have been investigated and used for induction. Selection is based on age, health status, and species. Known pre-existing disease conditions are also considered.

Opioid Combinations

Carfentanil has been used alone and in combination with xylazine for both immobilization and induction of anesthesia (Honnas et al. 1991; Cornick & Jensen 1992). Common complications include apnea, hypercapnia, excitability, agitation, and frenzied activity (Cornick & Jensen 1992). Naloxone or preferably naltrexone are used to reverse the effects of carfentanil, and tolazoline or atipamezole may be used to reverse the xylazine, making this a fully reversible combination. The addition of midazolam (0.1 mg/kg) to the carfentanil/xylazine combination (0.025/1 mg/kg) allowed for smooth induction and recovery in an adult ostrich; midazolam was not reversed (Citino, pers. comm.).

Other Combinations

Tiletamine/zolazepam IV produced rapid and smooth induction with sternal recumbency in adult ostriches, and allowed for endotracheal intubation in juvenile ostriches (Honnas et al. 1991; Lin et al. 1997; Gilsleider 1998; Ciboto et al. 2006). IV administration was facilitated by prior xylazine/butorphanol (X/B), xylazine, or acepromazine administration in adults; rheas required higher dosages of X/B than emus and ostriches to achieve the same level of sedation (Lin et al. 1997; Ciboto et al. 2006). Despite excellent induction, tiletamine/zolazepam IM is often associated with prolonged "rough" recoveries. These effects are lessened by diazepam before or after tiletamine/zolazepam administration (Cornick & Jensen 1992; Tully et al. 1996a). Midazolam IM would be expected to produce similar effects as diazepam; benzodiazepine administration is encouraged when using tiletamine/zolazepam combinations. Finally, tiletamine/zolazepam IV may result in apnea, necessitating assisted ventilation (Cornick & Jensen 1992).

Immobilization with medetomidine/ketamine, followed by IV propofol, allowed for safe, smooth induction and recovery of anesthesia in juvenile ostriches (Langan et al. 2000). Transient apnea occurred but spontaneously resolved; all birds were bradycardic throughout the procedure. Light anesthesia was maintained with a constant rate infusion of propofol; higher doses are necessary for a

surgical plane of anesthesia (Table 19.2). Successful sedation with IM acepromazine, followed by propofol IV has been reported in ostriches with minimal side effects, though the volume to administer was reportedly large (Ciboto et al. 2006).

Ketamine alone is not recommended due to excitation during induction and recovery, and possible convulsions. Rather, it is combined with other drugs (e.g., diazepam, midazolam, medetomidine, or xylazine) (Cornick & Jensen 1992; Burba et al. 1996; Tully et al. 1996b; Langan et al. 2000; Ciboto et al. 2006; Al-Sobayil et al. 2009). High-dosage diazepam/ketamine and other combinations result in "rough," unpredictable inductions, but smooth recoveries (Cornick & Jensen 1992). Diazepam (0.3–0.5 mg/kg IM) premedication facilitates induction with ketamine/diazepam IV (Cornick-Seahorn 1996). Xylazine combined with carfentanil (X/C) or ketamine (X/K) has resulted in successful induction in healthy ratites. However, rough recoveries were noted in some birds with X/K along with bradycardia and apnea (Matthews et al. 1991; Cornick & Jensen 1992; Fowler 1995; Gilsleider 1998). Xylazine/ketamine is not recommended in debilitated birds because of cardiopulmonary depression.

Pharmacokinetics in ostrich chicks premedicated with romifidine and induced with IM ketamine revealed rapid absorption and elimination half-life of ketamine, similar to that of mammals (De Lucas et al. 2007). However, there is considerable variation in the effectiveness of anesthetic agents used for induction. This variability may be related to dosage, route of administration, species, age and metabolic rate, degree of excitation, or individual variation (De Lucas et al. 2007). In general, diazepam appears to improve induction and recovery regardless of the other drugs used.

Maintenance

Isoflurane is the inhalant anesthetic of choice for chicks and juveniles, and lengthy procedures in adult birds. However, halothane, methoxyflurane, and nitrous oxide have also been used successfully. Significant decreases in respiratory rate and blood pressure have been recorded with isoflurane following X/K combinations in ostriches (Al-Sobayil et al. 2009). Administration of the inhalant anesthetic by a mask (Fig. 19.7) can be used to provide further relaxation for intubation following parenteral anesthetic induction.

Nonrebreathing systems are used in birds ≤7 kg, with an oxygen flow rate of 200 mL/kg/min. Circle rebreathing systems are used in larger birds (≥50 kg), with a flow rate of 20–30 mL/kg/min.

Injectable protocols have not provided adequate maintenance anesthesia for prolonged periods. Some success is possible using ketamine and xylazine for induction, followed by IV infusion of ketamine, xylazine, and guaifenesin (Cornick-Seahorn 1996) (Table 19.2). Repeated IV administration of ketamine (5 mg/kg) at 10–15-minute intervals can be used to prolong and/or maintain immobilization (Bruning & Dolensek 1986).

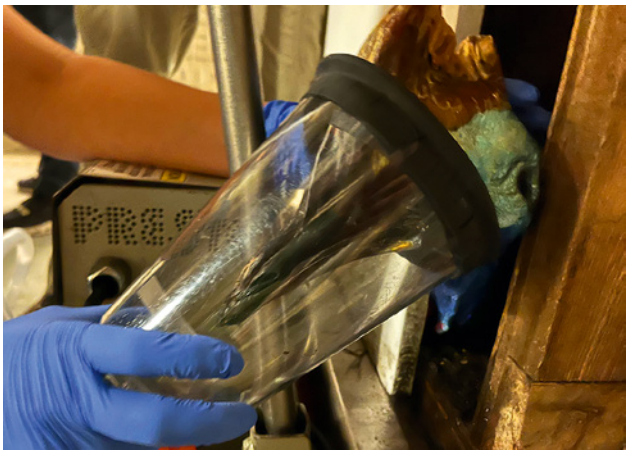


Figure 19.7 Administration of an inhalant anesthetic connected to an anesthesia machine can be used to provide further relaxation for intubation after induction with parenteral anesthetics.

Intravenous pentobarbital is not recommended because it has been associated with regurgitation and prolonged recoveries (Cornick-Seahorn 1996). Propofol may be a useful alternative for extended anesthetic procedures; clinical and research evaluation of its use in ratites is limited, but promising (Langan et al. 2000).

Recovery

Birds should be recovered in a dark, quiet, well-padded area to minimize stress and trauma. Use of diazepam (0.13–0.41 mg/kg IV) or midazolam (0.15 mg/kg IV) to produce a calming effect during the recovery period may help minimize self-trauma (Cornick & Jensen 1992; Cushing & McClean 2010). Alternatively, manual restraint of the bird in sternal recumbency until it is able to stand without assistance can be used. Some clinicians will restrain the bird in a towel or tarpaulin using tape or cargo straps until the bird is able to support itself. If this method of restraint is used, quick-release holding straps are recommended. Commercially available wraps are available for use in ratites (Raines 1998). An alternative method involves recovering the bird in sternal recumbency surrounded by hay bales, with a tent of bales over the top of the bird. The bird is not released from this enclosure until fully alert (Heard, pers. comm.).

Reversal agents available include yohimbine, atipamezole, naloxone, naltrexone, diprenorphine, and flumazenil (Table 19.2). Reversal agents, such as yohimbine for antagonism of xylazine, are not commonly employed in ratite anesthesia protocols. Atipamezole is used for reversal of alpha-2 adrenergic agonists (xylazine, detomidine, medetomidine), and flumazenil is used for reversal of the benzodiazepines. Flumazenil is not routinely used because of associated costs and lack of necessity (Cornick-Seahorn 1996). IM injection of diprenorphine has been used to reverse the effects of etorphine. IV naloxone administration followed by diprenorphine IM was noted to allow for smoother recovery following carfentanil administration than naloxone alone (Cornick & Jensen 1992).

In some cases, clinicians may prefer IM administration of reversal agents instead of intravascular administration to allow for a more gradual recovery. Extubation is not recommended until the bird is swallowing on its own and able to maintain its head in a normal position. The oral cavity should be examined prior to extubation to ensure excess secretions, blood, or debris are removed to maintain a clear airway. Renarcotization has not been reported, but birds should be monitored closely following reversal administration.

Field Anesthetic Techniques

There is presently no ideal technique for immobilization or anesthesia of ratites. Field immobilization is complicated by large drug volumes, and "rough" induction and recovery periods. There are also only limited reported investigations of field techniques. Both blowpipes and carbon dioxide-powered guns have been used, in combination with plain or barbed darts, for remote drug injection. Ideally reversible anesthetic regimens are used.

Administration of medications using darts delivered by CO_2 powered pistol has had mixed success for immobilization of cassowaries and ostriches (Fig. 19.5). Pole syringe use is hampered by difficulty in gaining proximity and access to injection sites (Stoskopf et al. 1982). Blowpipes and nonbarbed darts have also been used to deliver drugs to the thigh or lumbosacral muscles (Samour et al. 1990) (Fig. 19.5). For successful dart injection a perpendicular trajectory path into the muscle is required. Darts projected at an angle are likely to bounce out of the muscle prior to full delivery of medications (Stoskopf et al. 1982; Samour et al. 1990). Ratites accumulate fat over the pelvis and paralumbar musculature, and in obese captive birds this area is avoided for IM injection.

Evaluation of metodomidate/azaperone in captive ostrich chicks resulted in successful immobilization; although recommended for field use, it was not evaluated in adult ostriches or noncaptive settings (Van Heerden & Kefren 1991). Etorphine and etorphine/medetomidine combinations have been used to capture adult ostriches (Fowler 1995; Ostrowski & Ancrenaz 1995). Based on investigations in captive ratites, high-dosage ketamine/xylazine combinations may produce field capture and restraint; supplemental IV ketamine is necessary to prolong immobilization (Bruning & Dolensek 1986).

Carfentanil may cause induction excitement; this is lessened when combined with xylazine (Raath et al. 1992). This combination otherwise produced minimal to no adverse side effects, and was reversed with naltrexone and yohimbine without complication. Carfentanil/ketamine combinations have also been recommended (Fowler 1995).

Exertional rhabdomyolysis (capture myopathy) may occur in chemically immobilized ratites; field procedures are conducted by experienced personnel and at appropriate ambient temperatures. If excessive stress, excitement, or activity occurs prior to darting, it is prudent to abort the procedure. Medications and supplies necessary for treatment of exertional myopathy should be available during immobilization procedures.

Monitoring

Depth of anesthesia is assessed using heart rate and rhythm, respiratory rate and character, arterial blood pressure, wing and/or neck tone, and assessment of pedal, palpebral, and corneal reflexes. Continuous cardiac monitoring is achieved using an electrocardiogram or manual auscultation. Esophageal stethoscopes are used in chicks or small ratites. The brachial, medial metatarsal, or digital arteries are used for pulse assessment. Heart rates of 45–80 bpm are considered normal in anesthetized adults. The respiratory rate in an anesthetized adult ratite ranges from 25 to 40 breaths per minute (Gilsleider 1998).

Direct arterial blood pressures are measured by inserting catheters at the arterial sites listed above (Cornick & Jensen 1992; Lin et al. 1997). Additional arterial sites include the craniolateral aspect of the tibiotarsal bone, and parallel to the mandibular beak within the oral cavity (Cornick-Seahorn 1996). Indirect blood pressure monitoring has met with mixed success (Al-Sobayil et al. 2009; Cushing & McClean 2010). Based on information from mammalian species, a mean arterial pressure $\geq$60–70 mmHg is desirable. However, based on research it is proposed that ostriches normally have a higher arterial blood pressure than mammals (Cornick & Jensen 1992; Lin et al. 1997). Different drug combinations in different species and ages of animals are expected to affect the mean, systolic, and diastolic blood pressure; the limited ranges

Table 19.3 Systolic (SBP), mean (MAP), and diastolic (DAP) arterial blood pressures (mmHg) reported for anesthetized ratites.

		SBP		MAP		DAP		
Drugs	**Species**	**Minimum**	**Maximum**	**Minimum**	**Maximum**	**Minimum**	**Maximum**	**Reference**
X/B	R	68–72	82–120	49–56	60–99	32–51	52–91	Lin et al. (1997)
I	E, R	55–105	121–222	37–84	99–168	30–79	84–147	Lin et al. (1997)
	O	102–150	148–198	92–140	142–175	84–128	130–170	Cornick & Jensen (1992)
	O	145	206	118	171	90	147	Cornick-Seahorn et al. (1995)
TZ	E, R, O	47–178	186–232	44–126	135–210	39–103	122–192	Lin et al. (1997)
X/B/TZ	E, R, O	72–124	131–203	44–80	81–147	36–70	65–124	Lin et al. (1997)
D/K	O	160	254	126	212	85	198	Cornick & Jensen (1992)
X/D/K	O	162	275	134	232	104	200	Cornick & Jensen (1992)
X/C	O	160	185	132	158	90	122	Cornick & Jensen (1992)
X/K	O	136	175	82	105	52	60	Cornick & Jensen (1992)
	O	168–206	228	108–165	145–191	77–126	120–153	Matthews et al. (1991)
X/K/G	E	99	146	60	109	43	66	Cornick-Seahorn et al. (1995)

Species: O, ostrich; E, emu; R, rhea.
Drugs: X, xylazine; B, butorphanol; I, isoflurane; TZ, telazol (tiletamine/zolazepam); D, diazepam; K, ketamine; C, carfentanil; G, guaifenesin.

reported in the literature may serve as a rough guideline for acceptable values in ratites (Matthews et al. 1991; Cornick & Jensen 1992; Lin et al. 1997; Cornick-Seahorn et al. 1995) (Table 19.3). Arterial blood gases and pH can also be monitored, although normal values are limited or nonexistent. Venous blood gas samples have been used to monitor acid-base status during anesthesia (Cushing & McClean 2010) and may be affected by the age and sex of the bird (Bouda et al. 2009).

Additional monitoring includes capnography to assess ventilation, cloacal temperature, and pulse oximetry. The pulse oximetry probe can be applied at the wing web, tongue, intermandibular tissue, or tibiotarsal area. Juvenile birds in particular are susceptible to hypothermia, while adults may experience hyperthermia; frequent assessments of the cloacal temperature is recommended.

Complications

Complications associated with physical restraint either pre or post anesthesia include wing fractures, tibiotarsal fractures, tarsometatarsal joint luxation, lacerations caused by hooks or other restraint devices, cervical vertebrae dislocation or fracture, compression injury of the trachea, hypoxemia, peroneal nerve damage, and capture myopathy.

Anesthetic complications noted in the literature include hypothermia (especially very young and very thin birds), hyperthermia, regurgitation (especially in cases with preexisting gastrointestinal disease), hypoglycemia, neuropathy and myositis (due to insufficient padding during anesthesia), tracheal occlusion due to poor neck positioning, apnea, premature ventricular contractions (cause undetermined; Matthews et al. 1991), bradycardia, cardiac arrest, hypertension (Matthews et al. 1991), voluntary movement, self-trauma during recovery, excessive oral and respiratory secretions, hypocapnia (possibly related to excessive intermittent positive pressure ventilation), hypercapnia (Cornick & Jensen 1992; Cushing & McClean 2010), secondary fungal/yeast infections (Matthews et al. 1991), and rupture of great vessels (Honnas et al. 1991; Cullen et al. 1995).

Doxapram (5 mg/kg IV) can be used in cases of apnea, and hypotension can be treated using increased IV fluid administration, decreasing anesthetic depth, IV dobutamine (2–5 μg/kg/min) or IV dopamine (5 μg/kg/min). Epinephrine (0.02–0.2 mg/kg IV or intratracheal) can be used in cases of cardiac arrest, in conjunction with cardiac compression applied to the lateral aspect of the bird (Cornick-Seahorn 1996). Voluntary movement may be avoided by using butorphanol (0.02–0.05 mg/kg IV) to control pain, or by using ketamine intra-operatively (0.2 mg/kg IV). Bradycardia has been arbitrarily defined in the literature as heart rate <30 bpm. Anticholinergic agents such as glycopyrrolate or atropine have met with variable success in the treatment of bradycardia in ratites (Cornick-Seahorn 1996). Xylazine administration is thought to be associated with bradycardia in ratites, but conclusive evidence is lacking at this time.

Myopathy is treated with supportive care (IV fluids with bicarbonate, dextrose, corticosteroids, vitamin E–selenium, calcium, antibiotics, flunixin meglumine) and possibly dantrolene for muscle relaxation.

Diseases of Concern

Procedures requiring general anesthesia in the ratite include laceration repair, evaluation of traumatic injuries, evaluation and treatment of exertional myopathy (Smith et al. 2005; Tully et al. 1996b), sequestra removal (Tully et al. 1996a), castration (Pye 2007), removal of retained or infected yolk sacs, esophagostomy tube placement, proventriculotomy or ventriculotomy for foreign body removal, egg binding, orthopedic procedures, including correction of congenital or acquired musculoskeletal disorders, tumor removal, and impaction of the gastrointestinal tract (Ensley et al. 1984; Honnas et al. 1991; Cornick & Jensen 1992; Burba et al. 1996; Gilsleider 1998). Conditions causing a distended ventriculus or proventriculus (i.e., foreign body) necessitate rapid induction and intubation to minimize the risk of regurgitation and subsequent aspiration (Honnas et al. 1991; Cornick-Seahorn 1996).

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20

Penguins

Kate Bodley and Todd L. Schmitt

Introduction

The Order Sphenisciformes (penguins) consists of 18 species representing six genera (see Table 20.1). All occur in the southern hemisphere and are dependent on nutrient-rich, cool to cold water currents for their food sources. Most species are found in the northern cool temperate region of the Southern Ocean, up to latitude 30°S (Shirihai 2007). Several species are found in coastal and nearby waters of South Africa, South America, Australia, and New Zealand, and the most northerly species, the Galapagos penguin, occurs close to the equator. The emperor penguin and Adélie penguin live and breed exclusively on the Antarctic continent.

Anatomy and Physiology

Penguins are flightless birds that possess highly specialized anatomical and physiological features suitable for their pelagic lifestyle. Most penguin species spend >50% of their lives at sea. Many species make frequent, rapid, and prolonged dives while foraging. Emperor penguins may dive to depths greater than 500 m and remain submerged for more than 20 minutes (Meir & Ponganis 2009). Many species are exposed to extremely low environmental temperatures while on land, during their breeding and molting periods. The Magellanic penguin and the Galapagos penguin, however, must tolerate high environmental temperatures while on land, and then forage in cool ocean currents.

Penguins demonstrate remarkable development of various anatomical and physiological adaptations that allow them to forage and breed in such extreme environments. These adaptations are of potential significance during procedures involving restraint and anesthesia.

Penguins may be at greater risk of developing hyperthermia during restraint procedures than other avian species. Penguin feathers are not laid down in pterylae, rather they are densely packed over the entire skin surface. The lance-shaped contour feathers are very stiff and short, and have an attached downy afterfeather that provides insulation. Feathers are flattened during swimming, but feather shafts may be held erect while on land, providing a thick, air-filled, windproof coat (Dawson et al. 1999). During the pre-molting period, when most species gain significant body mass, a subcutaneous adipose layer provides further insulation.

One thermoregulatory adaptation is the humeral arterial plexus, a vascular counter-current heat exchanger that limits heat loss through the flipper. Evidence for the development of this structure arose in the fossil record during the late Cenozoic era, 49 million years ago, and it is believed to be a key adaptive feature that allowed penguins to successfully forage in cool and cold environments (Thomas et al. 2011). In addition, a post-orbital *rete mirabile* reduces heat loss from the head, and multiple–vein arteriovenous associations in the legs facilitate countercurrent heat exchange and assist heat retention (Frost et al. 1975). Penguins may be relatively overinsulated while on land, particularly when they live in warm terrestrial environments. The feet and flippers will function to dissipate excess heat at high temperatures via a general increase in blood flow to these structures and the bypassing of the counter-current heat exchange systems. When African penguins are heat-stressed, blood is shunted through a large marginal vein located in the axilla, which allows the axilla to be used as an efficient heat dissipater (Frost et al. 1975). Heat loss is also facilitated by panting and postural changes.

For the smallest species of penguins, the little blue penguin, thermoregulatory capacity is reduced due to size. Little blues occupy a relatively narrow range of distribution in the temperate zone around southern Australia and New Zealand. They come ashore at night to nest in burrows, where they are not subjected to considerable heat loads, and studies have demonstrated that this species differs

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Table 20.1 Species of penguins.

Genus	Species	Common Name	Habitat
Pygoscelis	*Pygoscelis adeliae*	Adelie penguin	Circumpolar Antarctica
	Pygoscelis antarctica	Chinstrap penguin	Circumpolar Antarctica
	Pygoscelis papua	Gentoo penguin	Antarctica and sub-Antarctic islands
Aptenodyptes	*Aptenodytes forsteri*	Emperor penguin	Circumpolar Antarctica
	Aptenodytes patagonicus	King penguin	Antarctica and sub-Antarctic islands
Eudyptes	*Eudyptes moseleyi*	Northern rockhopper penguin	Sub-Antarctic and south temperate islands
	Eudyptes chrysocome	Southern rockhopper penguin	Sub-Antarctic and south temperate islands
	Eudyptes chrysolophius	Macaroni penguin	Antarctica and sub-Antarctic islands
	Eudyptes pachyrhynchus	Fiordland penguin	New Zealand
	Eudyptes schllegeli	Royal penguin	Sub-Antarctic islands
	Eudyptes robustus	Snares Island penguin	New Zealand
	Eudyptes sclateri	Erect-crested penguin	New Zealand
Megadyptes	*Megadyptes antipodes*	Yellow-eyed penguin	New Zealand
Spheniscus	*Spheniscus demersus*	African penguin	South Africa and Namibia
	Spheniscus humboldti	Humboldt penguin	Peru and Chile
	Spheniscus magellanicus	Magellanic penguin	Chile and Argentina, Falkland Islands
	Spheniscus mendiculus	Galapagos penguin	Galapagos Islands
Eudyptula	*Eudyptula minor*	Little blue penguin	Australia and New Zealand

from other birds in that it lacks a typical panting response (Stahel & Nichol 1988). Therefore, little blue penguins are less able to withstand heat stress than other species. In addition, their small size limits their ability to maintain body temperature in water <5°C. Mean sea temperatures are >10°C within their range (Stahel & Nichol 1982).

The unique anatomical features of the penguin respiratory tract possess potential significance during anesthetic procedures. At the entry of the upper airway, when the glottis opens during respiration, one will notice the crista ventralis, a cartilaginous projection extending from the cricoid cartilage dorsally into the laryngeal lumen (McLelland 1989a). It forms an incomplete septum and may reduce the diameter of the endotracheal (ET) tube used during anesthesia. Further caudal in the tracheobronchial tree, a median septum divides the trachea into right and left bronchial channels. It is present in only certain penguin species (i.e., Magellanic, Humboldt, African, Emperor, and King) and is observed to bifurcate at the level of the second cervical vertebrae. It is therefore possible to insert the tip of an ET tube into one bronchus and provide incomplete unilateral ventilation (see Fig. 20.8). The physiological significance of varying median septum lengths in different penguin species is not known, but Ponganis et al. (2015) have postulated from pulmonary volume measurements that there may be a compensatory function to provide air volume expansion and prevent pulmonary barotrauma with air-sac compression during dives. There may be other evolutionary factors with divergent function of diving performance that led to anatomical adaptation as well. The septum extends cranially from the bronchial bifurcation, and each tracheal tube is completely encircled by a cartilaginous ring. In African penguins the septum terminates only a few centimeters short of the larynx, whereas in the rockhopper penguin, the septum is only 5 mm long and ends at the thoracic inlet (McLelland 1989a). In general, the septum is long in the Aptenodytes and Spheniscidae, but short in the Eudyptes and Pygosceles.

The network of secondary bronchi and paleopulmonic parabronchi in penguins permits continuous unidirectional airflow only, and neopulmonic anastomoses are poorly developed, which limits bidirectional flow (McLelland 1989b). Together with expansive air sacs, countercurrent gas exchange, and enhanced cellular hemoglobin capacity, the pulmonary apparatus can support the varied energetic lifestyle of penguins. The lungs and air sacs of various penguin species accounts for 30–45% of the total body oxygen store compared to 5–20% in most marine mammals (Ponganis et al. 2015). The avian lung volume only changes 1.4% between inspiration and expiration, and is relatively rigid when compared to the mammalian lung (Maina 2015). They have a well-developed cervical air sac, which reaches from anterior to the clavicle to the level of the lung hilus. Except for the clavicular air sac, all other air

sacs (cervical, craniothoracic, caudothoracic, and abdominal) are paired (Maina 2015). The skeleton is poorly pneumatized (McLelland 1989b).

Several penguin species have been found to have physiological adaptations that facilitate diving. Emperor penguins use a range of strategies to manage body oxygen stores while submerged, for example hyperventilation and tachycardia during the pre-dive period improves ventilation-perfusion matching during the dive, and arteriovenous shunts allow isolation of skeletal muscle from the circulation during a dive (Meir & Ponganis 2009; Ponganis et al. 2010). Additionally, wild diving emperor penguins demonstrate true diving bradycardia to maximize respiratory oxygen uptake and prolong the dive (Meir et al. 2008). In emperor penguins, the myoglobin concentration in pectoral muscle is among the highest measured in any vertebrate (Ponganis et al. 2010). Emperor, Adélie, gentoo, and chinstrap penguins were found to possess hemoglobin with enhanced oxygen affinity compared with other terrestrial birds. This increases their available oxygen when blood oxygen partial pressure is low during a dive (Meir & Ponganis 2009).

Most penguin species undergo periods of fasting during breeding, and all penguins will fast during their molt. Prolonged periods of fasting involve marked decreases in body mass. During the breeding fast, body mass loss averages 36–40% in macaroni penguins; during the molting fast, this species has total body mass loss of 45–50% (Williams 1995). During the molt, there is an increased energy requirement for heat production and for the breakdown of stored proteins to provide amino acids for synthesis of feathers. This results in an increase in metabolic rate. Studies have also demonstrated that there is a tradeoff between molting and the immune response in house sparrows (Moreno-Rueda 2010). The duration of the two fasting periods (the breeding fast and the molting fast) is greatest in the two largest penguin species: the emperor penguin and the king penguin (Williams 1995). Mazarro et al. (2013) determined that the behavior and appetite of captive African penguins remained constant during seven handling events (weighing and blood collection under manual restraint) carried out during molting; however, a molt-related decrease in hematocrit and red blood cell count was detected. Heat loss in molting little blue penguins is about 1.6 times higher than in nonmolting birds (Williams 1995).

Capture and Physical Restraint

Most penguin species may be captured by hand. Smaller species may be easily captured by hand from the burrow (Wallace et al. 1995) or while standing on land. Larger species may be caught by hand (Thil & Groscolas 2002a,b) or an appropriately sized hoop net may be used (Keymer et al. 2001). A metal rod, bent and covered with rubber at one end to form a hook, has been used to grasp the tarsometatarsus of free-ranging rockhopper (Karesh et al. 1999) and Magellanic (Gallo et al. 2019) penguins and draw them towards handlers, who would then restrain the birds. A remote injection device has been used to administer intramuscular (IM) ketamine to free-ranging Humboldt penguins (Luna-Jorquera et al. 1996).

Penguins are relatively robust and can tolerate periods of restraint for noninvasive procedures, but procedures must be planned so that they are performed quickly and efficiently to reduce the risk of hyperthermia. Most penguins in managed environments will require placement in a carrier or crate for transport to the examination site. Penguins weighing less than 7 kg can be placed easily in a large plastic dog kennel. For polar penguins, flat ice blocks are placed in the bottom of the kennel to aid with temperature regulation. Polar penguins larger than 7 kg require specially built wood or plastic transport crates that can accommodate flat ice blocks that are covered with a towel. Transport crates that have two folding doors opposite one another will provide adequate exposure to the penguin for restraint. The transport vehicle and receiving examination room must be air-conditioned to prevent extreme temperature fluctuations and subsequent overheating.

Penguins are best approached from behind so that the base of the head is grasped quickly and firmly. Penguin wings are powerful and may inflict injury during handling. The wings should not be grasped as the initial point of restraint as they may suffer significant injury (e.g., humeral fracture or joint injury). The wings should be held firmly against the body to avoid excessive flapping. If wing movement must then be controlled, a second hander may be required. The beak is large and sharp, so restraining the head is very important. Institutions housing king penguins include safety glasses as standard personal protection equipment during handling.

Penguins of less than 5 kg body mass may be quickly restrained by hand (Fig. 20.1). The rear of the head is grasped firmly at the base and then the limbs/body may be restrained. Very small penguins are grasped behind the head and then held around the body caudal to the wings.

Most often, the larger penguin species can be guided into a smaller enclosure and loaded into a carrier for transport prior to a procedure. Larger penguins may be tucked under the handler's elbow, facing caudally. The handler kneels, facing the bird, and pulls it towards them, tucking its head under the elbow and against the body. The bird's head will sit under the handler's hip, the bird lies along the thigh, and the elbow secures the head. The handler then holds the feet secure (Fig. 20.2). This level of restraint is suitable for minor procedures such as nail clipping.



Figure 20.1 Restraint technique for a penguin less than 5 kg (little blue penguin). The animal is grasped behind the head and then held around the body caudal to the wings. Image courtesy of Zoos Victoria.



Figure 20.2 Restraint technique for a large penguin undergoing a minor procedure: king penguin. Image courtesy of Village Roadshow Theme Parks.

Restraint for induction of anesthesia generally requires more controlled restraint of the head and neck. The penguin is approached from behind. The handler wraps their arms around the body of the bird and presses the wings tightly against the body. The body of the penguin may be tucked between the knees, such that the handler has both hands free to position the head and neck (Fig. 20.3).

Procedures that require the bird to be immobile (e.g., venipuncture, husbandry procedures, and anesthetic induction using a facemask) will generally require two or more handlers (Fig. 20.4). Safe restraint of penguins larger than 10 kg generally requires two handlers. One handler controls the body, and the other controls the head by firmly



Figure 20.3 Restraint technique, large penguin: king penguin. Image courtesy of Village Roadshow Theme Parks.



Figure 20.4 Blood can be collected from the external jugular vein (emperor penguin).

grasping the back of the head and top or bottom of the bill base (Fig. 20.4). Penguins may be hooded to reduce stress during restraint procedures (Thil & Groscolas 2002a,b).

Vascular Access

Venipuncture of superficial veins is accomplished for most diagnostic and therapeutic purposes with adequate manual restraint or during anesthesia. The jugular vein may be palpated along the right and left side of the neck. It is most easily accessible when the neck is extended and curved slightly away from the operator (Fowler & Fowler 2001; Redrobe 2000). Pressure is applied just anterior to the thoracic inlet, and the vein may be palpated ventral to the cervical muscles and dorsal to the trachea. A straight needle of size 22–19 gauge may be used for venipuncture for penguins of <7 kg and >10 kg, respectively. Butterfly needles or scalp catheters, 25–21 gauge, may also be used but require more dexterity for successful blood draw. The jugular vein is readily occluded following venipuncture to prevent hematoma formation.

The medial metatarsal vein is easily accessible in penguins, but may be small, and the wound site is easily contaminated by fecal pathogens from unsanitary conditions in a rookery. It is located just above the medial claw (Fig. 20.5) (Redrobe 2000).

In smaller species, the brachial, jugular, or sacral sinus may be more useful for collection of diagnostic blood samples. The cutaneous ulnar or basilic vein is not discernable in the wing of penguins, but the brachial vein can be raised via pressure in the axilla (Samour et al. 1983). In the African penguin, the marginal vein runs along the posterior edge of the humerus after branching from the brachial vein (Frost et al. 1975). This vein is readily accessible in the anesthetized penguin. In the conscious patient, the vein is more difficult to access and may be difficult to occlude following venipuncture (Fig. 20.6).



Figure 20.5 Blood can be collected from the medial metatarsal vein (Fiordland penguin), but the vein may be small and the skin must be carefully cleaned before venipuncture. Image courtesy of Zoos Victoria.

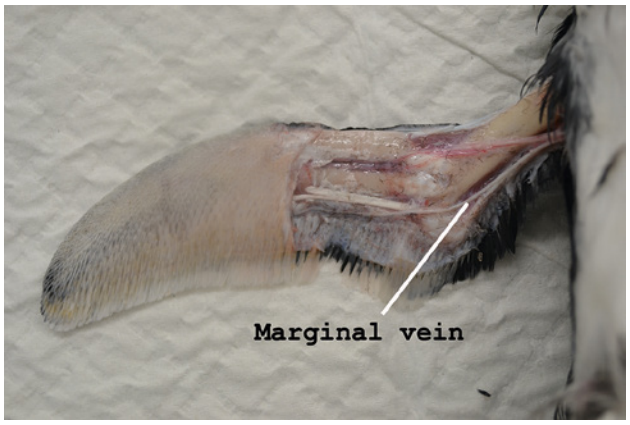


Figure 20.6 Venipuncture site located on the anterior aspect of the forelimb, little blue penguin. Anatomical nomenclature based on Thomas and Fordyce (2007). Image courtesy of Zoos Victoria.

Specially designed penguin restraint devices have been used to facilitate venipuncture without anesthesia. Keymer et al. (2001) described a device made to hold free-ranging penguins on the Falkland Islands, including Magellanic penguins, rockhopper penguins, and gentoo penguins. Birds were held in a plastic tube, with a slit in the side that enabled exposure of the flipper and access to the brachial vein.

In the zoological setting, training of aviculturists to restrain penguins for jugular venipuncture is paramount. For penguins <7 kg, the primary handler will restrain the body and a secondary handler can restrain the head if required. The primary handler can either kneel on the ground or sit on a chair or stool with the penguin (facing away from them) pinned/restrained using their knees (Fig. 20.7a). The secondary person can gently and firmly grasp the top of the bill and back of head to extend the bird's head right or left over the primary restrainer's leg to allow venous access (Fig. 20.7b,c).

Penguins larger than 10 kg require the primary handler to approach the bird from behind and wrap their arms, and sometimes legs, around the penguin. The secondary handler can restrain the bill and back of head firmly, and gently direct it over the primary handler's shoulder, allowing jugular venous access. Sometimes a third person is required to maintain restraint of the penguin by aiding the primary handler.

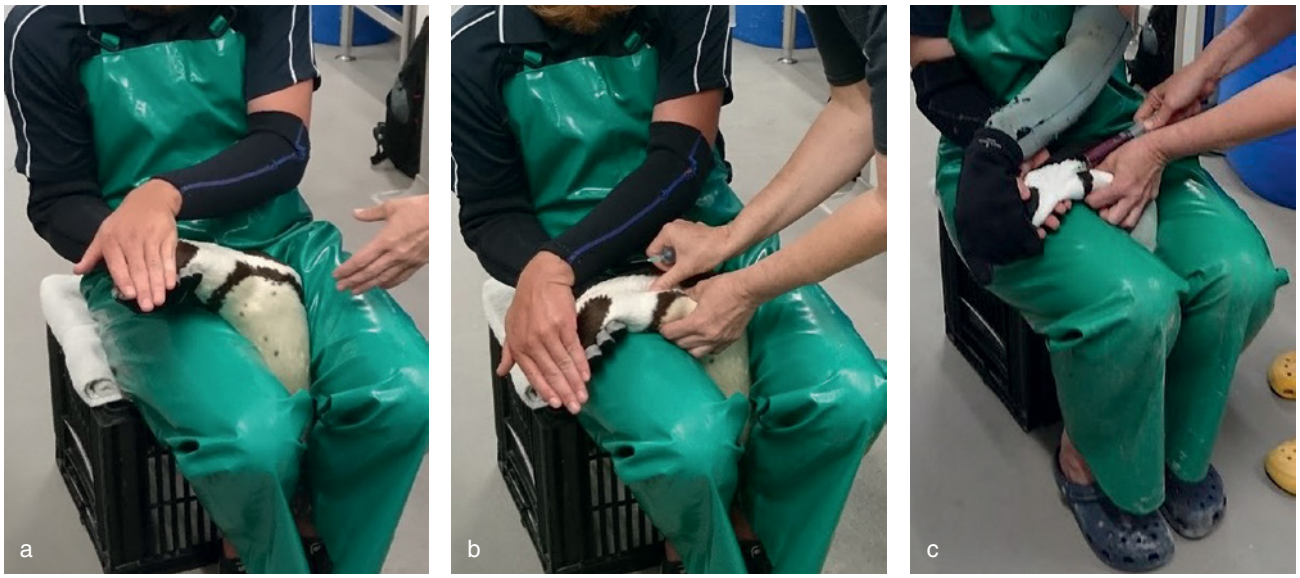


Figure 20.7 Restraint technique for blood collection from the jugular vein (African penguin). Images courtesy of David Roberts, SANCCOB.

Endotracheal Intubation

The technique for endotracheal intubation is as for other birds (Fig. 20.8). The presence of the crista ventralis may necessitate selection of an ET tube with a smaller external diameter. The median septum of the trachea may result in unilateral intubation and/or tracheal mucosal trauma. Some authors prefer to maintain penguins using a facemask because of the presence of the septum (Cranfield 2003). The point of separation of the two channels is generally distant enough from the glottis to allow insertion of a Cole ET tube (Stoskopf & Kennedy-Stoskopf 1986).

ET tubes with the appropriate diameter should be selected. Little blue penguins require ET sizes 2.5–3.5 mm. The largest penguin species, emperor penguins, have been intubated using 9.0-mm ET tubes (Kooyman et al. 1992). Inflation of the ET tube cuff has not been shown to be harmful to the tracheal mucosa in the author's (T.S.) experience and may be required to maintain adequate inspiratory gas pressure with assisted positive pressure ventilation and prevent possible exposure to refluxed gastric fluid. However, great care must be taken not to overinflate the cuff and cause subsequent tracheal membrane damage. Post-intubation obstruction is recognized as a potential complication after ET intubation in birds, and histologic

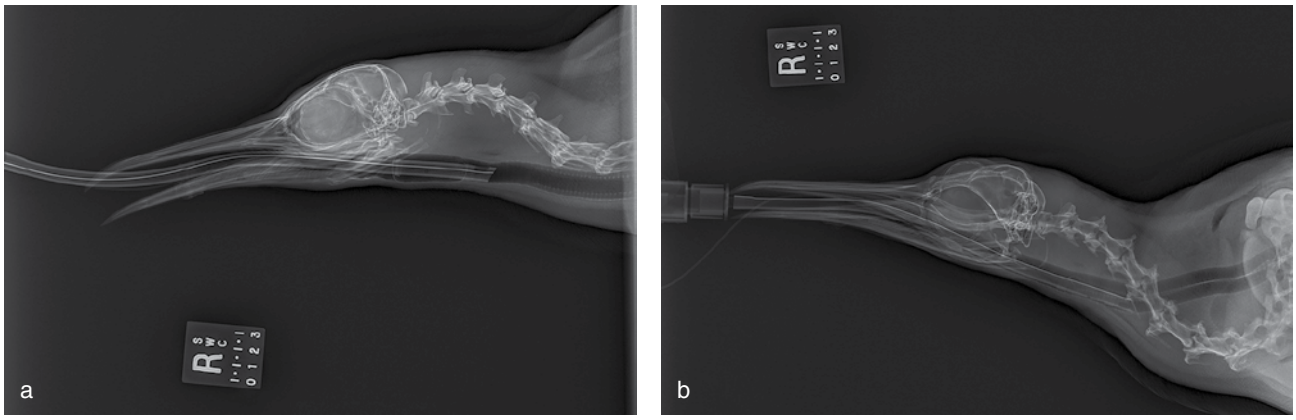


Figure 20.8 (a) Endotracheal tube placed correctly into the trachea, king penguin. (b) Endotracheal tube placed incorrectly into the trachea, king penguin: the tip of an ET tube has been inserted into one bronchus.

assessment suggests that it results from trauma or irritation to the tracheal mucosa (Sykes et al. 2013).

Laryngeal masks (LMA™, LMA North America Inc., San Diego, CA, USA) have also been used to deliver anesthetic gases in penguins. These masks are designed to sit over a human glottis and do not enter the trachea. Use of laryngeal masks will reduce risk of post-intubation trauma to the crista ventralis and tracheal mucosa. They require careful placement to prevent them slipping off the glottis: placing spacers within the mouth over the laryngeal mask and wrapping the neck to keep the mask in contact with the glottis are helpful manipulations (Sykes et al. 2013). The airway should be frequently evaluated during a procedure to ensure correct placement and patency.

Preanesthetic Considerations

In the zoological or rehabilitation setting, it is preferable to obtain a complete history, physical examination, and blood analysis of the penguin to formulate a safe and efficient anesthetic protocol. The clinical history of the patient is reviewed to prepare for additional testing, monitoring, and/or avoid unnecessary anesthetic complications. Physical examination should include evaluation of weight, body condition, hydration, nutritional status, and systematic evaluation of body organs. Apart from true emergencies, most anesthetic procedures should be conducted on stable patients. The clinical history and examination may identify physiological risks (i.e., respiratory disease) or the therapeutic needs of the patient prior to anesthesia. Based on the clinical risk assessment, anesthesia may be warranted to obtain appropriate diagnostic samples or images, or perform a more thorough examination of anatomy with an immobile patient and decrease staff exposure to radiation or harm. A preanesthetic blood analysis should include a cell blood count, hematocrit, total protein, albumin, globulins, glucose, uric acid, creatinine, aspartate aminotransferase, calcium, phosphorous, iron, and electrolytes (sodium, chloride, and potassium). Significant clinical pathology abnormalities should be corrected prior to anesthesia. Elective procedures should be postponed until the underlying condition is treated to alleviate risk of complications. Anesthetic procedures conducted during periods of physiological stress (i.e., molt, breeding, folliculogenesis) may carry greater risk of compromise for the patient due to anemia and metabolic changes. Hydration status should be corrected prior to anesthesia, and the patient should be held in an environment where the temperature is appropriate for the species (e.g., using air-conditioning). The desired temperature range for polar to temperate species is approximately 5–18°C. The age of anesthetized avian patients can carry associated risks with cardiovascular, respiratory, or metabolic disease. The type of induction, length of procedure, and methods of monitoring should be evaluated on an individual basis for geriatric and pediatric penguins. Penguin chicks are brooded by their parents, as they are unable to maintain constant body temperature. Hence, penguin chicks may need supplemental heat during anesthetic procedures, depending on the age and downy feather plumage. Adélie penguins are poikilothermic from hatching to approximately 9 days old (Williams 1995). Nonincubating adult birds (particularly during the period immediately prior to the molt) will have a thick subcutaneous fat layer, therefore injection depth must be taken into account to ensure adequate absorption. In king penguins, IM administration of drugs most often requires injection to at least 2 cm depth (Thil & Groscolas 2002a,b).

Capture and immobilization of wild penguins should be carried out in areas where there is no opportunity for escape into water. Where possible, fasting for a minimum of 8 hours is recommended to empty the stomach prior to anesthesia. Thil and Groscolas (2002a,b) repeatedly anesthetized king penguins with tiletamine-zolazepam during their breeding (nonmolting) fast, and did not detect significant differences between induction time, duration of immobilization, and measured parameters (including heart rate, cloacal temperature, and respiratory rate) during anesthesia carried out at different stages of the fast.

Induction and Maintenance Protocols

Inhalation anesthesia, using isoflurane or sevoflurane, is most frequently used for induction and maintenance in managed penguins. Anesthetic induction may be achieved by administration of 0.5–5% isoflurane and 3–8% sevoflurane via facemask. Maintenance of isoflurane is commonly 2.5–3%, whereas sevoflurane is 3–4.5%, depending on species and whether assisted ventilation is used. Inhalation agents delivered alone can produce cardiopulmonary depression and offer no analgesia, therefore the clinician is reminded to consider the patient's physiologic and disease status and provide supplemental analgesia or muscle relaxant to mitigate inhalant anesthetic side effects. Use of sevoflurane for anesthetic induction and/or maintenance has been reported in a number of penguin species (Ponganis et al. 2001; Bradford et al. 2008; Wallace & Walsh 2005). Sevoflurane has the potential for more rapid induction and recovery as its solubility is lower than that of isoflurane. Its less pungent odor may reduce the stress experienced during a facemask induction.

Intubation may be attempted when there is reduced beak tone, reduced menace or palpebral reflex, and recumbency. It is not uncommon for penguins to continue "swimming" with wings beating during the initial phase of anesthesia; this excitement phase will abate as anesthetic depth increases. Wing beating may persist if the penguin is hypoventilating. Assisted ventilation, 2–3 breaths per minute, may be necessary to obtain a smoother induction of anesthesia (Wallace & Walsh 2005). Once intubated, assisted manual ventilation of 6–8 breaths per minute may be necessary to achieve adequate maintenance anesthetic depth for diagnostic or surgical procedures. Most penguins will spontaneously ventilate under gas anesthesia, but continuous mechanical ventilation (CMV) may be needed to ensure adequate ventilation during long procedures. Before CMV, ensure that the ET cuff/tracheal is sealed to prevent air leakage and the tube is appropriately positioned. Inspiratory pressures up to 15–20 cmH_2O are recommended for adequate ventilation. The ET tube insertion depth must be evaluated by assessing patient ventilation, anesthetic depth, and/or with radiographic imaging to ensure that ET tube is in proper position. Endobronchial intubation can easily occur, as previously discussed, and may lead to inadequate ventilation, anesthetic depth, and poor patient compliance under anesthesia.

In diving animals, apnea and bradycardia can develop during mask induction, and have been ascribed to the cardiorespiratory "dive response" and dose-dependent effect of inhalant anesthetic agent. These changes, however, may be elicited as part of the defensive response to stress (Jones et al. 1988). This stress response can be ameliorated by the use of muscle relaxant sedatives (Ludders & Matthews 2007). Depending on the level of anesthesia needed, use of sedatives can provide adequate immobilization for procedures or be used to premedicate a more balanced anesthetic approach. Reversibility of injectable immobilization agents may be a key factor in decision-making for improving recovery when using injectable sedatives. Premedication of yellow-eyed penguins with midazolam (1.0–1.5 mg/kg IM) and butorphanol (2 mg/kg IM) has been found to produce smoother anesthetic inductions when using isoflurane in oxygen via facemask, and to reduce the incidence of regurgitation during mask induction (L. Argilla, pers. comm., Dunedin Wildlife Hospital). Midazolam 1 mg/kg and butorphanol 2 mg/kg IM is a useful premedicant combination in captive Fiordland penguins, and 2 mg/kg midazolam delivered intranasally has produced mild-to-moderate sedation in little blue penguins (K. Bodley, pers. obs.). Michael et al. (2012) found that administration of butorphanol 4 mg/kg plus tiletamine-zolazepam 0.15 mg/kg IM resulted in mild sedation and mild ataxia in little blue penguins. IM administration of medetomidine (25 μg/kg) and diazepam (0.38 mg/kg) to a captive male king penguin resulted in sedation sufficient for light restraint and radiographs (Bigby et al. 2016). General anesthesia was subsequently induced using 3.7 mg/kg propofol intravenous (IV), given over approximately 120 seconds, and was maintained via a propofol constant rate infusion (CRI) of at 0.3 mg/kg/min while magnetic resonance imaging (MRI) scans were performed. The patient was intubated and CMV was performed throughout the procedure. Anesthetic recovery was described as smooth, with return to spontaneous ventilation occurring approximately 10 minutes after the propofol CRI was discontinued. If required, both medetomidine and midazolam are reversible, using atipamezole and flumazenil, respectively.

Tiletamine and zolazepam (5 mg/kg IM) produced safe immobilization of free-ranging adult king penguins (Thil & Groscolas 2002a,b). Induction time (time to sternal recumbency) averaged 4 minutes and duration of immobilization was approximately 1 hour (mean = 69.3 ± 2.2 minutes). Transitory apnea (maximum duration 1.5 minutes) was noted in 30% of birds anaesthetized. The level of anesthesia was sufficient for noninvasive procedures. Preliminary trials suggested a higher dose rate (10 mg/kg IM) is suitable for immobilization for surgical adipose tissue biopsies (Thil & Groscolas 2002b). Five- to 7-month-old fasting chicks were immobilized for 80 minutes after receiving a 4 mg/kg dosage.

Administration of ketamine (2.0–7.5 mg/kg IM) resulted in sedation of free-ranging Humboldt penguins (Luna-Jorquera et al. 1996). Ketamine (5 mg/kg IM) facilitated handling for attachment of data-loggers, but did not result in anesthesia. Birds recovered after 40–45 minutes. Higher dosages (7.5 mg/kg) resulted in salivation, muscular rigidity, reduced consciousness, and more prolonged recovery. Higher ketamine dosages (5–10 mg/kg IM) administered to nesting African penguins resulted in prolonged anesthetic recovery (Wilson & Wilson 1989).

A combination of medetomidine (0.05 mg/kg), ketamine (5 mg/kg), and butorphanol (0.5 mg/kg) was administered to 22 captive Humboldt penguins and resulted in sedation, muscle relaxation, and analgesia, but a surgical plane of anesthesia was not achieved (Widmer et al. 2021). Recovery following administration of atipamezole (0.25 mg/kg) was smooth but prolonged. Respiratory depression was not noted in any penguin, but a significant reduction in heart rate was observed. One penguin developed second-degree atrioventricular (AV) block, and electrocardiographs (ECGs) revealed ventricular premature contractions in two penguins. One penguin died during recovery from a ruptured left ventricle and pericardial tamponade.

Monitoring

Monitoring of penguins during anesthesia is accomplished using physical assessment and noninvasive monitoring instrumentation methods to evaluate temperature, heart rate and rhythm, respiratory rate, percentage oxygen saturation, end-tidal carbon dioxide levels, blood pressure, and inspiratory and expiratory anesthetic gas levels. Physical assessment includes monitoring beak tone, ocular reflexes, and wing/tail/head movement. Temperature can be measured with small thermometers, but a commercial cable thermistor provides more length if core temperature is desired with an esophageal approach. The mean internal body temperature in little blue penguins in their thermoneutral zone in air was 38.4 ± 0.8°C (Stahel & Nichol 1982). Core temperature in male emperor penguins incubating eggs must be maintained at 37.6–38.5°C during the Antarctic winter via metabolic heat production and huddling behavior (Williams 1995). Deep body temperature measured in free-ranging emperor penguins during nocturnal rest (i.e., when birds were not diving) ranged from 36.0 to 38.7°C (Ponganis et al. 2001). Esophageal probes may provide a more accurate measure of core temperature during anesthesia: the temperature taken 5 cm inside the cloaca represented core temperature in little blue penguins, whereas cloacal temperatures taken 3 cm from the vent were considerably lower (Stahel & Nichol 1982).

Mild hypothermia has been observed in king penguins undergoing prolonged anesthesia (duration approximately 75 minutes) using tiletamine-zolazepam in the field. This was addressed by placing the birds on insulative covers during the procedures (Thil & Groscolas 2002a,b). Prolonged inhalant anesthetic procedures can cause hypothermia due to inhalation of dry cold oxygen, therefore constant temperature monitoring is required. Hypothermia can reduce cardiac contractility as well as prolong recovery. Supplemental thermal support measures, such as warm-water gloves or warmed IV bags, can be placed on the feet where counter-current circulation is present to limit the rate of patient heat loss. The presence of the highly insulative feathers will limit the effectiveness of contact heating methods.

In general, hyperthermia is considered a more likely adverse effect than hypothermia during restraint and anesthesia of penguins because of the presence of an insulative subcutaneous fat layer and densely packed feathers. The anatomical adaptations that allow rapid cooling when penguins are exposed to high environmental temperatures may be utilized during anesthesia. In the field, application of snow to the underside of flippers and the feet has been used to cool penguins at risk of hyperthermia. In the zoological setting, air-conditioned examination rooms are prepared prior to an anesthetic event. Additionally, frozen ice blocks are initially placed on the feet and under the flippers to lower the risk of hyperthermia (Fig. 20.9).



Figure 20.9 Inhalant anesthesia in an Emperor penguin. Note the positioning of the animal on ice to minimize hyperthermia.

Respiratory rate and character should be constantly monitored during anesthesia by observation of thoracic movements and those of the re-breathing bag during gaseous anesthesia. Pulmonary auscultation is best achieved over the dorsum. Hypoventilation can occur with increased anesthetic time, type of anesthetic agent used, and depth of anesthesia. CMV can be utilized to improve consistent ventilation during long procedures or aid with obtaining detailed imaging of air sacs during the inspiratory phase. Inspiratory pressures of 20–25 cmH_2O are optimal for most species. Depth of anesthesia must be monitored carefully with CMV, as anesthetic gases are delivered throughout the air sac system and lungs, and a gradual decrease of anesthetic gas percentage can improve recovery time. Hypoventilation during recovery, following discontinuation of anesthesia with 100% oxygen, can be assisted with room air ventilation (oxygen 21%) using an AMBU bag or manual resuscitating bag prior to extubation of the ET tube. Penguin patients may cough or shake their heads during recovery when not completely conscious, so the ET tube and head of the penguin should be carefully observed and managed during recovery. Ventilatory support should be provided until the patient is breathing spontaneously on its own.

Heart rate and rhythm can be first assessed with a stethoscope in the axillary region bilaterally before other instrumentation is applied. The heart rate of a medium-sized penguin should be between 85 and 120 bpm (Stoskopf & Kennedy-Stoskopf 1986). Sinus arrhythmia is not a common feature during cardiac auscultation. The heart rate of adult king penguins anesthetized using

tiletamine-zolazepam was 99–115 bpm (Thil & Groscolas 2002b). Heart rate and rhythm should be monitored throughout anesthesia by external auscultation, esophageal stethoscope, audible Doppler ultrasonic (US) probe or ECG. The Doppler US probe can be placed over the brachial artery or medial saphenous artery.

A standardized technique for ECG lead placement on the wing feathers and foot webbing, moistened with 70% isopropyl alcohol, and monitoring of heart rate and rhythm has been reported (Stoskopf & Kennedy-Stoskopf 1986). Heart rhythm must be monitored so that abnormal rhythms, such as AV block, tachycardia, or bradycardia, will be noted and corrected (by administering appropriate treatment or by ending the procedure). Pulse oximeter probes can be placed on nonpigmented skin (feet, cloaca, or beak) to monitor trends of percentage oxygen saturation. Caution with interpretation of real oximetry values is advised as oxygen saturation values in birds do not correlate well with arterial saturation derived from blood gas analyses (Schmitt et al. 1998). At the same oxygen saturation, the high absorption ratio in birds compared with humans resulted in a low saturation value on the human calibration curve used by pulse oximeters. It is notable the oxygen–hemoglobin dissociation curve determined in gentoo, chinstrap, Adélie, and emperor penguins is significantly left-shifted when compared with most other birds. In these penguin species the partial pressure of oxygen at which hemoglobin is 50% saturated (P_{50}) lies within the mammalian range rather than the avian (Meir & Ponganis 2009). Cardiopulmonary suppression in the form of bradycardia can occur with gas anesthesia. Anesthetic depth and ventilation rate should be adjusted accordingly to improve cardiac function. Continued ventilatory support with hyperventilation is often needed to improve bradycardia before resuscitative medications (i.e., anticholinergics) are used.

ET attachments for capnography and gas anesthetic concentration sampling can be attached to monitor anesthetic depth and ventilation. Capnography measures maximum inspiratory and expiratory CO_2 concentrations and respiratory rate. Monitoring CO_2 levels can provide information about ventilation, tracheal extubation, airway obstruction, hypo- and hyperventilation, and apnea. Anesthetic gas concentration can aid in the assessment of anesthetic depth and quality of anesthesia. Currently, trends of anesthetic gas level are monitored to assess anesthetic depth and gauge recovery time, as validation of minimum alveolar concentration levels has not been reported in penguins. Noninvasive blood pressure (NIBP) cuffs placed around the tarsus can be used to monitor trends in blood pressure, but NIBP cuffs have not been validated in penguins (Fig. 20.10). A Doppler US probe, pneumatic cuff, and manometer can be used for the same purpose, but to the authors' knowledge mean blood pressure has not been reported in penguins.



Figure 20.10 Noninvasive blood pressure cuff placed around tarsus, little blue penguin.

Patient position during anesthesia can affect ventilation and perfusion, especially with spontaneous respiration. Positioning in dorsal recumbency can adversely impact respiratory function. Thil and Groscolas (2002a,b) observed nonintubated sedated king penguins in dorsal recumbency develop tracheal obstruction due to accumulation of salivary secretions. The birds were observed to lift their heads to facilitate swallowing. Penguins immobilized and placed in ventral recumbency had a reduced incidence of apnea and "head lifting" compared with those in dorsal recumbency. In addition, duration of immobilization was significantly prolonged in dorsally immobilized penguins. Nevitt et al. (2014) examined air-sac volumes, lung volumes, and lung densities in conscious and anesthetized Humboldt penguins using quantitative computed tomography image analysis, and evaluated the effect of body position (dorsal, ventral, and right lateral recumbencies) on the values of those variables. When under anesthesia, birds in dorsal recumbency had the lowest air-sac volume. The radiodensity of lung tissue was also highest in dorsal recumbency. On the basis of these findings, the authors suggested that dorsal recumbency should be avoided for extended procedures in penguins because of possible hypoventilation and ventilation-perfusion mismatch.

Penguins maintained with inhalant anesthesia can be manually or mechanically ventilated to help compensate for the effects of dorsal recumbency.

Recovery

Gaseous anesthetic agents generally result in a more rapid recovery from anesthesia than injectable agents. A rapid anesthetic recovery is preferable, particularly in free-ranging penguins, as prolonged interruption of normal behaviors may result in negative effects such as disturbance of breeding and nest abandonment. Signs of recovery include "swimming" or flapping of the flippers, and leg and head movement. Recovering penguins should be supported upright to prevent regurgitation or trauma to the flippers. Mild gastric reflux is not uncommon and should be managed by close observation and gentle swabbing of the oropharynx with gauze to prevent aspiration of fluid. The ET tube can be removed when the penguin displays a cough reflex and appears to swallow. Once extubated, penguins should not be allowed access to water until they have completely recovered from the effects of anesthetic agents. Free-ranging penguins can be housed inside portable temporary enclosures, situated close to the colony, until they have completely recovered. They must be protected from extremes of temperature and closely monitored while they are still demonstrating effects from anesthetic agents. Once recovered, managed penguins can generally eat prepared thawed frozen-fish diets within 2–3 hours of anesthetic recovery.

Fluid therapy

Fluid therapy can be administered to penguins by different methods based on stage of illness, hydration status, or metabolic need. Oral fluids, electrolyte solutions, or fresh water can be administered with a long red rubber feeding tube of appropriate length for the species and large volume syringe. Fluids deposited in the distal esophagus will easily descend into the ventriculus. Often the first choice for penguins, based on ease of administration, is the subcutaneous route. Subcutaneous fluids, indicated for maintenance or treatment of deficits, are administered using a 19- or 20-gauge needle with a standard fluid administration set. The skin behind the nape of the neck or dorsal scapular region is tented and the needle is inserted into the subcutaneous tissue space. Fluid volumes of 50–300 mL per site can be administered for penguins <7 kg. Fluid boluses of 500 mL to 1 L can be safely and efficiently administered in king and emperor penguins. Most penguins need only to be restrained briefly for placement of the needle and then can be allowed to roam in a confined space as the fluids are delivered. IV catheters have been successfully maintained in the brachial vein and the medial metatarsal vein in several penguin species (Wallace & Walsh 2005; Bradford et al. 2008). Intraosseous fluid administration is difficult due to dense, poorly pneumatized bones. Breitweiser (1994) described a technique for repeated administration of large volumes of intracelomic fluids to gentoo and rockhopper penguins that was well-tolerated by conscious birds. The needle was placed just caudal to the keel and slightly left of the midline, and warmed fluids were administered into the celomic cavity, between the body wall and the distal end of the proventriculus.

Field Anesthesia

Field anesthesia techniques should be chosen carefully. The environmental conditions and the physiological status and behavioral features of the species concerned must be evaluated. Planning of immobilization procedures must include consideration of the potential detrimental impacts that the intervention produces. Living in an extreme environment is energetically costly, and stressful interventions may compromise survivorship and/or reproductive success.

Use of injectable agents will facilitate remote delivery of immobilizing drugs, potentially reducing the stress induced by capture and manipulation. When remote delivery techniques are used, anesthetic drug delivery is less precise and adjustments in dose rate are not possible. The use of inhalational anesthetic agents to induce and maintain anesthesia allows the operator greater control over anesthetic depth and duration than the use of injectable agents for this purpose. Precision vaporizers must be housed in insulated containers when environmental temperatures are low because they function efficiently only within a limited temperature range (Gales et al. 2005). The apparatus used to deliver gaseous anesthetic agents may prove cumbersome and difficult to deploy under the environmental conditions encountered in sub-Antarctic and Antarctic habitats. Use of injectable anesthetic agents may be logistically preferable in such circumstances.

Analgesia

Kilburn et al. (2014) investigated the pharmacokinetics of tramadol and its primary metabolite, O-desmethyltramadol (M1), in African penguins after oral administration of crushed tramadol hydrochloride tablets in fish. Both tramadol and M1 reached human therapeutic concentrations

within 30 minutes of ingestion. Based on this study, a dose of 10 mg/kg orally once a day will result in plasma levels of M1 that remain above human therapeutic concentrations in African penguins. The authors noted that there is large species variability in the pharmacokinetics and pharmacodynamics of drugs, therefore appropriate dosing regimens may vary between penguin species. Empirical use of butorphanol (1 mg/kg IM) has been reported for postsurgical analgesia (Bradford et al. 2008).

Morrison et al. (2018) examined the single-dose pharmacokinetics of IM and oral meloxicam in African penguins. The results of the study suggested that dosages of 0.5 mg/kg IM q24h (once a day) and 1 mg/kg PO q48h are appropriate, but further studies are needed to determine multiple-dose pharmacokinetics and analgesic effects. Dosage and administration of nonsteroidal anti-inflammatory drugs (NSAIDs) should always be carefully considered prior to their use. A clinical study by Baert and de Backer (2003) compared the plasma clearance rates of three NSAIDs in five bird species. Between species, the difference in protein binding alone was so great that the authors recommended the pharmacokinetics of each NSAID should be independently assessed for each target avian species.

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21

Ducks, Geese, and Swans (Waterfowl)

Daniel Mulcahy and Darryl Heard

Introduction

Waterfowl (ducks, geese, and swans) are aquatic birds within the Family Anatidae, Order Anseriformes (del Hoyo et al. 1992). They vary widely in body mass from several hundred grams to more than 13 kg (del Hoyo et al. 1992). Several species have been domesticated for food (meat and eggs), as well as their aesthetic value (e.g., mute swans). Free-living waterfowl are also significant for their value to hunters, including food. They are an important if not essential component of wetland and coastal biota. There are many threatened and endangered species (del Hoyo et al. 1992) due mostly to loss of habitat, but overhunting, introduced vermin, and lead poisoning have had significant impacts on many species.

Avian influenza virus is an important potential zoonosis that can be present within both free-living and domestic waterfowl populations (Shriner & Root 2020). Appropriate protective gear should be worn when working with free-living, and in some cases domestic, species.

Since many waterfowl and their eggs are consumed it is also important to know the regulations regarding the use of drugs (including analgesics and anesthetics) in these species. There are laws and rules in many countries to prevent drugs entering the human food chain. This includes waterfowl that are hunted.

Anatomy and Physiology

Avian anatomy and physiology relevant to anesthesia are discussed in detail in Chapter 15. A feature of waterfowl and other birds is the presence of intrapulmonary chemoreceptors that respond to partial pressure of carbon dioxide (pCO_2). They interface respiratory control and gas exchange by being more responsive to alterations in pCO_2 than in pO_2 (Fedde et al. 1974; Hempleman et al. 1986; Hempleman & Burger 1984). These receptors provide feedback control to ventilation and match respiration with metabolism (Shoemaker & Hempleman 2001). Intrapulmonary chemoreceptors are part of a reflex arc that inhibits respiration when intrapulmonary pCO_2 decreases (Burger & Estavillo 1978).

Some male waterfowl have an asymmetrical bulbous expansion of the trachea, while some geese and swans have tracheal loops that lie in the caudal cervical or anterior coelomic areas (McLelland 1989a). The avian trachea is 2.7 times as long and 1.29 times as wide as the trachea of a similarly sized mammal (McLelland 1989b). Consequently, the anatomical dead space is about 4.5 times that of a mammal (McLelland 1989b). The increased dead space is compensated for by a low respiratory frequency about one-third that of similar sized mammals. This results in minute tracheal ventilation of about 1.5–1.9 times that of mammals (McLelland 1989b). Anesthetic respiratory depression causes more minute ventilation to be devoted to anatomical dead space. Assisted ventilation is, therefore, indicated even when anesthetized birds are spontaneously breathing.

Physical Restraint

Physical restraint alone can be used for short duration procedures that cause minimal pain or distress. The main goal is completion of the procedure in the minimum time required with the least stress on the bird. If a bird shows marked distress, place it back in its cage or container and allow it to recover. A healthy bird should recover to normal respiration within 15 minutes.

Wild birds are always alert for a relaxed grip. They will then make an explosive attempt to escape or inflict harm on the restrainer. To prevent escapes, flighted birds should be handled in an enclosed space. Appropriate-sized nets should also be available for recapture.

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Although small waterfowl are a minimal injury risk, medium to large species can harm personnel. Swans and geese use boney/keratinized thickenings in the carpal areas (knobs) for defense. They will hit potential threats, including humans, with the carpal areas of the wings. These hits are of sufficient force to cause blunt force trauma. Many species (e.g., tundra swans, *Cygnus columbianus*) also possess claws on their feet for extra traction on slippery surfaces, especially ice. These claws can be large and sharp enough to inflict unintentional, but significant lacerations if the handler does not take care. Fortunately, even large free-living waterfowl seem to calm down quickly once appropriately restrained.

Covering the eyes with a hood or a stocking reduces stress during transportation and handling. Some birds, however, will dislodge these covers by shaking their heads. Ducks and geese are picked up for short periods by grasping the base of both wings in one hand and supporting the feet and body with the other (Fig. 21.1). This places considerable stress on the wings and is used only with additional support and not for fractious birds. It can be used for removing birds from a transport container.

Tucking their heads under a wing, which appears to cause mild sedation, conveniently holds ducks and some geese. For additional brief restraint "hook-and-loop" strapping is wrapped snugly around the bird, incorporating both folded wings. Care is taken not to restrict respiration. Restrained birds can then be weighed on a scale (Fig. 21.2).



Figure 21.1 Restraint technique used for ducks and small geese. The humeri are grasped with the fingers of one hand. For heavier birds, the other hand should be placed under the feet to support the weight of the bird. Using this technique, birds should not be held for more than a minute or two to avoid damage.



Figure 21.2 Temporary restraint of a male surf scoter (*Melanitta perspicillata*), here used to weigh the bird on a scale, by tucking the head under a wing and wrapping the bird snugly with "hook-and-loop" strapping. Care is taken to avoid interference with respiratory excursions of the keel and the duration of such restraint should be measured in seconds. Photograph courtesy of Dan Esler.

Handling of free-living waterfowl can cause significant hyperthermia that is exacerbated by environmental temperature (Davenport et al. 2004; Phalen et al. 1996). Plumage provides superb heat retention, especially in cold water adapted species. Excess heat is lost by evaporation through panting, transdermally in featherless areas, and through the feet.

Vascular Access

As in other birds, the jugular, medial metatarsal or basilic (ulna) vein is used for access. The jugular is used for blood samples greater than 1 mL and for placement of relatively large catheters in anesthetized birds. It is the largest peripheral vein, has a fairly thick wall, and hematoma formation is uncommon. The right jugular vein is often larger than the left, but either can be used. Waterfowl generally do not have a bare area of feathers (apterylae) that can be used to visualize the jugular. For blood collection the feathers over the vein are wet down with alcohol. The vessel can then be either seen or palpated through the feathers for venipuncture (Fig. 21.3).

The basilic (ulna) vein crosses the medial distal humerus. Its narrow lumen, thin walls, and curving course make it difficult to obtain more than a small blood sample. Hematoma formation is common. The metatarsal (saphenous) vein courses along the medial tarsometatarsus, crossing the tibiotarso-tarsometatarsal joint. The vein is usually visible and the featherless skin facilitates good disinfection.



Figure 21.3 Blood collection from the right jugular vein of a male red-headed duck. Note alcohol has been used to wet the feathers down to locate the vessel. Palpation is also used to locate the appropriate place for venipuncture using a 1-mL syringe and 25-gauge needle.

The tightness of the skin discourages hematoma formation. Blood is obtained using the needle-nick technique, a needle and syringe, or a butterfly catheter. Its small diameter minimizes the volume of blood that can be obtained, especially in small birds. It is, however, useful for administration of drugs, including propofol and alfaxalone.

Preanesthetic Considerations

Awake or recovering birds are caged in an area that is quiet and protected from the elements. Lightly anesthetized birds are aroused by loud noises (e.g., laughter, motor noises, and raised voices).

Obesity, a very common problem in domestic waterfowl, reduces tidal volume due to air-sac compression. This can lead to hypercapnia, respiratory acidemia, and possibly death (Phalen et al. 1996). Free-living birds have increased intracoelomic fat at times during their life cycle and similar complications should be expected. Fatty liver, in addition to causing dysfunction, makes this organ friable and easily fractured, leading to sometimes rapid death due to hemorrhage.

Fasting before anesthesia is controversial. A fast of 3–12 hours is recommended to empty the crop to reduce regurgitation and aspiration (Curro 1998; Harrison 1991; Redig 1998). In wild-caught waterfowl a pre-induction fast of an hour is sufficient for ingested food to clear. As a precaution, the anesthetized bird is laid on a foam pad or other platform slightly elevated (3–5 cm) above the anesthetic table. The bird's head is positioned on the table lower than the rest of its body. This lessens aspiration of refluxing esophageal or gastric contents.

Ideally, avian blood glucose levels are ≥200 mg/dL before anesthesia. Inexpensive (about $100), over-the-counter blood glucose monitors require little blood, gives rapid results, and are relatively accurate (Lieske et al. 2002).

Intubation

Except for brief procedures all birds are intubated and ventilated. Waterfowl have long necks, allowing for a long endotracheal tube. The length of the neck is used to measure the maximum endotracheal tube length. In some the trachea narrows slightly about midway between the head and thoracic inlet. When resistance is encountered to the tube, stop and withdraw a small distance.

Uncuffed endotracheal tubes are recommended to prevent trauma since birds have complete tracheal rings. Careful use of low-pressure cuffed endotracheal tubes has, however, been suggested for a good seal (Curro 1998). Overinflation of a cuffed endotracheal tube can cause ischemic necrosis of the tracheal mucosa lesion. This can lead to septum formation and narrowing of the tracheal lumen 1–2 weeks after intubation (Ludders 1998). Some mucosal trauma can also occur during transport or movement of the bird that causes rubbing at the end of the tube. A Cole tube is appropriate for very small birds or chicks and ducklings to prevent passing the tube too far into the trachea. Palpating the throat can be used for an estimate of the external tracheal diameter. In waterfowl, females may require a half to a full size larger endotracheal tube than males of the same species. All ducks and geese can be intubated and ventilated with 2–4-mm (internal diameter) cuffless tubes.

As in most birds, intubation is relatively easy; the glottis is easily seen at the base of the tongue. For intubation the upper and lower bills are held agape with the fingers of one hand while inserting the endotracheal tube into the glottis with the other. Alternatively, in large-billed birds an assistant holds both bills, so the person intubating can use one hand to pull the tongue forward while passing the endotracheal tube with the other. Endotracheal tubes are inserted without lubrication.

Correct tube position is confirmed by direct visualization, condensation inside the tube, chest excursions during ventilation, or capnography. It is a good habit to

immediately confirm proper placement by palpating the throat of the bird. If the tube is within the trachea, only one hard tubular structure, the trachea, will be felt ventral to the cervical vertebral column. The endotracheal tube is secured in place by securing it to the mandible.

Oxygen and Anesthesia

As in mammals, inhalant anesthetics depress spontaneous ventilation in waterfowl and other birds (Ludders et al. 1988a, 1989a, 1990; Goelz et al. 1990). It is essential to avoid hypoventilation during anesthesia because birds lack the respiratory reserve capacity to compensate. Oxygen within air sacs does not diffuse into the blood to any great extent (Magnussen et al. 1976).

Using oxygen to deliver inhalant anesthetics further alters respiratory variables in spontaneously breathing birds. In domestic ducks, respiratory rate decreased (but not significantly) as the fraction inspired oxygen increased to more than 90% (Seaman et al. 1994). Increasing oxygen concentration above 40% decreased tidal volume, a decrease that was significantly correlated with arterial CO_2 (Seaman et al. 1994). High oxygen concentrations may depress ventilation by acting on O_2-responsive chemoreceptors (Ludders et al. 1995). The use of air instead of oxygen during anesthesia does not depress the O_2-sensitive chemoreceptors and is less likely to cause hypoventilation. Unfortunately, this is difficult to do with modern inhalant anesthetic machines since most use oxygen as the carrier gas. Switching to ventilation with room air during recovery may, however, assist transition to full spontaneous ventilation as the bird wakens.

Parenteral Anesthesia

The response of waterfowl to many of the anesthetics used in parenteral anesthesia is, unfortunately, problematic at best (see below). Many of the drugs and combinations produce poor immobilization and are associated with adverse effects that can include difficult inductions and recoveries, and even death.

Parenteral anesthesia does, however, have the advantages of ease of use, rapid onset, minimal equipment, reasonable cost, and reduced contamination of the workspace. Like inhalants, most parenteral anesthetic drugs and combinations do produce dose-dependent cardiopulmonary depression. Few parenteral anesthetics are reversible. Exceptions include benzodiazepines, alpha-2 agonists and opioids. Other potential disadvantages include species and individual differences, the need to determine body weight for accurate administration, and a relatively narrow margin of safety. In waterfowl most intramuscular (IM) anesthetics are delivered into the pectoral muscles, although the large leg muscles can be used. Vascular access is discussed above. Some of the parenteral anesthetic drugs used in waterfowl are summarized in Table 21.1.

Alpha-2 Adrenergic Agonists

Xylazine/ketamine combinations used to be commonly used for avian field anesthesia. Xylazine has largely been replaced by the more potent and receptor selective medetomidine and dexmedetomidine. In mallards intravenous (IV), but not IM, medetomidine/midazolam/ketamine produced adequate analgesia and anesthesia for a 30-minute period (Machin & Caulkett 1998a). In the same study, various combinations of medetomidine, ketamine, fentanyl, midazolam, butorphanol, methohexital, or alphaxalone-alphadolone delivered intramuscularly or intranasally were either ineffective or lethal. Medetomidine and xylazine, alone or in combination with other drugs, are used with caution. Sometimes they fail to immobilize birds or else they produce significant cardiopulmonary side effects (Atalan et al. 2002; Pollock et al. 2001; Sandmeier 2000; Uzun et al. 2003; Varner et al. 2004). An advantage to the use of alpha-2 agonists alone or in combination with other drugs is their reversibility with atipamezole.

Midazolam

Diazepam has been supplanted by midazolam for use in waterfowl and other birds. Midazolam produces minimal cardiopulmonary depression and is generally very safe to use even in debilitated birds. It offers the advantages of reversibility with flumazenil and water solubility. The latter allows it to be readily mixed with other parenteral drugs such as ketamine.

Midazolam is usually administered intravenously or intramuscularly, but more recently intranasal (IN) administration has been investigated (Le Net et al. 2019). The latter route allows for ease of administration and rapid mucosal absorption. In Canada geese (*Branta canadensis*) midazolam (2.0 mg/kg IM) provided a satisfactory level of restraint for radiography with minimal cardiopulmonary changes (Valverde et al. 1990). Midazolam has been also used to reduce stress in the perianesthetic period of captured free-living waterfowl (Le Net et al. 2019).

Tiletamine/Zolazepam

Tiletamine/zolazepam is not used because it does not provide adequate analgesia. In Pekin ducks (*Anas platyrhynchos*) tiletamine/zolazepam (13 mg/kg IM), with lidocaine (100 mg) infiltrated into the skin and musculature at the incision site, was used for anesthesia to surgically collect liver biopsies (Carp et al. 1991).

Table 21.1 Injectable drugs used in waterfowl anesthesia.

Common Name	Purpose	Primary Drug	Dosage (mg/kg) and Route	Second Drug	Dosage (mg/kg) and Route	Additional Drug	Dosage (mg/kg) and Route	Reference
Pekin duck (*Anas platyrhynchos*)	Liver biopsy	Tiletamine/ zolazepam	13 IM[a]	Lidocaine	100 mg infiltrated			Carp et al. (1991)
Canada goose (*Branta canadensis*)	Sedation for radiology	Midazolam	2.0 IM					Valverde et al. (1990)
Pekin duck	Anesthesia research	Xylazine	1 IV					Ludders et al. (1989b)
		Ketamine	20 IV					
		Ketamine	20 IV	Xylazine	1 IV			
Mallard duck (*Anas platyrhynchos*)	Anesthesia research	Ketamine	10 IV	Midazolam	2 IV	Medetomidine	0.05 IV	Machin & Caulkett (1998a)
Mallard duck	Preanesthetic sedation	Midazolam	2 IM	Butorphanol	1 IM			Wilson & Pettifer (2004)
Mallard duck	Neuromuscular blockade	Cis-atracurium	0.25 IV					Wilson & Pettifer (2004)
Tufted duck (*Aythya fuligula*)	Surgery	Ketamine	10 IV	Midazolam	2 IV	Medetomidine	0.05 IV	Blogg et al. (1998)
						Buprenorphine	0.06 IM	
Pekin duck	Surgery	Ketamine	10 IV	Midazolam	2 IV	Medetomidine	0.05 IV	Blogg et al. (1998)
						Buprenorphine	0.06 IM	
Canvasback duck (*Aythya valisneria*)	Anesthesia research	Propofol	15 IV induction; 0.8/min IV infusion					Machin & Caulkett (1999)
Wood duck (*Aix sponsa*)	Prevent nest abandonment	Propofol	9-10 IV					Hepp & Manlove (2001)
Pekin duck	Anesthesia research	Pentobarbital	160 IV					Rode et al. (2003)
Mallard duck	Anesthesia research	Ketoprofen	5 IM					Machin & Livingston (2002)
Spectacled eider (*Somateria fischeri*)	Transmitter implantation	Ketoprofen	5.4 IM					Mulcahy et al. (2003)
King eider (*Somateria spectabilis*)	Transmitter implantation	Ketoprofen	2.2 IM					Mulcahy et al. (2003)

(*Continued*)

Table 21.1 (Continued)

Common Name	Purpose	Primary Drug	Dosage (mg/kg) and Route	Second Drug	Dosage (mg/kg) and Route	Additional Drug	Dosage (mg/kg) and Route	Reference
Common eider (*Somateria mollisima*)	Transmitter implantation	Ketoprofen	3.4 IM					Mulcahy et al. (2003)
Pekin duck	Preanesthetic sedation	Buprenorphine	0.05 IM					Wilberg (2005)
Canvasback duck	Transmitter implantation	Propofol	10 IV induction; 1-2 IV bolus	Bupivacaine	2 IM			Machin & Caulkett (2000)
Bar-tailed godwit (*Limosa lapponica*)	Transmitter implantation	Propofol	8-15 IV induction; 1-4 IV bolus	2:1 bupivacaine/ lidocaine	1.5-2.0 IM			Mulcahy et al. (2011)
Mallard duck	Anesthesia research	Xylazine	5 IM	Midazolam	5 IM			Machin & Caulkett (1998b)
		Midazolam	0.1 IM	Medetomidine	0.1 IM			
		Ketamine	8 IM	Medetomidine	0.1 IM			
		Ketamine	8 IM	Medetomidine	0.2 IM			
		Ketamine	8 IM	Medetomidine	0.3 IM			
		Ketamine	8 IM	Medetomidine	0.4 IM			
		Ketamine	8 IM	Medetomidine	1 IM			
		Ketamine	8 IM	Medetomidine	2 IM			
		Ketamine	20 IM	Medetomidine	2 IM			
		Midazolam	2.5 IM	Fentanyl	0.025 IM			
		Midazolam	5 IM	Fentanyl	0.05 IM			
		Midazolam	5 IM	Sufentanil	0.025 IM			
		Midazolam	5 IM	Butorphanol	1 IM			
		Midazolam	2 IM	Ketamine	20 IM			
		Midazolam	2 IM	Methohexital	10 IM			
		Midazolam	10 IM	Alphaxalone-Alphadolone	36 IM			
		Midazolam	1 IV	Alphaxalone-Alphadolone	18 IV			
		Midazolam	1 IV	Ketamine	20 IV			
		Midazolam	1 IV	Ketamine	40 IV			
		Midazolam	2 IV	Ketamine	40 IV			
		Midazolam	5 IV	Ketamine	50 IV			

		Midazolam	1 IV	Ketamine	20 IV	Xylazine	5 IV	
		Midazolam	1 IV	Ketamine	10 IV	Xylazine	3 IV	
		Midazolam	1 IV	Ketamine	10 IV	Xylazine	1 IV	
		Midazolam	1 IV	Ketamine	10 IV	Medetomidine	0.03 IV	
		Midazolam	2 IV	Ketamine	10 IV	Medetomidine	0.05 IV	
Mute swan (*Cygnus olor*)	Induction	Alphaxalone-Alphadolone	3.0-4.2 IV					Cooke (1995)
	Anesthesia research	Propofol	8 IV induction; 2.9 IV bolus					Müller et al. (2011)
	Anesthesia research	Propofol	8 IV induction; 0.85 IV infusion					
Mallard duck	Sedation for handling	Ketamine	24 IM					Samour et al. (1984)
Muscovy duck (*Calrina moschata*)		Ketamine	20 IM					
Hawaiian goose (*Branta sandvicensis*)		Ketamine	20 IM					
Mallard duck		Alphaxalone-Alphadolone	23 IM					
Muscovy duck		Alphaxalone-Alphadolone	11 IM					
Hawaiian goose		Alphaxalone-Alphadolone	3 IM					
Mallard duck		Xlazine	9 IM					
Muscovy duck		Xlazine	8 IM					
Muscovy duck		Xlazine	51 IM					
Mallard duck		Ketamine	20 IM	Xlazine	5 IM			
Muscovy duck		Ketamine	70 IM	Xlazine	10 IM			
Hawaiian goose		Ketamine	20 IM	Xlazine	5 IM			
Mallard duck	Analgesia research	Ketoprofen	5 IM					Machin & Livingston (2002)

IM, intramuscular; IV, intravenous.
[a] Additional doses of 3 mg/kg were used to extend anesthesia.

Ketamine

As in mammals and other birds, ketamine alone is not used because of poor muscle relaxation and spontaneous movement, even at high dosages. It is often, however, combined with other drugs to minimize these unwanted side effects. In Pekin ducks xylazine alone (1 mg/kg IV) or combined with ketamine (20 mg/kg IV) induced hypoventilation and hypoxemia (Ludders et al. 1989b). In Pekin, mallard, and tufted ducks (*Aythya fuligula*) a combination of ketamine (10 mg/kg IV), midazolam (2 mg/kg IV), and medetomidine (0.05 mg/kg IV) was effective for anesthesia and surgery (Machin & Caulkett 1998b). In domestic ducks, however, Abass et al. (2007) found intramuscular ketamine combined with acepromazine, xylazine or medetomidine failed to provide either adequate analgesia or anesthesia.

Propofol

Propofol can be used for induction followed by an inhalant for maintenance. It can also be administered by a constant rate infusion. Canvasback ducks (*Aythya valisneria*) were maintained with a constant rate infusion (0.8 mg/kg/min) following a bolus induction (15 mg/kg) (Machin & Caulkett 1999). More commonly, it is given by slow bolus, both to induce and to maintain anesthesia. The frequency and bolus sizes are titrated to maintain the desired anesthetic depth. Propofol, however, has a narrow therapeutic index. Apnea and hypotension should be expected in all individuals. Artificial ventilation may mask overdosage because the initial sign of toxicity is hypoventilation (Machin & Caulkett 1999).

Alfaxalone

The physiological effects, induction, duration, and recovery of alfaxalone are very similar to those of propofol. Furthermore, it has the advantage of being able to be given intramuscularly. The commercially available concentration (10 mg/mL) limits its use alone for induction in small birds if inhumane IM injection volumes are to be avoided. Subcutaneous injection of larger volumes may be effective and less stressful. Unfortunately, Kruse (2019; Kruse et al. 2019) showed alfaxalone (10 mg/kg IV and IM) alone in mallard ducks (*Anas platyrhynchos*) provided inadequate sedation with associated hyperexcitement during induction and recovery. Lower dosages, however, might be combined with other drugs (midazolam, alpha-2 adrenergic agonists) for improved sedation and induction.

Analgesia

In waterfowl any procedure that would cause pain in humans or result in tissue damage should be performed under anesthesia with consideration for analgesia (see Chapter 2). Species differences in response to analgesics, and the relative paucity of published research in waterfowl make selection and dosing difficult. As with mammals, preemptive administration of analgesics is more effective in easing the pain caused by tissue damage during surgery than postoperative analgesic administration.

Nonsteroidal Anti-iInflammatory Drugs

Flunixin meglumine, ketoprofen, meloxicam, and carprofen have all been used in waterfowl. Flunixin meglumine is not recommended because of a greater risk of adverse effects than in mammals (Clyde & Paul-Murphy 1999). These effects, noted in other bird species, include renal toxicity, regurgitation, tenesmus, and injection site necrosis (Clyde & Paul-Murphy 1999; Machin et al. 2001; Machin 2005).

Nonsteroidal drugs that are not selective for cycloxygenase-2 are used with caution. In free-living male eiders, the nonselective nonsteroidal anti-inflammatory drugs (NSAID) ketoprofen was implicated in renal toxicosis and death when given perioperatively (Mulcahy et al. 2003). Female eiders were not adversely affected. This sex-related difference was thought to be due to physiologic changes associated with male behavior on the nesting grounds. Ketoprofen (5 mg/kg IM) takes about 30 minutes from injection to the onset of analgesia (Machin & Livingston 2002).

Birds eliminate NSAIDs rapidly, but differences in elimination rates occur between species (Baert & De Backer 2003). Compared to chickens, ostriches (*Struthio camelus*), turkeys (*Meleagris gallopavo*), and pigeons (*Columba livia*), ducks (*Anas platyrhynchos*) are intermediate in elimination half-life for meloxicam (0.72 hours), a NSAID selective for cyclooxygenase-2 (Baert & De Backer 2003).

Opioids

Birds often differ from mammals in their response to μ-agonist opioids. This appears to be due to a preponderance of κ opioid receptors over μ in some, but not all species. Butorphanol (1 mg/kg) combined with midazolam (2 mg/kg) was used as premedication for isoflurane anesthesia in a mallard duck (Wilson & Pettifer 2004). In domestic ducks, buprenorphine (0.05 mg/kg IM) 1 hour before induction with isoflurane effectively reduced reaction to painful stimuli, but had strong respiratory depressant

effects (Wilberg 2005). In tufted ducks, buprenorphine (0.06 mg/kg IM) was given at the time of anesthetic induction to provide postsurgical analgesia (Blogg et al. 1998).

Local Anesthetics

Lidocaine and bupivacaine are most commonly used in waterfowl. Their duration of effect has not been determined in birds, but in mammals lidocaine lasts 1–2 hours and bupivacaine 4–6 hours (Lemke & Dawson 2000; Skarda 1996). Use of local anesthetics in birds has been limited by fear of toxicity. To avoid adverse side effects (i.e., depression, drowsiness, seizures, and cardiovascular collapse) the maximum dose is calculated prior to the start of the procedure (4–6 mg/kg lidocaine, 2 mg/kg bupivacaine) (Hocking et al. 1997; Machin 2005).

Brenner et al. (2010) described a technique for brachial plexus nerve blockade in mallard ducks using either lidocaine or bupivacaine. This was based on studies of the anatomy (Alam et al. 2017), as well as nerve conduction (Brenner et al. 2008). Unfortunately, the technique showed variable effectiveness (Brenner et al. 2010) and further evaluation was recommended to improve consistency. Trujanovic et al. (2021) described ultrasound and nerve stimulator-guided blockade of the sciatic and femoral nerves in a domestic duck undergoing tibiotarsal fracture repair.

Inhalation Anesthesia

Isoflurane has been the primary inhalant anesthetic for birds since the mid-1980s (Bednarski et al. 1985; Ludders et al. 1989a, 1988b). Other inhalant anesthetics (i.e., methoxyflurane and halothane) are rarely used now because their manufacture has been discontinued (Goelz et al. 1990; Greenlees et al. 1990; Ludders et al. 1988a). Sevoflurane is increasingly used in clinical settings. Because of its lower blood gas partition coefficient, induction and recovery of birds occur more rapidly than with isoflurane (Quandt & Greenacre 1999). This effect, however, is generally not clinically significant. Sevoflurane is less pungent than isoflurane for human beings (TerRiet et al. 2000). The pungency of volatile anesthetics may contribute to the breath-holding seen in birds when an anesthetic mask is placed over their faces.

In mallard ducks, isoflurane has a minimum anesthetic concentration of 1.3% (Ludders et al. 1990). In birds generally, it causes dose-dependent reduction in spontaneous ventilation that extends to apnea at high concentrations (Ludders et al. 1990). The calculated anesthetic index (anesthetic concentration causing apnea/minimal anesthetic concentration) for ducks (1.65) is lower than for dogs (2.51), cats (2.40), and horses (2.33) (Ludders et al. 1990, 1995; Steffey et al. 1977; Steffey & Howland 1977). The lower anesthetic index for ducks indicates hypoventilation occurs at lower isoflurane concentrations in this species than in others. In Pekin ducks, isoflurane caused tachycardia and hypotension (Goelz et al. 1990). Although arrhythmias were uncommon, one duck died when ventricular bigeminy and multifocal ventricular rhythms progressed to ventricular fibrillation (Goelz et al. 1990). In other avian species, arrhythmias, cardiac irritability, and premature ventricular contractions have also been observed (Aguilar 1996; Greenlees et al. 1990; Jaensch et al. 1999; Langlois et al. 2003; Ludders et al. 1989a, 1988a; Matthews et al. 1991; Naganobu & Hagio 2000; Straub et al. 2003).

Induction

Inhalant anesthetics are usually administered through a mask for induction. Commercially available cat or dog masks are used for small ducks and geese. The mask must include the nares at the base of the upper bill. The mask aperture can be altered with a piece of surgical glove stretched over the opening, taped around the edges and with a slit cut into the center.

The apnea and bradycardia that occur when an induction mask is placed over a bird's beak and face are commonly attributed to a "dive response", but more likely result from a stress response caused by stimulation of trigeminal nerve receptors (Butler 1988; Jones et al. 1988; Woakes 1988). Pre-oxygenating ducks with 100% oxygen for several minutes reduced this response in dabbling, but not diving ducks (Furilla & Jones 1986).

The isoflurane vaporizer is set to 3–5% for induction. In ducks and geese the oxygen flow rate is 1–3 L/min to allow relatively rapid changes in anesthetic concentration as the vaporizer setting is altered. A system for scavenging or venting waste anesthetic gases is used for safety (Altman 1992). Alternatively, for portable anesthetic machines a canister filled with activated charcoal is used. However, not all cartridge brands work equally well (Smith & Bolon 2004). The charcoal canister is always laid on its side to avoid blocking the bottom vents, causing unwanted backpressure on the nonrebreathing circuit.

If apnea is prolonged during induction, respiration is encouraged by lifting the bird at the base of the wings, then gently pressing its body down on the table. Inflation and deflation of the reservoir bag is used to monitor breathing and ventilation, assuming the mask is snugly fitted against the face of the bird. Pulling out a wing or a foot and releasing it judges anesthetic depth. A conscious bird will withdraw into the folded position. When the bird is

assessed as unconscious, oxygen flow is turned to zero. It is preferable to turn the oxygen flow on and off (stopping flow of anesthetic through the vaporizer) rather than turning the vaporizer down and then back up again (during which time isoflurane vapor continues to flow through the dead space and into the room).

Monitoring and Supportive Care

Monitoring begins as soon as a bird is placed in front of the anesthetist, with observation of respiration and attitude. It ends when the bird is fully recovered and returned to its source. As is often stated, there is no better monitoring technique or device than a trained, experienced, and attentive anesthetist to assure the greatest patient stability and safety. Changes in anesthetic depth, body temperature, and cardiopulmonary status occur quickly in birds and must be identified and responded to just as quickly. In fieldwork, a biologist is often drafted in as anesthetist and given on-the-job training. To assure maximum efficacy it is preferable to concentrate acquisition of anesthesia experience in one person, rather than rotate the responsibility between multiple biologists. A trusted anesthetist allows the surgeon to concentrate on their job, contributing to quality work and reduced anesthesia time.

There are several schemes for staging anesthetic depth (Korbel 1998; Sandmeier 2000). In practice, most are too complicated, especially for relatively short procedures, and only serve to divert the attention of the anesthetist away from directly observing the patient. A simpler scheme for fieldwork with a biologist anesthetist is given in Table 21.2 (Curro 1998; Rosskopf & Woerpel 1996). Successful induction has occurred when the legs and wings can be extended without being withdrawn and in most cases this signals readiness for intubation.

Table 21.2 Simplified anesthesia levels of birds (stages are continuous).

Induction	Muscle relaxation, lowered head, drooping eyelids, wings and legs can be extended without being withdrawn
Light	No response to positional change; corneal, palpebral and pedal withdrawal reflexes present; no volitional movement
Medium	Respirations slow and deep; palpebral reflex absent; corneal and pedal reflexes sluggish or absent
Deep	Respirations very slow and progressively shallow; reflexes absent

Source: After Curro (1998).

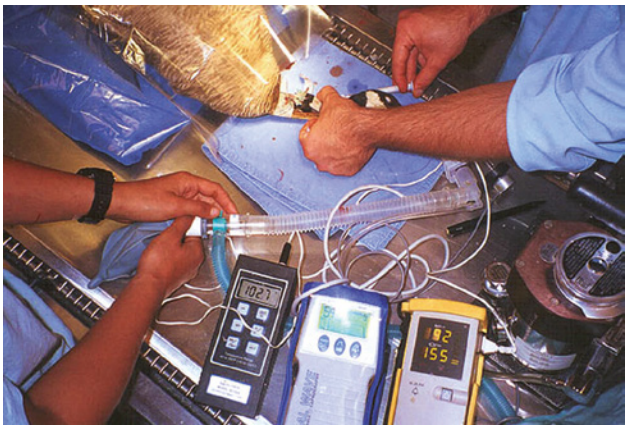


Figure 21.4 A lesser Canada goose (*Branta canadensis*) anesthetized with isoflurane with anesthetic circuit shown. The patient, prepared for surgery, is being electronically monitored with a digital thermometer, capnograph, and pulse oximeter, and a blood sample is being drawn from the jugular vein for blood gas determination.

Once intubated, the appropriate monitoring instrumentation is applied. Respiratory monitors, stethoscopes, electrocardiographs, capnographs, blood gas analyzers, blood pressure monitors, and cloacal and esophageal temperature probes have been used to assess the anesthetic status of waterfowl (Fig. 21.4). Deciding the instrumentation to use depends on practicality and procedure length. It is contrary to the best interests of the patient to significantly extend anesthetic duration to place additional monitoring sensors and instruments. The essential physiologic variables to monitor include heart rate and rhythm, respiration rate and depth, and body temperature.

Respiration is evaluated by observation. Depth is judged by the extent of sternal movement. Movement of the re-breathing bag does not reliably reflect occurrence and depth of respiration, as the cuffless endotracheal tube may not form a sufficient seal. Arterial blood gas analysis is the definitive means of evaluating ventilation, but is rarely done.

Tracheal secretions tend to be very thick. Clicking or gurgling noises indicate partial tracheal or endotracheal blockage; the endotracheal tube is withdrawn and cleaned if necessary. Sometimes the plug is located in the trachea instead of the tube. Complete tracheal obstruction (as from a plug) is suggested by marked inspiratory and expiratory efforts with little to no air movement. In many cases, the anesthetist can force air past the obstruction with positive pressure, but the material then re-obstructs the tube. End-tidal CO_2 readings will be low, despite assisted ventilation. If this occurs, the tube is removed immediately and either replaced or cleaned and reinserted. Tracheal mucous plugs are sometimes removed by inserting a longer, smaller diameter endotracheal tube, rotating, then withdrawing

with the mucus plug attached. Obstructions occur more often with dehydration, which thickens secretions. Since they rarely drink water provided in a holding container wild birds held for hours prior to surgery are assumed to be dehydrated.

Manipulations of the bird's body can cause excursions of air through the trachea that are not part of the respiratory cycle. Observation of the graphic waveform of a capnograph can confirm observed respiration rates that reflect a true respiratory cycle (Fig. 21.4). However, not every capnograph is accurate at small tidal volumes (see Chapter 4). Capnography is considered accurate only during positive pressure ventilation (Sap et al. 1993). When monitoring with a capnograph, manual or positive pressure ventilation is adjusted to keep end-tidal CO_2 partial pressures at 30–45 mmHg (Edling et al. 2001).

The purpose of cardiovascular monitoring includes ensuring that the heart is beating and the blood is circulating. Pulses are palpable at the tibiotarsal or elbow (cubital) joints if the hands of the anesthetist and extension of a leg or wing will not disturb the procedure. A stethoscope, esophageal stethoscope, electrocardiograph, or Doppler flow detector is used for cardiovascular monitoring. It is useful to have redundancy in monitoring in case a sensor is dislodged.

Pulse oximetry can be undependable due to motion artifact, inaccuracy, lack of calibration to avian hemoglobin, and discontinuity of values during surgical emergencies (Schmitt et al. 1998). Pulse oximeters are calibrated for human blood and will give a lower saturation value for avian blood (Schmitt et al. 1998). For routine monitoring the relative inaccuracy of oxygen saturation is not critical and the pulse oximeter can be used to monitor trends in heart rate and oxygen saturation. Relying solely on pulse oximetry to monitor birds anesthetized with isoflurane in 100% oxygen is inadequate as they may be poorly ventilated despite adequate oxygenation (Edling et al. 2001).

It is often difficult to find a suitable site for placing the pulse oximeter probe. The inter-digital webbing of the feet is used, but the presence of pigment may make the site unsuitable for a transmittance probe. Similarly, clamp probes are placed on the tip of the upper bill of ducks with lightly pigmented bills (Fig. 21.5). Reflectance probes are placed into either the esophagus or cloaca. Maintaining a constant, proper position with reflectance probes is a problem; the anesthetist may have to make frequent adjustments to assure adequate tissue surface contact.

Auscultation of the heart is a simple and direct means for monitoring heart rate and rhythm. The large pectoral muscle mass of waterfowl reduces transmission of cardiac sounds; the stethoscope diaphragm is placed on the dorsal thorax, lateral thorax or thoracic inlet. However, placing a stethoscope under the surgical drape may be disruptive to the surgeon. Alternatively, an esophageal stethoscope is used. This consists of a hollow plastic tube with multiple openings at the distal end, covered with a plastic cuff. Sensor tubes are available in a variety of diameters; the largest tube compatible with the esophagus is used for the best signal. The tube is inserted to the level of the heart. Positioning is evaluated by listening to the volume and clarity of the signal. The long necks of waterfowl and shorebirds facilitate intra-operative adjustments without disturbing the surgeon. The sensor tube is placed immediately after intubation. Sometimes respiratory sounds are also heard. Diminished or no heart sounds are usually due to inadvertent displacement of the sensor.



Figure 21.5 Placement of a pulse oximeter transmittance probe on the bill of a female mallard duck (*Anas platyrhynchos*). This technique works when there is little or no pigment on the bill. Photograph courtesy of Scott Larsen.

An ultrasonic Doppler flow detector (Parks Medical®, Parks Medical Electronics Inc., Aloha, Oregon, USA; Minidop®, Jorgensen Laboratories, Inc., Burlington, Wisconsin, USA) is most commonly used for cardiac monitoring. The ultrasound probe is commonly taped over the cranial tibial artery, but the superficial ulnar artery at the distal humerus and the carotid artery are also used (Lichtenberger 2005; Zantop & Bowles 2000). The Doppler flow detector allows indirect monitoring of systolic blood pressures, using the appropriate pressure cuff size (40% of appendage circumference) around the leg proximal to the probe. Diastolic, and therefore mean, blood pressure cannot be obtained with this method. Birds with systolic blood pressures $\leq$90 or $\geq$145 mmHg are evaluated for causes of hypotension and hypertension, respectively (Lichtenberger 2005). Hypovolemia is treated with bolus administration of crystalloids (10–20 mL/kg) or colloids (5 mL/kg) until systolic pressures are restored (Lichtenberger 2004). For immediate effect, fluids are given intravenously or intraosseously (Valverde et al. 1993).

Digital thermometers are more useful than traditional thermometers because their displays are easier to read. Digital thermometers are placed in either the cloaca or deep in the esophagus (Fig. 21.4). Cloacal sensors are taped in place, but the tape is easily dislodged by fecal fluid and the thermometer is difficult to read if covered by a surgical drape. Digital thermometers with long, flexible extension sensors are preferred for esophageal placement. To read the core temperature the sensor is inserted until it is past the thoracic inlet. Normal body temperature in waterfowl is 40–42°C, but it tends to decline during anesthesia.

Supportive Care

Body Temperature

Body temperature maintenance within a normal range begins with a patient that is dry, clean, and minimally stressed. Hypothermia is more likely to occur in a patient with feathers wetted during capture and handling or fouled by feces and urine during transportation. Conversely, birds severely stressed during capture, transported in a poorly ventilated container, and held for hours before a procedure at high environmental temperatures are very likely to be hyperthermic. In the author's experience with Arctic waterfowl, hyperthermia occurs more commonly than hypothermia.

During normal respiration the turbinates warm and humidify inspired air (Schmidt-Nielsen et al. 1970). The efficiency of evaporative heat exchange by the turbinates is such that the nasal surface temperature may be less than that of the ambient air (Jackson & Schmidt-Nielsen 1964). The air being cooled and supersaturated by passing over the turbinates during exhalation minimizes water and heat losses. The reduction in evaporative water loss ranges from 55% to 71% in birds (Geist 2000). Exhaled air temperature at the external nares averaged 19.6°C lower than core temperature while oropharyngeal temperature measured only 3.5°C lower, indicating the trachea is minimally involved in heat exchange (Geist 2000). The condensed moisture and heat recovered at the turbinates are returned to the body. In the intubated bird during anesthesia, breathing is shifted from nasopharyngeal to oropharyngeal, bypassing the countercurrent heat-exchange and moisture recovery mechanisms in the nasal cavity. This accelerates heat and moisture loss. The type of breathing system used for avian anesthesia has little effect on body temperature loss.

Correction of abnormal body temperatures is begun as soon as it is recognized. Wetting the unfeathered legs and feet with isopropyl alcohol treats hyperthermia. The feet of waterfowl efficiently control body temperature due to the presence of the rete tibiotarsale, a vascular network (Midtgård 1980). In severe hyperthermia, rapid correction requires other concerns are ignored. It may be helpful to also wet the axilla with alcohol, despite the risk of removing waterproofing of the feathers.

Correction of hypothermia is more difficult and is best avoided. If body temperature decreases suddenly, dislodgment of the temperature sensor from within the thorax is suspected first. To treat a hypothermic bird, external heat is applied to the exposed skin of the feet and lower legs. Bags of water or saline heated up to 43°C or chemical heat packs wrapped in a layer of cloth are placed on the feet. Leaks in the bags should be avoided to prevent feather wetting, which will exacerbate hypothermia. Waterfowl reduce heat loss by decreasing blood flow to their hindlimbs, making external heat application to the feet less efficient.

Hypothermic birds recover very slowly from anesthesia. They are held wrapped in a towel to conserve body heat during recovery. It is best to correct the body temperature abnormality during anesthesia rather than to expect the postanesthetic patient to recover on its own. Hypothermic birds are recovered and re-warmed with caution and with constant observation. Rewarming reverses peripheral vasoconstriction and increases metabolic demand for glucose (Heard 2000). Deaths of hypothermic birds that occur within several hours of the end of anesthesia may be due to the effects of induced hypothermia.

Efforts to reduce thermal loss under anesthesia usually involve placing the bird on an insulated pad, a heated circulating water mattress, or wrapping in bubble wrap (Harrison 1994). These methods have little effect because of the high insulating value of feathers. A radiant energy source placed just above anesthetized birds was the only effective technique for maintaining a constant body temperature (Phalen et al. 1996; Rembert et al. 2001). The effectiveness of radiant heat was demonstrated, however, in a sun conure (*Aratinga solstitialis*) that died of heat stroke (body temperature 48.1°C) during surgery under an unusually hot surgical lamp (Hofmeister & Hernandez-Divers 2005).

Ventilation

Most surgical procedures are performed in dorsal recumbency, which can cause profound respiratory alteration. In conscious chickens placed in dorsal recumbency, tidal volume decreased 40–50% although breathing frequency increased by 20–50% (King & Payne 1964). Respiratory compromise may be worsened in waterfowl by the inertial resistance of the relatively large pectoral muscle mass to respiratory excursions of the keel. The pressure of viscera on the abdominal air sacs also reduces their effective volume.

Inhalant anesthetics cause a dose-dependent depression of spontaneous ventilation (Ludders 1992; Ludders et al. 1990, 1989a, 1988b). Intermittent positive pressure ventilation is used in anesthetized birds, even if some spontaneous breathing is continuing, to ensure adequate oxygenation of the blood (Edling et al. 2001). In geese, an average arterial partial pressure of carbon dioxide ($PaCO_2$) of 53 mmHg was necessary for spontaneous respiration to occur; no respiration occurred with $PaCO_2$ ≤40 mmHg (Pizarro et al. 1990). Ventilation is assisted manually using the reservoir bag on the breathing system or a mechanical ventilator (Hernandez-Divers 2001; Pettifer et al. 2002). Analysis of blood gases has showed that effective gas exchange is achieved using mechanical ventilation (Edling et al. 2001; Ludders et al. 1989a; Mitchell et al. 2001; Pettifer et al. 2002; Piiper et al. 1970).

In mammals, a decrease in mean arterial blood pressure is usually observed during positive pressure ventilation. In a variety of birds, including sandhill cranes (*Grus canadensis*), pigeons (*Columba livia*), and Amazon parrots (*Amazona ventralis*), blood pressures either increased or were maintained during ventilation (Ludders et al. 1989a; Pettifer et al. 2002; Wilson & Pettifer 2004). An exception was hypotension observed in positive pressure-ventilated chickens anesthetized with sevoflurane (Naganobu et al. 2003). The cardiovascular effects of positive pressure ventilation in birds are still uncertain and have not been examined in waterfowl.

A spontaneously breathing bird is given at least two assisted breaths per minute. If an anesthetized bird is apneic the assisted ventilation rate is 8 to 15 breaths per minute depending on size (large birds require fewer breaths than small). If pulse oximetry and capnography are used to monitor respiration the rate is guided by the end tidal CO_2 level and the relative hemoglobin saturation (Fig. 21.4).

Air-sac Cannulation

Airflow through the lung is continuous and unidirectional. It is therefore possible to ventilate and provide anesthesia through an air-sac cannula (Brown & Pilny 2006; Jaensch et al. 2001; Rode et al. 2003; Whittow & Ossario 1970) (Chapter 16). A common application of this technique is in patients with tracheal obstructions (Clippinger & Bennett 1998; Mama et al. 1996; Rode et al. 2003). The abdominal or caudal thoracic air sacs are generally used. The clavicular air sac has been used, but it appears to participate less in ventilation than the thoracic and abdominal air sacs (Jaensch et al. 2002; Rode et al. 2003). Cannulation of the caudal thoracic air sac has been used to anesthetize zebra finches (*Taeneopygia guttata*) as small as 10 g (Nilson et al. 2004). The technique could easily be adapted for anesthesia of very small ducklings.

Placing an air-sac cannula requires the selected site (on the lateral abdominal wall well ventral to the spine so as to avoid damage to the kidney) to be prepared as with any surgical site. Feathers are taped aside and the skin is prepped. While general anesthesia makes placement easier, in conscious birds the surgical site is infiltrated with lidocaine (≤2 mg/kg). The skin is incised with a scalpel blade. The muscle layer is penetrated with either sharp dissection by making a puncture with a blade or by blunt dissection using hemostats to work through the muscles and air sac membrane. The cannula, often an endotracheal tube, is pushed into the air sac. The tube is secured by suturing tape butterfly wings to the skin. The breathing system is then connected and the animal ventilated. Waste anesthetic gases exit through the trachea and are an exposure risk to personnel. The cannula is removed when spontaneous ventilation is reliable. Sutures or surgical glue are used to close the incision.

Ducks anesthetized with phenobarbital and breathing room air through clavicular air sac cannulas had no significant differences in arterial blood gas values compared to ducks that were endotracheal intubated (Rode et al. 2003). Caudal thoracic air-sac cannulation in sulfur-crested cockatoos (*Cacatua galerita*), anesthetized with isoflurane in 100% oxygen, provided adequate blood oxygenation and maintained tidal and minute volumes (Jaensch et al. 2001). However, clavicular air-sac cannulation did not provide adequate ventilation or anesthetic maintenance (Jaensch et al. 2001).

Recovery

For recovery, the anesthetized bird is positioned in lateral to slightly ventral recumbency. The bird remains intubated and respiration is assisted until it shows controlled, voluntary motion and objects to the presence of the endotracheal tube. The tube and esophageal monitoring sensors are removed at that time. Newly extubated birds remain sedated by the anesthetic and may become quiescent.

Many recovering birds go through a period of disorientation, wing flapping, and struggling (emergence delirium) that may result in self-inflicted trauma (Curro 1998). To avoid this, recovering birds are wrapped in a towel (unless hyperthermic) and observed closely for continued respirations. Only when the bird holds its head erect and steady is it replaced in the recovery container. It is then regularly observed for flexion of its head and neck that may obstruct the airway. If this occurs, the bird is repositioned or removed from the recovery container and held until fully recovered. Recovery time depends on the choice of anesthetic, anesthetic duration, and extent of physiologic

alteration that has occurred. A bird that is hypothermic, hypoglycemic, or has impaired drug elimination mechanisms will take longer to recover.

Field Techniques

Free-living waterfowl are anesthetized for a variety of reasons, including restraint. An increasing number of field anesthesias and surgeries are done to collect liver biopsies for determination of cytochrome P450 1A, a hepatic enzyme induced by exposure to hydrocarbons from spilled oil (Trust et al. 2000; Esler et al. 2002; Golet et al. 2002; Jewett et al. 2002; Peterson et al. 2003; Mulcahy et al. 2011; Mulcahy & Esler 2010). Isoflurane is the anesthetic of choice for taking surgical liver biopsies from birds (Degernes et al. 2002). The cytochrome P450 isoenzyme responsible for the limited isoflurane metabolism that occurs is different from that assayed for oil spill exposure (Kharasch & Thummel 1993).

There is also a need for field anesthesia to surgically implant transmitters and data loggers (Butler & Woakes 1979; Olsen et al. 1992). Many waterfowl species, especially diving birds, do not tolerate external attachment of transmitters. Percutaneous antennas allowed recently miniaturized satellite transmitters (PTT-100, Microwave Telemetry, Columbia, Maryland, USA) to be implanted in waterfowl, especially sea ducks (Petersen et al. 1995, 1999, 2003, 2006). In spontaneously breathing pigeons anesthetized with isoflurane, the opening of an air sac for endoscopic splenic biopsy worsened hypoventilation, despite an increased respiratory rate (Touzot-Jourde et al. 2005). This response was possibly due to high $PaCO_2$ or to a lighter anesthetic plane following dilution with room air entering the incision. If the birds were ventilated mechanically, the ventilator did not achieve the selected inspiratory pressure due to leakage through the open air sac. In those birds respiratory alkalemia developed and $PaCO_2$, HCO_3, base excess, heart rate, and mean arterial blood pressure were all significantly decreased, although PaO_2 was maintained (Touzot-Jourde et al. 2005). The incision required to implant a transmitter creates a much larger opening in the abdominal air sac than that for an endoscopic biopsy. This suggests the cardiovascular effects during implantation are the same or worse.

When free-living birds require anesthesia it is rarely practical to do more than a quick physical examination prior to induction. The ability to do hematology and serum chemistries is rarely available. The emergence of point-of-care blood analyzers, however, has begun to permit at least some screening of patients in the field (Stoskopf et al. 2010). Consumer-grade blood glucose analyzers have begun to be used in seabird rehabilitation (Lieske et al. 2002). The prandial status of wild avian anesthetic candidates is usually unknown, and it is advisable to hold wild birds for as short a time as possible to limit stress. It is recommended to hold birds for about an hour before anesthesia to prevent intra-operative draining of crop contents with subsequent aspiration.

Holding, Transportation, and Handling

Surgical facilities for field research are usually centralized and the birds transported by truck, boat, aircraft, or by being hand-carried from the capture site. Birds are transported in soft bags, boxes, or animal carriers. Cardboard boxes are rarely suitable because of the lack of air circulation, even if holes are punched through the sides. Techniques for carrying are directed at protection from trauma, minimizing stress, and preserving the protective function of the feathers. It is preferable to transport birds individually to prevent fighting. If more than one bird must be placed in a transport container, mixing birds of the same sex is avoided.

The size of the container should be sufficient to allow the bird to stand and turn around. If too many birds are placed into a single container, trauma or death from suffocation may result from birds piling up in a corner.

The insulation of feathers and aquatic lifestyle of waterfowl contribute to hyperthermia during dry transportation. A transport container must have adequate ventilation to prevent hyperthermia. Commercial cat and dog crates have grated windows that let air circulate (Fig. 21.6). However, the grid may permit bird bills to pass through and suffer damage. The existing grid is covered with finer mesh netting that prevents trauma, but still allows air circulation and observation of the bird.

Prevention of feather soiling during transportation and holding is essential. Soiled feathers are a source of infection during surgery and are less capable of maintaining a constant body temperature during anesthesia and recovery. Following release, a soiled bird has to devote more time to preening. This leads to increased energy expended, reduced feed consumption, and increased risk of predation. A towel or other absorbent material is placed on the bottom of the transport container. If the bird is permitted to rest directly on the bottom of the container, the towels are changed frequently to assure a clean and dry substrate. It is preferable to have waterfowl rest on netting suspended from a frame on the bottom of the container. The mesh size should be small enough to prevent toe entanglement, but allow excreta to pass through. Alternatively, artificial turf is used for the substrate (Fig. 21.6).

When captured, wild birds rarely eat or drink in transport or temporary holding facilities, especially with humans nearby. Pretreatment holding times are therefore



Figure 21.6 Examples of holding and recovering cages made by modifying an animal carrier by the addition of artificial turf (top) or mesh surrounding a PVC-pipe frame (bottom) to reduce fecal soiling of feathers. A turf bottom (top) is safer for a bird like the bar-tailed godwit (*Limosa lapponica*), which has a long bill and toes, to reduce the chance of entanglement. A finer mesh net should be attached to the inside of the wire-grid door and air holes to prevent damage to the bills of shorebirds and ducks such as the common eider (*Somateria mollissima*), shown in the bottom picture.

usually limited to 1–2 hours to reduce stress and dehydration. For most procedures, birds are returned to their holding containers for about an hour after they have recovered, then released.

The feathers are often disarranged or damaged during capture and initial handling to free the bird from nets or traps. Handling must be gently done to maintain feather integrity and waterproofing, especially for waterfowl that will be released into cold waters. If surgery is done on wild-caught water birds intended for immediate release, feathers are not plucked because that would increase the amount of heat lost when the bird is released into cold water. It also imposes an increase in energy demand during feather replacement.

Lingering sedative effects are undesirable in field anesthesia of wild birds. Birds are released relatively quickly after recovery from anesthesia, placing them at risk of injury or predation or unable to maintain social status in a flock or a pair bond commitment. Due to these risks, analgesics that might compromise reactivity (e.g., opioids) are not used.

Oral Drug Administration

Waterfowl have been captured using bait treated with alpha-chloralose, a centrally active chloral derivative of glucose (Bailey et al. 1999; Belant & Seamans 1999, 1997; Belant et al. 1999). Other oral drugs used to capture waterfowl have not had the same level of use and experimentation (Cline & Greenwood 1972). Alpha-chloralose is soporific and narcotic; it does not produce general anesthesia. It has been most used as an avicide to control nuisance birds. Although usually added to corn, it has also been combined (30 mg/kg) with margarine and used in tablet form to capture Canada geese (*Branta canadensis*) (Belant & Seamans 1997; Crider 1967). This approach is used for birds that habitually use a certain area. When applied to a substrate like bread, individual birds can be targeted if they can be approached and thrown the bait. However, induction is very long and recovery may take many hours. As a result, this drug is not suitable for birds that are to be quickly released after a procedure. Multiple exposures may be complicated by drug accumulation in the tissues.

Alpha-chloralose is hazardous to use and a current Material Safety Data Sheet must be obtained from the manufacturer and consulted for the proper personal protective equipment. Legal use of alpha-chloralose in the United States requires an Investigational New Animal Drug Application (#6602) issued by the Food and Drug Administration to the Animal and Plant Health Inspection Service, US Department of Agriculture. In mallard ducks the effective dose (ED_{50}) is 15 mg/kg and the lethal dose (LD_{50}) is 34 mg/kg, resulting in a therapeutic index ($TI = LD_{50}/ED_{50}$) of 2.2 (Cline & Greenwood 1972). Alpha-chloralose is much less safe in mallard ducks than chickens, where ED_{50} = 45 mg/kg, LD_{50} = 300 mg/kg, and TI = 6.7 (Loibl et al. 1988). This difference indicates that interspecies variability in susceptibility must be carefully considered. Overdosing is a potential problem; birds that have ingested alpha-chloralose are at risk of drowning if they enter the water. Drugged birds that escape and die in wetlands are a slight risk for starting an outbreak of avian botulism in waterfowl (Goldberg et al. 2004). Care is taken to prevent secondary poisoning of nontarget species, including domestic animals (Segev et al. 2006).

Inhalation Anesthesia

Inhalation anesthesia in free-living birds is usually performed with isoflurane. The minimum equipment for administration includes a tank of oxygen, regulator and pressure tubing, flow meter, vaporizer, and breathing system. Most people prefer the vaporizer and flow meter mounted on a stand for convenience (Small et al. 2004).

Use of compressed oxygen in the field at low ambient temperatures may contribute to loss of body heat. If safely possible oxygen cylinders are kept in a warmed environment. Exposure to very cold temperatures can shrink metal parts and seals, causing gas leakage. Cylinder valves transported to cold environments should be tightened more than usual and checked on arrival at the field location. It is prudent to always have a plan for an alternative anesthetic technique (e.g., injectable drugs).

Induction of wild-caught waterfowl is done using isoflurane and a mask. The vaporizer is set at 4% with a minimum oxygen flow of 1 L/min for most ducks and small geese. Occasionally a wild bird is sufficiently stressed to resist induction and the vaporizer is turned to 5%. If induction resistance occurs regularly, consideration should be given to preanesthetic sedation of the birds.

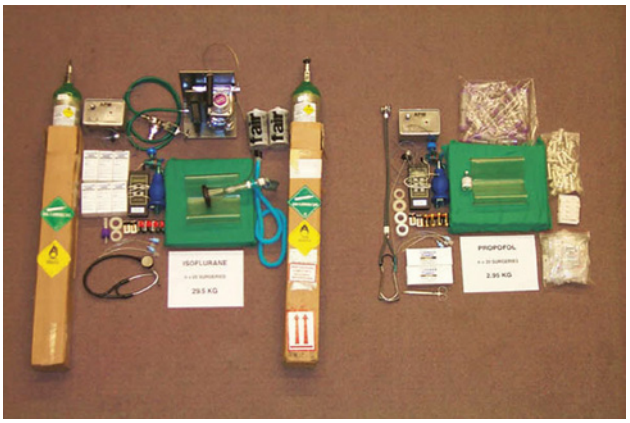


Figure 21.7 Comparison of equipment and supplies required to perform an identical number of surgeries using isoflurane (left) or propofol (right). The latter system totals about 10% of the weight of the former. The cartons containing the oxygen cylinders bear hazardous materials labels.

Intranasal Drug Administration

In mallard ducks intranasal alphaxalone-alphadolone had no effect (Machin & Caulkett 1998a). Intranasal ketamine, midazolam, methohexital, and butorphanol alone or in combination produced light sedation at best, as did intranasal ketamine and midazolam when combined with IV propofol (Machin & Caulkett 1998a). However, intranasal delivery was not combined with isoflurane administration. Intranasal midazolam (2–8 mg/kg) decreased postsurgical mortality in female surf scoters (Le Net et al. 2019). Alternatively, this author has used 2 mg/kg IM in surf and white scotors immediately after capture to reduce stress in the perisurgical period for transmitter implantation. The drug was administered intramuscularly by a member of the capture team using a predrawn dose.



Figure 21.8 A 0.508-mm (25-gallon), 1-cm butterfly catheter placed in the tibiotarsal vein of a yellow-billed loon (*Gavia adamsii*) and connected to a syringe holding propofol. The wings of the "butterfly" have been cut off to reduce the chance of dislodging the needle.

Injectable Anesthesia

For the intracoelomic implantation of radio transmitters, propofol has been used as a general anesthetic, combined with bupivacaine or a 2:1 mixture of bupivacaine/lidocaine infused at the incision site (Machin & Caulkett 1999, 2000; Mulcahy et al. 2011). The propofol/bupivacaine anesthetic system eliminates shipping hazardous materials. In addition, the equipment required for propofol/bupivacaine is much less expensive, and the mass of materials required is a fraction of that required using isoflurane as an anesthetic (Fig. 21.7).

The medial aspect of the tibiotarsus is prepared for catheter placement by cleaning and disinfecting with nondetergent iodophor solution. A 0.508-mm (25-gauge), 1-cm butterfly catheter (No. 4573, Abbott Laboratories, North Chicago, Illinois, USA), or an alternative catheter of suitable size and length for the bird, is placed in the medial metatarsal vein (Fig. 21.8). Stability of the catheter is improved by snipping the plastic butterfly wings from the needle. Other butterfly catheters and over-the-needle catheters can also be used, depending on the length of the bird's leg. Birds are induced by slow administration of propofol (20 mg/kg or to effect, depending on the temperament and level of excitement of the bird). Following induction, which occurs within seconds, the catheter and its tubing are taped in place. Following preparation of the surgical site, bupivacaine or bupivacaine/lidocaine mixture (2:1 v/v) is infused at and around the incision site to a maximum of 2 mg/kg. Additional propofol is given by bolus (1–4 mg/kg) to maintain a plane of anesthesia suitable for

the procedure being done. Clues to indicate the need for additional propofol are movement or tone in the legs and wings, or opening of the eye with the presence of a reflex movement of the nictitating membrane.

Following induction with 8 mg/kg of propofol, a continuous rate infusion (0.85 mg/kg/min) was compared to bolus administration (2.9 mg/kg) in mute swans (*Cygnus olor*) (Müller et al. 2011). In that study, bolus administration of propofol was considered to be unsatisfactory due to sudden awakening of the swans. However, that result suggests a difficulty by the researchers in detecting signs of anesthetic lightening in time to administer additional propofol. The present author has used propofol administered by bolus to anesthetize tundra swans (*Cygnus columbianus*) without problems with unexpected awakenings.

Hazardous Material Shipping

Inhalant anesthetics and compressed oxygen cylinders are classified as hazardous materials for air transportation and can only be shipped as cargo, never as checked baggage (Anon. 2006). Failure to follow regulations governing shipment of hazardous materials may result in significant legal sanctions. They must be shipped in specific packaging, with appropriate hazard labels and forms. Hazardous materials shipping agents should be consulted to ensure proper packaging and labeling. Adequate time and planning must be allowed to ensure the anesthetic and oxygen will arrive when needed. Additional regulations apply to moving hazardous materials on other forms of public transportation (e.g., buses, trains, and ferries) and via transportation corridors such as tunnels and bridges. Empty oxygen cylinders are not classified as hazardous materials and may be transported on passenger aircraft. To avoid confusion and delay, empty oxygen tanks and their packaging should have all hazardous materials labels removed or covered. It is prudent to leave the valves of empty cylinders open during shipping to avoid partial re-pressurization due to temperature or air pressure changes, and to attach a large label stating "Empty" to the container.

Properly packaged and labeled isoflurane and other inhalant anesthetics can be shipped (as cargo) on an aircraft bearing passengers, but compressed oxygen cylinders can only be carried on purely cargo flights. In some cases it may be possible to transport isoflurane, but not compressed oxygen, to a field site because of the types of aircraft services available to the nearest staging area. If medical-grade oxygen cannot be shipped to a location, a large tank regulator can be fitted to a tank of welder's oxygen, which can often be found in remote villages and on commercial fishing boats. Alternatively, it is possible to drive an anesthetic vaporizer using compressed air. A small electric air compressor and a low-pressure, 22-L portable air tank, such as those used by house painters to power paint sprayers, can be shipped to the field as baggage without concern for hazardous material shipping regulations. Most field camps have small electrical generators for recharging batteries. The air tank is filled using the air compressor and then is connected to a flowmeter and thence to the vaporizer. The air pressure in the tank should not fall below 0.34 MPa (50 psi), limiting this technique to short duration procedures unless the compressor is run continuously. It is theoretically possible to fill the air tank using a hand-driven bicycle tire air pump, assuming sufficient enthusiasm for prolonged physical exertion. Specialized draw-over vaporizers, developed for military use, use ambient air and have been adapted for use in wild animals (Lewis 2004). With any inhalant anesthetic system that uses air, it is critical to provide adequate ventilation to ensure oxygenation.

Anesthesia to Prevent Nest Abandonment

Waterfowl are commonly captured while sitting on nests during laying or incubating eggs. These captures may be of short duration for the purposes of marking, measuring, or sampling. The stress of removing a sitting bird and the presence of humans when the bird is replaced on the nest causes a high rate of nest abandonment. Briefly anesthetizing gray partridges (*Perdix perdix*) and mallards being returned to the nests on which they had been captured almost eliminated nest abandonment (Rotella & Ratti 1990; Smith et al. 1980).

Despite widespread use, it is considered inappropriate and hazardous to use any inhalant anesthetic by pouring it onto cotton balls. In that technique, methoxyflurane is placed on cotton in a container at the nest site; the head of the bird is then placed into the container until muscle relaxation occurs. The bird is then placed on the nest with its head tucked under its wing and the researcher quickly withdraws. The bird is closely monitored to prevent anesthesia becoming too deep because no vaporizer is used. A light anesthetic depth is sufficient because the bird only needs to be obtunded for the length of time it takes to place it on the nest and withdraw. When methoxyflurane manufacture was discontinued in the 1990s some biologists switched to isoflurane delivered via cotton ball to birds being replaced on nests. However, the properties of isoflurane make it more hazardous than methoxyflurane to use for this purpose.

Propofol has recently been used to render birds unconscious to prevent nest abandonment (Hepp & Manlove 2001; Machin & Caulkett 2000). Propofol (10 mg/kg over

1 minute followed by additional 1–2 mg/kg boluses until induction) is delivered via a catheter in the medial metatarsal vein (Machin & Caulkett 2000).

Induction of wood ducks (*Aix sponsa*) with methoxyflurane averaged 5 minutes; although not stated it is presumed that wood ducks given propofol IV were immediately induced (Hepp & Manlove 2001). There was no significant difference in mean time to recovery for wood ducks anesthetized with methoxyflurane (11.8 ± 1.6 minutes) compared to propofol (9.2 ± 0.8 minutes) (Hepp & Manlove 2001). The disadvantage of using propofol is that the biologist must be able to deliver it into a vein at the nest site. An advantage of propofol is that it is not classified as a hazardous material for the purpose of shipping.

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22

Birds: Miscellaneous

Darryl Heard

Introduction

Although many of the major orders (groups) of birds warrant separate chapters (Chapters 15–21), many others are either uncommon in captivity or research. Consequently, there are few to no publications; this chapter covers the anesthesia of bird groups not specifically covered elsewhere. The range of physiologies and anatomies of birds across the living orders are very similar. Consequently, the anesthetic principles, regimens, and drug dosages described in the other avian chapters can be extrapolated to the birds of a similar size in this chapter.

Anatomy and Physiology

For those readers interested in a more detailed discussion of avian anatomy and physiology I recommend King and McLelland (1984) and Whittow (2000). The anatomy and physiology of birds relevant to anesthesia are summarized in Chapter 16. As mentioned, they are similar across avian orders due probably to the evolutionary constraints of flight. These include the needs to minimize weight (lightweight bone structure, rapid digestion, and assimilation of nutrients) while at the same time maximize cardiopulmonary and muscular function. The main differences between species are related to capture and prehension of food (e.g., beak shape and size), and life-style (aquatic, terrestrial, arboreal). For example, in one study (Mortola & Seguin 2009) the respiration rate in aquatic birds was lower (allometric equation 14.5 $W(kg)^{-0.56}$) compared to terrestrial species (13.4 $W^{-0.26}$).

All birds, except kiwis, have their nares at the base of the upper beak. The nares of toucans and related birds (Piciformes) are also in this position, but covered by feathers and the edge of the beak. Gannets, pelicans (Pelecaniformes), and some other diving birds have partially or fully occluded nares and breathe through a gap in the commissure of the beak (Fig. 22.1a) (King & McLelland 1984). Many species of marine as well as terrestrial birds from arid environments secrete salt through their nares from glands located within the head (Gerstberger & Gray 1993). The operculum in procellariiformes (albatrosses, petrels) is converted into a tube on the dorsal aspect of the bill (King & McLelland 1984).

The large beaks of hornbills (Coraciformes), toucans (Piciformes), storks (Ciconiiformes), and cranes (Gruiiformes) are lightweight, yet able to deliver powerful blows to kill small vertebrates, excavate tree cavities for nests, and defend themselves (Seki et al. 2010). Unfortunately, the beaks of these animals are easily damaged if too much side to side pressure is applied. The toco toucan (*Ramphastos toco*) possesses the largest beak relative to body size of all birds. It is able regulate heat distribution by modifying blood flow, using the bill as a transient thermal radiator (Tattersall et al. 2009) (Fig. 22.2a).

Cranes, similar to currasows and guans discussed in Chapter 29, possess long convolutes tracheas that may extend back into their sternum. This anatomy makes these species very susceptible to the adverse effects of fluid accumulation in the trachea. Pelicans possess subcutaneous air cells not connected to the respiratory system. These cells can expand during administration of nitrous oxide (Reynolds 1983).

Capture and Physical Restraint

The main defensive weapon of birds is the beak, although the sharp talons of some species can also cause pain and injury (Fig. 22.1b). When restrained, birds will often orient on the handler's eyes as a place to strike. This is because the eyes are constantly moving and attract the attention of the bird. Long-necked birds such as egrets, herons, cranes, loons,

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Figure 22.1 (a) The nares of brown pelicans (*Pelecanus occidentalis*) and other pelicans are partially occluded, making them predominantly mouth breathers. As in most birds, the nares are located at the base of the upper bill. (b) An aggressive American white pelican (*Pelecanus erythrorhynchos*) demonstrating the potential danger of the beak to handlers. Birds will orient on the human eyes to attack because they are constantly moving. The glottis is located deep within the caudal portion of the oropharynx and is very mobile. (c) The closed glottis of a brown pelican (*Pelecanus occidentalis*) deep in the caudal portion of the oropharynx. (d) The open glottis of a brown pelican (*Pelecanus occidentalis*). The cartilaginous septum in the larynx can be gently displaced by the tube for endotracheal intubation. Stabilization of the glottis from outside the pouch and a good light source will facilitate intubation. (e) An intubated pelican connected to a nonrebreathing system. A circle breathing system would also be appropriate for this size bird. The cuff of the endotracheal tube is not inflated to prevent damage to the tracheal mucosa. This bird was induced with propofol administered to effect into a catheter placed in the medial metatarsal vein.

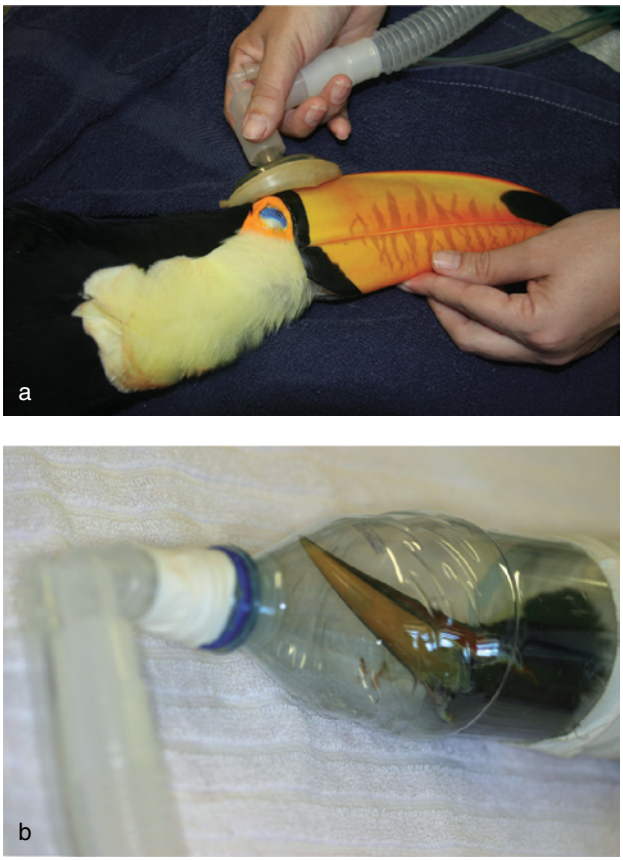


Figure 22.2 (a) Inhalant anesthetic induction of a toco toucan (*Ramphastos toco*) using a small human pediatric mask placed over the nares at the base of the bill and connected to a nonrebreathing system. (b) An aracari being induced using a mask made from a plastic bottle to accommodate the long beak.



Figure 22.3 A hospitalized sandhill crane (*Grus canadensis*) demonstrating the use of a purpose-made hood to keep the animal quiet. This can also be used during physical restraint and examination or for transportation.

and pelicans are particularly dangerous. Consequently, protective glasses are recommended when working with these species.

Restraint is similar for most bird species. For large species protective gloves may be worn. They, however, reduce the dexterity of the handler, and also may act as a fomite for pathogens if not properly cleaned. Towels are a useful alternative because they are more easily cleaned or discarded after use. They are perceived as a barrier by the birds and facilitate holding the wings and the legs at the same time. Covering the head and eyes will also calm many species (Fig. 22.3).

Regardless of size, care must always be taken to prevent inhibiting respiration when holding any bird. The breathing pattern is similar, yet different from mammals. For a bird to inhale the sternum must be able to move rostral and outward, along with the ribs.

Hyperthermia is common during restraint. This is exacerbated in birds adapted to cold environments. Prolonged muscle contraction including isometric, will produce heat, lactic acidemia, and hyperkalemia. Death may occur due to cardiac arrhythmia and muscle injury (capture myopathy or exertional rhabdomyolysis) (Burgdorf-Moisuk et al. 2012; Businga et al. 2007; Hanley et al. 2005; Marco et al. 2006; Ruder et al. 2012; Windingstad et al. 1983; Chapter 5). Physical restraint, whether it be using a towel or gloves, or tying the legs, will also potentially inhibit a bird's ability to dissipate heat. Dehydration and malnutrition exacerbate hyperthermia and muscle damage.

Conversely, care must be taken with cold-adapted species to not interfere with their adaptive thermoregulatory anatomy and physiology, for example anesthetic drugs may alter blood flow, affecting countercurrent heat-exchange. Disruption of their protective feather covering with alcohol or plucking to facilitate jugular blood collection and surgery can impair their ability to return immediately to a cold or aquatic environment.

Restraint devices have been designed to facilitate handling many avian species. These include body wraps and hoods with Velcro attachments (Fig. 22.3). As mentioned previously, care must be taken using these devices to ensure adequacy of breathing and thermoregulation. Many, but not all, species are quieter when their eyes and ears are covered, or they are maintained in a quiet darkened environment (Fig. 22.3).

Good-quality nets are essential regardless of a bird's ability to fly. Many can outrun humans and a long-handled net can be invaluable for capture. It is important to have a variety of small to large nets available.

Diurnal birds will often stay still in a dark environment and are unable to perceive red light. If a handler approaches slowly, deliberately, and directly at a bird they may stay still long enough to allow a close approach and then a grab by hand or with a towel.

Vascular Access

The main sites for blood collection in all avian species are the external jugular vein, the basilic vein, and the medial saphenous vein. As the species gets smaller, the main site is the jugular vein. The right jugular vein is usually the most developed. In some individuals, however, the left is most prominent. Even when the right is prominent the left will often be identifiable, but smaller. The ulnar (basilic) vein on the medial surface of the elbow can be used in large birds. It is problematic, however, because hemostasis is difficult and keeping the wing still to prevent accidental movement of the needle is difficult. The medial saphenous vein is useful for collecting blood from birds restrained by a handler in the upright position. In hornbills the jugular veins are often covered by extension of the air sacs, making accurate venipuncture difficult. This author consequently uses the medial saphenous vein for this group of birds.

Not all birds, especially aquatic and cold-adapted birds, have feather spaces (apterylae) over the jugular. In birds without apterylae the author wets the feathers over the jugular vein with alcohol and treats the feathers as the outer skin. Wetting the feathers down will often allow the occluded jugular vein to be identified. Alternatively, it can be palpated through the feathers.

In healthy birds 10% of the blood volume can be collected safely without any adverse effects. Since the blood volume is approximately 10% of the bodyweight (1 g = 1 mL) then 1% of the bodyweight can be collected. More athletic birds are able to tolerate greater blood loss than ground-dwelling species. Obese animals have proportionately smaller blood volumes, since fat has a relatively small blood supply.

Although not recommended in the living bird, blood can also be collected terminally or after death from the vertebral vessels, as well as the heart. To collect blood from the vertebral vessels the needle is placed as for a cerebrospinal fluid tap in a mammal. That is, the head is flexed ventrally and a 22–25-gauge needle is inserted into the space between the back of the skull and the atlas. A 1- or 3-mL syringe is then used to collect the blood. Cardiac puncture in most birds is made difficult by the complete sternum. A long needle must be introduced in the midline from the caudal or rostral aspect of the sternum.

Depending on the size of the bird, catheters for fluid administration can be placed in either the jugular or medial saphenous veins. Keeping a catheter in the jugular vein of an awake bird is not recommended because of the potential for hemorrhage if the bird struggles. Intraosseous catheters in either the proximal and distal ulna or the proximal tibiotarsal bones are alternatives to intravenous catheterization. In very small birds regular hypodermic needles can be used, but in spinal needles are recommended in larger birds. In pelicans the ulna and tibiotarsal bones are pneumatic and, therefore, contraindicated for intraosseous catheterization.

Endotracheal Intubation

Despite the extreme variation in tongues of some birds, the glottal opening is always at its base (Figs 22.1c,d and 22.4a,b). The jaws of flamingos do not open very far, inhibiting visualization of the glottis and placement of the endotracheal tube. The tube is either placed blindly by palpation or with the use of an endoscope. Some birds have septa at the glottal opening; these can be gently displaced to the side with the endotracheal tube (Fig. 22.1d). The glottis of pelecaniformes is located deep in the pouch and is very mobile (Fig. 22.1b–d). Outside manipulation may be necessary to keep it still to allow intubation. A good light source is necessary for the intubation of some species. A head lamp makes glottal visualization easier in some species.

Preanesthetic Considerations

Regurgitation or vomiting in the perianesthetic period must be prepared for in many avian species. Some birds will regurgitate as a defensive mechanism when handled (e.g., both New and Old World vultures). Fish-eating and fruit-eating birds seem particularly prone to regurgitation or reflux of stomach contents under anesthesia. Fasting is usually not an option in birds either because of the situation or the size of the bird. The smaller the bird the higher the metabolic rate and the more likely it will develop hypoglycemia. It is virtually impossible and not recommended to fast a bird to the point of no gastrointestinal



Figure 22.4 (a) The oral cavity of an aracari demonstrating the position of the glottis at the base of the thin tongue. (b) The oral cavity of a kookaburra (*Dacelo novaeguineae*) also showing the closed glottis at the base of the tongue.

contents. Water may be removed a couple hours before a procedure. When reflux is a concern, use a gauze roll placed past the glottis to prevent the liquid from entering the glottal area. The gauze is attached to tape that extends outside the bird's head so it is not forgotten at the end of the procedure.

The tracheal rings of birds are complete. Consequently, it is recommended cuffed endotracheal tubes not be used and the cuffs inflated. This is because of the greater potential for tracheal mucosal damage. Trauma also occurs from the tip of endotracheal tube. The trachea of most birds also narrows from the glottis. If a large tube is jammed into the trachea, mucosal damage will occur. Head and neck movements exacerbate this trauma during anesthesia.

Analgesia

Analgesia is described in detail in Chapters 2 and 16. Nonsteroidal anti-inflammatory drugs are highly variable in their effects and ability to cause injury across avian species. Great care must therefore be taken in drug and dosage selection. Birds appear to respond predominantly to κ-opioid agonists, but there are some studies indicating μ opioids may produce analgesia in some species (Chapter 16). Tramadol is an alternative for use postoperatively in avian species. The judicial use of local anesthetics and blocks can also be a valuable part of a multimodal analgesia plan.

Induction/Maintenance Protocols

Parenteral anesthetic regimens and response to drugs are similar across all birds and are described in Chapters 15–21. Ketamine alone is not recommended because of poor muscle relaxation. Consequently, parenteral anesthetic regimens based around this drug usually include either a benzodiazepine (diazepam, midazolam) or an alpha-2 adrenergic agonist (xylazine, detomidine, medetomidine, dexmedetomidine). Unfortunately birds seem to be very resistant to the effects of the latter drugs, requiring dosages much higher than in mammals of a similar size.

Propofol and alfaxolone can be used in all species of birds when vascular access is available, but they do produce dose and administration rate-dependent cardiopulmonary depression. Although alfaxalone can be given intramuscularly, the large injection volume of drug required in anything but the smallest of birds is inhumane. To decrease the volume of alfaxalone injected it can be used as part of a combination of anesthetic drugs and analgesics.

All birds can be induced and maintained with an inhalant anesthetic. For some species, however, mask induction is problematic. In birds with long or large beaks commercially available masks do not extend to cover the nares at the base of the beak. In these species masks can be made from water bottles or a plastic bag (Fig. 22.2b). Alternatively, a small mask can be placed over the nares (Fig. 22.2a). Some species of birds do not have patent nares, but rather breathe around the side of the mouth (Fig. 22.1a). It is important to ensure the nares are patent in obligate nasal breathers when using a mask that closes the beak.

Monitoring

Mortality during anesthesia appears higher for birds than mammals. Monitoring is therefore very important in preventing injury and death. One person should always be dedicated to monitoring during the perianesthetic period. Clear surgical drapes facilitate visualization of respiration and auscultation of small patients during surgery. Redundancy in monitoring when possible is also important, for example the use of both a Doppler flow detection device and an esophageal stethoscope to monitor heart rate.

Anesthetic depth is determined using basic reflexes and responses: muscle and cloacal tone, pupil size, palpebral and corneal response, toe pinch, response to surgical incision, feather plucking, heart rate etc. Interestingly, birds appear more likely to respond to feather plucking than a skin incision. This may be related to the clustering of nociceptors and mechanoreceptors around the feather follicles. Palpebral response is usually absent at light surgical planes of anesthesia. Sudden pilo-erection under anesthesia can be an indication of cardiac arrest rather than decreased anesthetic depth.

Hypothermia is common in anesthetized birds and temperature monitoring is essential. Unfortunately, cloacal may not accurately reflect core body temperature. Forced air warmers are preferred for maintaining normothermia in anesthetized birds (Rembert et al. 2001).

Heart rate is monitored by palpation or placement of a Doppler flow probe on a peripheral artery (metatarsal, ulnar), auscultation of the heart (stethoscope, including esophageal), pulse oximeter or by electrocardiography. Positional maintenance of the Doppler flow probe is sometimes difficult. A soft clamp can be constructed from two tongue depressors and used to keep the probe in place over the ulna artery. Alternatively, in large birds the flow probe can be placed in the oropharynx or esophagus and directed at the major arteries ventral to the neck vertebra. Pulse oximetry is inaccurate and unreliable in birds. Capnography can be used to monitor respiration, but is also inaccurate for the reasons discussed in Chapter 15.

Recovery Considerations

The recovery period is a critical period for anesthetized avian patients and a common time for mortality. This may be related to the physiologic instability associated with transitioning from an anesthetized to an awake animal. For example, as a hypothermic bird becomes warmer, peripheral vessels dilate and metabolic rate increases. The former may unmask hypovolemia and hypotension, leading to decreased cardiac output. Increased metabolic rate increases glucose and oxygen use, exacerbating or precipitating hypoglycemia and hypoxemia, respectively.

Field Immobilization (Wild Capture)

Physical capture of most birds is well described by Bub (1991). The main issues when working with free-living birds is injury due to struggling, hyperthermia, and exertional rhabdomyolysis (capture myopathy) (Burgdorf-Moisuk et al. 2012; Businga et al. 2007; Hanley et al. 2005; Marco et al. 2006; Ruder et al. 2012; Windingstad et al. 1983; Chapter 5). Restraint and anesthesia time should be minimized by planning and preparation, and rapid processing. When birds are to be kept for periods of time care must be taken to use appropriately designed crates or holding structures appropriate to the species.

Intranasal midazolam (0.5–2.0 mg/kg) administration may be a rapid way to provide sedation in wild birds (Ward et al. 2011). It can be reversed with flumazenil. Propofol or alfaxalone can be used for short-term immobilization, as well as maintenance of anesthesia (Fig. 22.5a,b). Neither drug provides good analgesia and other drugs must be added to the anesthetic regimen when painful procedures are planned. As with all avian anesthesias, respiratory support must be provided. Inhalation anesthesia can also be used for induction and maintenance. Administration of the inhalant anesthetic is preferably done using a precision vaporizer. The use of isoflurane without a vaporizer is not recommended because of the potential for anesthetic overdosage.



Figure 22.5 (a) Intravenous administration of propofol into the medial metatarsal vein of a purple swamp hen (*Porhyrio porphyrio*). (b) A purple swamp hen (*Porhyrio porphyrio*) anesthetized with propofol for surgical implantation of a radiotransmitter. The mid-line surgical site was infiltrated with a combination of lidocaine and bupivacaine. Meloxicam was also administered for additional analgesia. Note the use of a flexible esophageal thermometer (white line) and esophageal stethoscope for monitoring. The bird is intubated and ventilated four to six times a minute using an Ambu bag.

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23

Mice, Rats, Guinea Pigs, Gerbils, Hamsters, Chinchillas, and Other Rodents

Darryl Heard

Introduction

Rather than a comprehensive review, the objective of this chapter is to provide the necessary information to safely anesthetize the most common pet rodents seen in veterinary clinical practice. Since many of these species are also used in research there is a plethora of papers describing anesthesia. Care, however, must be taken when extrapolating research anesthesia to the clinical setting. Research animals are often young and more physiologically resilient to the adverse effects of some drugs and combinations. Furthermore, the goals of research anesthesia may not be a rapid recovery, but rather to have a relaxed, pain–free anesthetic combination that provides prolonged unconsciousness and not necessarily recovery. Similarly, drug combinations and dosages obtained from formularies that collate information from these research papers must be critically evaluated before use in the clinical setting.

The order Rodentia includes the most living mammalian species (2277 or more; Wilson & Reeder 2005). Common pets include the house mouse (*Mus musculus*), rat (*Rattus norvegicus*), chinchilla (*Chinchilla laniger*), golden (*Mesocricetus auratus*) and Siberian (*Phodopus sungorus*) hamsters, guinea pig (*Cavia porcellus*), and Mongolian gerbil (*Meriones unguiculatus*).

Although usually small (≤200 g), several are very large (e.g., marmots, *Marmota*; giant squirrels, *Ratufa*; pacas, *Agouti*; maras, *Dolichotis*; capybara, *Hydrochaeris hydrochaeris*; beaver, *Castor*; and porcupines, *Hystrix*). Rodents have four incisors, no canines, and there is a gap between the incisors and the cheek teeth (Nowak 1999). Some have cheek pouches, internal or external, that open near the angle of the mouth (Nowak 1999). During anesthesia these pouches can be a source of aspirated food material.

Consequences of Small Body Size

Schmidt-Nielsen (1984) describes the relationship between body size and vertebrate physiology. As small animals, rodents have high metabolic and oxygen consumption rates and therefore low tolerance to even brief hypoxemia. Irreversible central nervous system injury occurs within ≤30 seconds of respiratory arrest. Increased oxygen uptake requires increased alveolar ventilation, resulting in more rapid inhalant anesthetic uptake and excretion. High metabolic rates increase the speed of elimination of parenteral drugs. In herbivores this is enhanced by adaptations for detoxification of chemicals in their food. Consequently, drugs generally have shorter duration of effect than in larger mammals and require higher dosages.

High metabolic rates and small glycogen reserves predispose to hypoglycemia. A small body has a large surface area to volume ratio and usually higher temperature. Convective heat loss is rapid and hypothermia assured unless supplemental heat is provided. Loss of even small amounts of blood may lead to hemorrhagic shock and death. Airway resistance is inversely related to radius^4; slight changes in diameter (e.g., from edema and mucous accumulation) will have a dramatic effect on respiratory work.

Zoonotic Diseases

Many species harbor pathogens that infect humans (Padovan 2006), for example deer mice (*Peromyscus maniculatus*) are the reservoir for the virus that causes hantavirus pulmonary syndrome in people in the south-western United States (Elliott et al. 1994). *Giardia* spp. are present in beavers (*Castor* spp.) and capybaras (Thompson 2004). Handling rodents awake is minimized to prevent bites and

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scratches. The use of physical barriers (i.e., gloves, breathing masks, and biological hazard suits) is based on the predetermined risk, the species, and the procedure.

Physical Restraint

All rodents bite, including many kept as pets. In an animal of unknown temperament, inhalant anesthesia is an acceptable alternative for physical examination. Care is taken with small rodents to avoid physical restraint in place of adequate analgesia and anesthesia. Large rodents are restrained in squeeze cages or remotely injected for drug administration.

Pet rodents can often be gently picked up in the palm of the hand. Guinea pigs and similar sized rodents are supported under the rump while being held (Fig. 23.1). Some rodents may be grasped at the tail base for transfer from cage to cage. This technique, however, is avoided in animals that shed their tails in response to a threat (e.g., spiny mice, *Acomys* spp.) or are able to turn and bite (Nowak 1999).

Grasping the nape is used to restrain some small rodents. Hamsters and others with loose skin require a very tight grasp to prevent them turning and biting (Fig. 23.2). Small to medium-sized rodents are restrained with a hand around the neck and the thumb positioned under the jaw to prevent biting. In laboratory animal facilities mice and other small rodents can be transferred from cage to cage using soft forceps. This technique is also used for small free-living rodents caught in traps. Leather or chainmail gloves can be used to handle aggressive rodents, but they limit feel and the former do not protect against a direct bite.



Figure 23.1 Tame rodents such as this guinea pig can be held, but should be supported below the rump.



Figure 23.2 Some rodents (e.g., Siberian hamsters) can be restrained by grasping the skin at the nape of the neck. Sufficient skin, however, must be grasped to prevent the animal turning and biting the handler.

Porcupines offer a unique challenge. Although they do not "shoot" their sharp quills they will back rapidly and with great force into a threat. The quills of New World porcupines have barbs that make their removal very difficult. Additionally, the quills of porcupines may be covered in potentially pathogenic bacteria. They also make remote injection difficult. The author uses a purpose-built restraint box to allow drug injection into the leg muscles of Southern African crested porcupines (*Hystrix africaeaustralis*) (Fig. 23.3). The metal box has one side of wire with spaces sufficient to allow legs to drop through when the cage is turned. A leg is then grabbed and injected with a parenteral anesthetic. This porcupine species, however, has skin that tears very easily.

Preanesthetic Preparation

Rodents are primary or obligate nasal breathers and upper respiratory disease is common (e.g., pseudo-odontoma in prairie dogs, mycoplasmosis/respiratory complex in rats). The nares are assessed for patency before induction with an inhalant anesthetic and mask. This author does not routinely remove food or water prior to anesthesia. Fasting exhausts glycogen stores. It may also contribute to ileus and pregnancy ketosis in guinea pigs and other herbivores.



Figure 23.3 A restraint cage for Southern African crested porcupines. The cage is metal to prevent the animal chewing. One side has large openings that cause the legs to fall through when the cage is turned. This allows an unprotected leg to be grasped and injected with immobilization drugs. Care must be taken in this species to prevent skin tearing.

Premedication

Recommended dosages are given in Table 23.1. In rats, atropine sulfate (0.05 mg/kg) and glycopyrrolate (0.5 mg/kg) increased heart rate for 30 and 240 minutes, respectively (Olson 1994). Although both reduce bradycardia in rodents anesthetized with ketamine/alpha-2 adrenergic agonist combinations, glycopyrrolate is more effective in maintaining heart rate within normal range (Olson 1994). Neither glycopyrrolate nor atropine influence respiration rate, core body temperature or systolic blood pressure alone or combined with injectable anesthetics.

Benzodiazepines provide good sedation and relaxation and are useful for induction of debilitated patients because of their minimal cardiopulmonary effects. Xylazine, medetomidine or dexmedetomidine are combined with ketamine to improve muscle relaxation, analgesia, and duration of effect. However, they produce respiratory depression and bradycardia. Interestingly, midazolam may ameliorate the adverse cardiovascular effects of dexmedetomidine in rats (Cornelis et al. 2000). Alpha-2 adrenergic agonists are reversed with yohimbine, tolazoline or atipamezole. Tolazoline (10–50 mg/kg), when compared to yohimbine (1 mg/kg), appeared most effective and safe for the reversal of xylazine/ketamine anesthesia in rats (Komulainen & Olson 1991). In rats, yohimbine (20 mg/kg IP) produced a high (22%) mortality.

Analgesia

The principles and techniques for rodent analgesia are reviewed in Chapter 2, and by Robertson (2001) and Flecknell (2018). The two main groups of analgesic premedicants, opioids and nonsteroidal anti-inflammatory drugs (NSAIDS), are combined or used alone. Even low-dosage ketamine provides analgesia and for this reason is worthwhile including in some anesthetic regimens (Robertson 2001). Local and regional anesthesia (see below) also have the potential to further enhance analgesia. Tramadol is an additional analgesic that can be used in the perianesthetic period, but only oral or compounded formulations are available in North America. Effective drug dosages are still to be determined for many species. Recommended dosages for analgesics are given in Table 23.2.

Local and Regional Anesthesia

Many large captive species (e.g., guinea pigs) are amenable to local and epidural anesthesia for minor and occasionally major (e.g., caesarian section) procedures, respectively

Table 23.1 Drugs used for premedication in rodents.

Drug	Rat	Mouse	Gerbil	Hamster	Guinea pig, Chinchilla, Prairie Dog	Beaver, Capybara, Porcupine
Acepromazine	0.5–2.5 IM IP	0.5–2.5 IP	Not recommended	0.5–2.5 IM IP	0.5–2.5 IM	0.1 IM
Diazepam	3–5 IP PO	3–5 IM IP PO	3–5 IP PO	3–5 IP PO	1–2.5 IM IP PO	0.1–1.0 IM PO
Midazolam	1–2 IP	1–2 IM IP	1–2 IP	1–2 IP	1–2 IM IP	0.1–0.5 IM
Xylazine	10–15 IP	10–15 IP	5–10 IP	5–10 IP	5–10 IP SC	1–5 IM SC
Atropine	0.05 SC IM	0.05 SC IM	0.05 SC IM	0.05 SC IM	0.05 SC IM	0.03 SC IM
Glycopyrrolate	0.01–0.02 SC IM	0.01–0.02 SC IM	0.01–0.02 SC IM	0.01–0.02 SC IM	0.01–0.02 SC IM	0.01 SC IM

IM, intramuscular; IP, intraperitoneal; PO, per os; SC, subcutaneous.
Use lower dosages for debilitated, geriatric, or obese animals and for those that are relatively large for the species. Acepromazine is not recommended for use in gerbils because it may lower the seizure threshold.
Source: Flecknell (1991) and Mason (1997). Doses are based on mg/kg basis.

Table 23.2 Suggested analgesic dosages (mg/kg) for rodents.

Analgesic	Rat	Mouse, Gerbil, Hamster	Chinchilla, Guinea pig, Prairie dog	Beaver, Capybara, Porcupine
Buprenorphine	0.03–0.05 SC q8–12h 0.5–0.6 orally	0.1–0.2 SC q6–12h	0.05 IM, SC q6–12h	0.01–0.03 IM, SC q8–12h
Buprenorphine SR (current US slow –release formulation)	1.2 SC	0.6 SC	0.3–0.48 SC	
Butorphanol	2 SC q2–4h	1–5 SC q4h	2 IM, SC q4h	0.5 IM, SC q4h
Carprofen	5 SC, PO q24h	20 SC q12h	4 IM, SC q24h	
Ketoprofen	5 SC, PO q24h	20 SC		1–3 IM, SC q24h
Meloxicam	1 SC, PO q24h	5–20 SC PO q12h	0.2 SC, PO q12–24h	0.1–0.3 SC, PO q12–24h
Morphine	2–5 SC q4h	2–5 SC q4h	2–5 IM, SC q4h	1–3 IM, SC q4–6h
Tramadol	20–40 orally q12–24h 5 SC	80 SC	2–5 PO 12–24h	0.5–5 PO once or twice a day

IM, intramuscular; PO, per os; q2–4h, ; SC, subcutaneous.
Source: Flecknell (1991, 2001, 2018), Foley et al. (2019), and Mason (1997).

(Eisele et al. 1994). Most local anesthetics have a low therapeutic index (particularly the long-acting drugs such as bupivicaine) and commercial preparations usually contain drug concentrations suitable for humans. Consequently, great care must be taken to calculate and prepare appropriate volumes of local anesthetic for infiltration.

Parenteral Anesthesia

Small to medium-sized rodents are preferably induced and maintained with an inhalant anesthetic (see below). Parenteral anesthetic regimens are used where inhalant anesthesia is not available (e.g., for field immobilizations), to reduce inhalant anesthetic pollution, to enhance analgesia, to facilitate mask induction with an inhalant, and for convenience in research facilities. Representative parenteral anesthetic regimens and dosages are described in Table 23.3.

Drug Administration

Injection routes include subcutaneous (SC), intramuscular (IM), intraperitoneal (IP), intravenous (IV), and intraosseous (IO). In some species, intranasal administration of midazolam and other nonirritating drugs may be appropriate. Potentially irritant solutions (e.g., high or low pH solutions) should not be administered SC or IM because of the risk of self-mutilation (Gaertner et al. 1987; Leash et al. 1973). Diluting the solution, avoiding large volume injections, and injecting in the proximal muscles of the legs reduce the risk of developing this adverse effect. Alternatively, drugs are administered by IP injection. Large rodents are enclosed in squeeze cages (Fig. 23.3) or administered drugs using a remote injection system.

Vascular Access

Small size makes venous and intraosseous catheterization difficult, but practice and attention to technique enable attainment of these essential skills. Potential catheterization sites include the cephalic, saphenous, and auricular veins. The lateral coccygeal veins can be accessed in rats with small gauge needles. Penetration of the skin before placement, with either a hypodermic needle or scalpel blade, is done to prevent catheter buckling. Intraosseous catheterization using 18–22-gauge spinal needles can be performed at the proximal femur (via the trochanteric fossa), tibia (tibial crest), and humerus.

Venipuncture and Blood Collection

Depending on size and species, blood samples can be collected in clinical cases from the jugular, cephalic, saphenous (Hem et al. 1998), femoral, perineal (agoutis and related species), and lateral coccygeal veins. The cranial vena cava, femoral artery, and ventral coccygeal vessels are alternative sites in some species. The heart and retro-bulbar sinus are used in research species, but are not recommended for clinical patients.

For collection of blood from the saphenous vein the rodent can be placed head first into a plastic tube for restraint (Hem et al. 1998). The hair over the proximal tarsus is gently clipped to allow visualization of the vessel and microhematocrit tubes are used to collect blood from small rodents (Hem et al. 1998).

Table 23.3 Parenteral anesthetic regimens and dosages (mg/kg) for representative rodents.

Species	Ketamine/acepromazine	Ketamine/xylazine	Ketamine/medetomidine	Ketamine/midazolam	Tiletamine/zolazepam	Propofol
Mouse	50–150/2.5–5.0 IP	50–200/5–10 IP		40–150/3–5 IP	50–80 IP	NA
Hamster	50–150/2.5–5.0 IP	50–150/5–10 IP		50–150/5 IP	50–80 IP	NA
Gerbil	NA	50–70/2–3 IP		40–150/3–5 IP	50–80 IP	NA
Rat	50–150/2.5–5.0 IP IV	40–90/5 IP		40–100/3–5 IP IV	50–80 IP IV	10 IV
Guinea pig, Chinchilla	20–50/0.5–1.0 IP IV	20–40/3–5 IP IV	5/0.06 IM (Henke et al., 2004)	20–50/3–5 IP IV	20–40 IP IV	10 IV
Beaver, capybara, porcupine		5–10/1–2 IM	3–4/0.03–0.04 IM IV		4–6 IM IV	6–8 IV

IM, intramuscular; IP, intraperitoneal; IV, intravenous; NA, not applicable.
Source: Adapted, in part, from Flecknell (1991), Henke et al. (2004) and Mason (1997). Use the lower dosages for debilitated animals and for IV injection.

The restraint tube can also be used to facilitate blood collection from lateral coccygeal veins in rats. The major problem with the use of these vessels is ensuring an adequate blood flow (Conybeare et al. 1988). One technique briefly warms the tail by immersion in a water bath (up to 45°C). This causes local vasodilation. Prolonged vasodilatation can be achieved by using a heating lamp placed above the rodent cage, but a major disadvantage is the lack of temperature control and the danger of burns. Instead, controlled warming of the total environment of the rat or mouse to temperatures around 40°C induces increased blood flow through the tail, making it possible to collect blood from the lateral coccygeal (caudal) vein (Conybeare et al. 1988).

Parenteral Anesthetics

Some rodents (e.g., guinea pigs) have limb movement at ketamine or tiletamine/zolazepam dosages expected to produce surgical anesthesia. Ketamine (44 mg/kg) takes 8–10 minutes for induction and has a very short duration of effect (15–20 minutes) (Weisbroth & Fudens 1972). Ketamine and ketamine/xylazine may be associated with self-mutilation (Gaertner et al. 1987).

Xylazine and other alpha-2 adrenergic agonists are frequently combined with ketamine for short-term immobilization and surgical anesthesia. These combinations, however, produce mild to severe dose-dependent hypotension, bradyarrhythmias, and respiratory depression (Hart et al. 1984; Wixson et al. 1987). Oxygen supplementation and assisted ventilation are recommended. Ketamine/benzodiazepine combinations produce less cardiopulmonary depression and analgesia, but good muscle relaxation.

In rats and mice acute reversible lens opacity has been observed with xylazine and xylazine/ketamine (Calderone et al. 1986). These "cataracts" were associated to a varying degree with proptosis, obtunded blink response, corneal surface drying, and mydriasis. Reversible lens opacity due to dehydration has been observed by this author in some rodents (e.g., young squirrels).

Although moderately effective for minor surgery in rats and gerbils, very high tiletamine/zolazepam dosages are required to prevent response to noxious stimuli in other species (i.e., mice, hamsters, and guinea pigs) (Silverman et al. 1983).

Propofol is used for induction and maintenance of anesthesia when administered as a continuous IV infusion or intermittent bolus. The propofol can be diluted with saline for injection in very small patients. Apnea is related to dose, rate of injection, and the presence of other drugs. The induction dose is dependent on the rate of administration (Larsson & Wahlstrőm 1994). In rats, both fast (20 mg/kg/min) and slow (2.5 mg/kg/min) rates result in larger doses than those at an intermediate rate (10 mg/kg/min). Propofol is a poor analgesic. It is indicated for induction of healthy rodents in which vascular access can be attained.

Alfaxalone is a potent steroid hypnotic agent whose poor water solubility prompted the development of a 2-hydroxypropyl-β-cyclodextrin (HPβCD) formulation. It is similar to propofol, but can also be given intramuscularly. Subcutaneous administration may be preferable to intramuscular injection, especially with larger volumes. This author uses alfaxalone as part of a combination rather than alone for sedation or induction (Table 23.4). The cardiopulmonary effects are the same as propofol, and induction dosages may result in apnea, even when given intramuscularly or subcutaneously. Alfaxalone produces sedation to unconsciousness, but no analgesia. It should not be used alone for invasive or surgical procedures.

Table 23.4 Alfaxalone regimens and dosages (mg/kg) for representative rodents.

Species	Alfaxalone	Alfaxalone/ dexmedetomidine	Alfaxalone/midazolam	Alfaxalone/ ketamine	Alfaxalone/ dexmedetomidine/ buprenorphine	Alfaxalone/ ketamine/ midazolam	Alfaxalone/ ketamine/ dexmedetomidine	Alfaxalone/ butorphanol	Alfaxalone/ butorphanol/ midazolam
Rat (*Rattus norvegicus*)	20 IP for sedation More variable duration and depth in males (West et al. 2020)	30/0.05 IP for surgical anesthesia in females Males showed shorter and more variable anesthesia (West et al. 2020) Atipamezole IP at 60 minutes after induction							
Chinchilla (*Chinchilla lanigera*)								5/0.5 IM Rapid induction of short-term variable sedation (Parkinson & Mans 2017)	
Guinea pig (*Cavia porcellus*)	5 IM Moderate sedation for 30 minutes for noninvasive procedures (Alvarez et al. 2022; d'Ovidio et al. 2018) Bruxism, hectic movements, twitching, and some degree of hyperreactivity 20 mg/kg SC induction 6.8–8 minutes, recumbency 50–90 minutes, retained pedal withdrawl, bruxism, and twitching in some animals (Doerning et al. 2018)		5/0.5 SC Provided more profound sedation than alfaxalone Adequate for nonpainful, noninvasive procedures. Bruxism, hectic movements, twitching, and some degree of hyperreactivity (Alvarez et al. 2022)		15–20/0.25/0.05 SC Dexmedetomidine reversed at 90 minutes with atipamezole 0.025 SC Addition of dexmedetomidine/ buprenorphine increased duration of sedation and immobility, but no general anesthesia (Doerning et al. 2018) One death				
Naked mole rats (Esher et al. 2019) (*Heterocephalus glaber*)				20/4 IM Induction smooth and rapid with males taking longer than females Moderate sedation (Ambar et al. 2020)			2/20/0.02 IM thigh Rapid induction, profound immobilization, atipamezole (1 IM) reversal at 40 minutes after induction		2/2/1 IM thigh Slow induction to moderate sedation Reversal with flumazenil (0.1 IM) at 40 minutes after induction

Five-striped palm squirrels (*Funambulus pennantii*)	6/40 IM rapid induction, recovery in ~60 minutes (Eshar & Beaufrere 2020) Twitching and abnormal vocalizations during recovery Oxygen and thermal support recommended		6/20/0.1 IM Rapid induction, partial reversal with atipamezole (0.15 IM) at 40 minutes after induction (Eshar & Beaufrere 2020) Oxygen and thermal support recommended	8/1/1 IM Rapid induction, partial reversal with flumazenil (0.1 IM) at 40 minutes after induction (Eshar & Beaufrere 2020) Oxygen and thermal support recommended
Black-tailed prairie dog (*Cynomys ludovicianus*		6/30/0.15 IM Rapid induction with reversal at 45 minutes with atipamezole 1.5 Deep anesthetic plane associated with hypothermia, bradycardia, hypotension, and suspected hypoxemia/ hypercapnia (Hiebert et al. 2022)	6/30/0.15 Rapid induction with reversal at 45 minutes with atipamezole 1.5 Deep anesthetic plane associated with hypothermia, bradycardia, hypotension, and suspected hypoxemia/ hypercapnia (Hiebert et al. 2022)	

Use the lower dosages for debilitated animals and for intravenous injection. IM, intramuscular; IP, intraperitoneal; SC, subcutaneous.

Alfaxalone is more readily eliminated from males than females due to differential clearance (Brewster et al. 1996). This can result in faster recovery for males. In rats alfaxalone (10 mg/kg IP) was not analgesic and did not potentiate the antinocioception of opioids (Winter et al. 2003).

Inhalation Anesthesia

Inhalation anesthesia is the primary component of most, if not all, clinical anesthetic regimens.

Inhalant Anesthetics

Isoflurane is associated with rapid induction and recovery, and rapid control of anesthetic depth. It produces a dose-dependent cardiopulmonary depression, does not sensitize the myocardium to catecholamine-induced arrhythmias, and is a poor analgesic (Imai et al. 1999). Sevoflurane is similar to isoflurane, except it produces even more rapid induction and recovery. The decision whether to use sevoflurane rather than isoflurane is usually related to cost.

Inhalant Induction

For induction, inhalant anesthesia is used alone or as an adjunct to parenteral drugs. The anesthetic is administered into a chamber or through a mask. The advantage of an induction chamber is the animal is not manually restrained during the involuntary excitement phase of induction. This reduces injury to handler and patient. The disadvantages include greater potential for environmental contamination with inhalation anesthetic and difficulty in monitoring.

Mask induction of manually restrained animals, without premedication and supplemental injectable anesthesia, is not recommended. Anesthetic chambers and masks are opaque to allow visualization of the patient. Chambers can be made from commercial plastic containers and sized to the animal (Fig. 23.4). The chamber top should be able to be secured to prevent the animal forcibly opening it and escaping. For induction of an awake or lightly sedated animal, inhalant anesthetic is introduced into the container through one opening and waste gas removed from another opening. The vaporizer is set at maximum concentration, and oxygen flow rate is set at 2–4 L/min depending on the size of the container. It will take a period of time for the concentration in the induction chamber to equilibrate with the vaporizer setting. The animal loses its righting response in 5–10 minutes and is removed from the chamber. A mask is placed over its nose and mouth, and the chamber is removed outside or closed to allow waste gases to be safely voided to the atmosphere. The animal is then either maintained using the mask or intubated when it is sufficiently relaxed.



Figure 23.4 Small to medium-sized rodents (e.g., agouti) can be induced with inhalant anesthetics administered into a chamber. These induction chambers can be made from commercially available plastic boxes that should be opaque and have a secure top.

When maintaining anesthesia with a mask, it is important to have the animal's head and neck in extension to facilitate air movement. Respiratory pattern, rate, and noise should also be assessed to ensure minimum resistance to breathing. If the animal appears to be having respiratory difficulty, move the head and neck to see whether the obstruction can be corrected. If not, use cotton-tipped applicators to clear the oropharynx and nares. If this fails to relieve the problem, intubate or wake the animal and cancel the procedure.

Equipment

Small size is an indication for a nonrebreathing system for administration of inhalant anesthetics. T-piece breathing systems are recommended for the smallest. Rebreathing bags can be constructed from small balloons to facilitate visualization of respiratory movement. Fresh gas flow rate for nonrebreathing systems is about 200 mL/kg/min.

Inhalation anesthesia is often maintained with a mask connected to the breathing system. Systems have been developed for small rodents that also allow concurrent scavenging of waste anesthetic gases (Levy et al. 1980; Mauderly 1975). These usually include the fresh gas line entering the mask and an exit line for removal of waste gases.

Endotracheal Intubation

Respiratory obstruction and hypoventilation are common limitations to diagnostic and surgical procedures. With practice and the use of appropriate technique and equipment, intubation should be a routine standard of care in some rodents.

There are a variety of commercially available endotracheal tubes; the smallest cuffed and uncuffed tubes have 3- and 1-mm internal diameters, respectively. Guidelines for endotracheal tube size are given in Table 23.5. Endotracheal tubes are preferably opaque for visualization of condensation or occlusion with mucous or blood. For the smallest patients, endotracheal tubes are constructed from over-the-needle catheters or urinary catheters.

Guinea pigs present many obstacles to routine intubation. Their cheek pouches frequently contain stored food and they readily regurgitate if the oropharynx is stimulated. They produce profuse salivary secretions that can be controlled, in part, by glycopyrrolate. The soft tissue at the base of the tongue is readily traumatized by a laryngoscope blade, resulting in profuse hemorrhage. The soft palate is fused to the base of the tongue, and entry to the glottis is through the small opening of the palatal ostium (Timm et al. 1987). The palatal ostium is also present in chinchillas and capybaras, and probably other hystericomorph rodents. The glottis is also very small relative to the size of the animal. This author has had success using a blind technique in some animals, but more recently has routinely used a 1.9-mm semiflexible straight scope to place a 2-mm internal diameter uncuffed endotracheal tube. Washing the mouth before anesthesia removes any food material and facilitates visualization of the glottis. Another author (Kujime & Natelson 1981) describes intubation of dorsally recumbent guinea pigs using direct visualization techniques with modified pediatric #0 blades and 14-gauge over-the-needle catheters.

Table 23.5 Guidelines for endotracheal tube size selection in rodents.

Species	Endotracheal Tube Size
Rat	16–18-gauge over-the-needle catheter
Guinea pig, chinchilla	14–16-gauge over-the-needle catheter, ≤2 mm ID
Hamster	16-gauge over-the-needle catheter
Eastern gray squirrel	≤2 mm ID
Prairie dog	2.0–2.5 mm ID
Capybara	6.0 mm ID

ID, internal diameter.

Rat intubation usually involves direct visualization of the glottis. It requires magnification and a focused light source (e.g., rigid endoscope). One technique describes transillumination with a high intensity light source in contact with the skin surface in front of the neck near the pharyngoepiglottic region (Yasaki & Dyck 1991). This author uses a rigid endoscope or an otoscope attached to a #2 ear speculum that has had the distal two-thirds of the tip along the right side removed (Tran & Lawson 1986). The rat is positioned in dorsal recumbency on a board. An elastic band is then affixed to the upper incisors and fastened to the board to extend the head and neck. The tongue is pulled forward and to the side, and a cotton-tipped applicator is used to clear any secretions from around the glottis. Topical application of local anesthetic on the glottis will reduce laryngospasm. A slight pressure exerted on the ventral surface of the neck may further facilitate visualization of the glottis. A blind technique, similar to that described above for other rodents, has also been reported (Stark et al. 1981).

Endotracheal tubes for rats are constructed from 14–16-gauge over-the-needle catheters. The needle stylette is cut to the same length as the catheter, and the end is then filed smooth so that the smoothed needle is approximately 1 mm shorter than the catheter (Stark et al. 1981). Alternatively, a 70-mm length of malleable 20-gauge wire is used as a stylette (Tran & Lawson 1986). At 1.5 cm from the end of the catheter, the stylette is bent at a 30° angle. A surgical suture can be tied to the catheter at a point 4.5 cm from its end to prevent excessive insertion of the catheter into the trachea. Mucous obstruction is common and changing the tube may be necessary. This technique can also be used for hamsters.

Prairie dogs, chinchillas, squirrels, and other medium to moderately large rodents (e.g., African pouched rats, maras) can routinely be intubated for inhalation anesthesia using a blind technique. The anesthetized rodent is laid in lateral recumbency, with the head and neck moderately extended. The tube is then passed in a similar manner to that described for the rabbit (Chapter 25). Alternatively, an endotracheal tube can be placed with the assistance of an endoscope. The tube is placed over the scope or alongside it (Figs 23.5 and 23.6).

When in doubt remove the endotracheal tube and reassess placement. The use of a pulse oximeter is invaluable for determining potential oxygenation problems due to airway obstruction. Correct endotracheal tube placement is determined by (1) visualizing condensation on either the inside of the endotracheal tube or a metal surface placed at the end of the tube; (2) detecting air movement with hair placed in front of the tube; (3) watching the nonrebreathing bag; (4) the response to intubation (coughing etc.); and (5) the detection of exhaled carbon dioxide on a capnograph. To ensure the tube has not been placed into a single

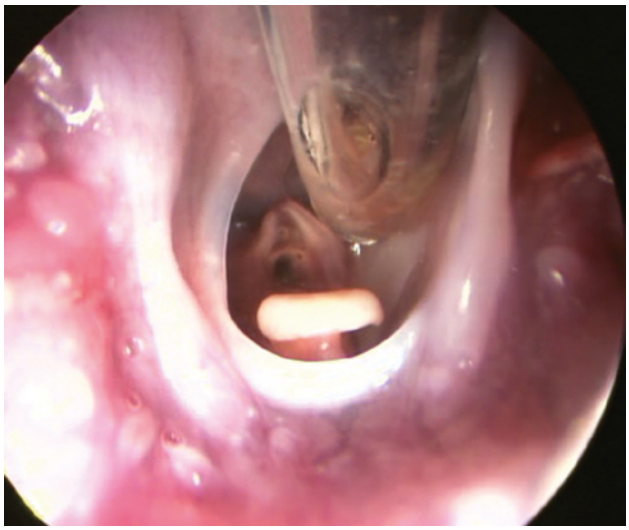


Figure 23.5 For endotracheal intubation of chinchillas and other medium to large rodents the glottis can be visualized with an endoscope.



Figure 23.6 Although large, capybara are difficult to intubate. In this animal an endoscope is being placed directly into the glottis of an anesthetized animal, and the endotracheal tube is then slid off the endoscope.

bronchus, premeasure the tube before use and auscultate both lung fields for respiratory sounds after intubation.

Monitoring

Monitoring is described in Chapter 3. It is recommended a trained person be assigned as anesthetist for each patient. This facilitates monitoring, recording, and supportive care, and saves time when intervention is required.

Unconsciousness is based on anesthetic dose and vaporizer setting, muscle relaxation, decreased reflex activity, and absence of limb and body movement. Palpebral and corneal reflexes are observed at 0.8 MAC (minimum alveolar concentration), but are abolished at >2.0 MAC (Imai 1999). The corneal reflex, however, is a poor guide to anesthetic depth (Imai 1999). A fixed dilated pupil, unresponsive to light, is a cross-species indicator of excessive depth. Anal tone is retained until deep anesthetic levels, but is difficult to assess in small rodents.

Pain and nocioceptor responses are assessed with a toe, ear, and tail pinch, or a skin incision. Increasing depth is assumed when muscle tone (e.g., jaw muscle, anal sphincter) decreases, palpebral and corneal reflexes are obtunded, and respiration pattern becomes regular and even. Sudden tachycardia, hypertension, or tachypnea in response to stimuli is indicative of inadequate anesthetic depth or analgesia.

Rodent heart rates are determined by temperature, size, metabolism, respiratory state, and the presence or absence of painful stimuli. Heart rate is inversely related to body size. The resting heart rate for mammals is calculated from the allometric equation $241 \times M_b^{-0.25}$, where M_b is bodyweight (kg) (Schmidt-Nielsen 1984). A heart rate 20% above or below the calculated rate for an individual is considered either tachycardic or bradycardic, respectively.

The esophageal stethoscope is not practical to use in small rodents and it may induce regurgitation in guinea pigs. Alternatively, a quality pediatric stethoscope is used. The electrocardiograph (Fig. 23.7) should have a multichannel oscilloscope with nonfade tracing and freeze capabilities. Additionally, it must be able to record at speeds of 100 mm/s and amplify the signal to at least 1 mV equal to 1 cm. Standard lead positions are used.

The Doppler flow detector is used anywhere there are major arteries close to the skin. These include the ventral aspect of the tail base, the carotid, femoral and auricular arteries, and directly over the heart. Potential sites for indirect blood pressure measurement include the legs, forearms, tail, and ears. Indirect blood pressure measurement techniques have been designed and validated for use in rats (e.g., Ibrahim et al. 2006; Widdop & Li 1997).

As with cardiac auscultation, evaluation of the respiratory system requires a good-quality stethoscope with appropriate head and length of tubing, and an experienced ear. Pulse oximetry has been evaluated in rats and appears accurate at hemoglobin saturation levels greater than 70% (Decker et al. 1989). Potential sites for placement of transmission pulse oximeter sensors include the ear, tongue, buccal mucosa, paw, vulva, prepuce, and proximal tail



Figure 23.7 Anesthetized Prevost's squirrel (*Callosciurus prevostii*). Note the use of a mask and attached nonrebreathing system. The squirrel was induced with isoflurane in oxygen in an induction box. This animal could have been intubated blindly with a 2-mm internal diameter uncuffed endotracheal tube. The heart rate and rhythm are being monitored with a lightweight portable electrocardiogram (Vetcorder).



Figure 23.8 An anesthetized fox squirrel. The animal was intubated with an uncuffed 2-mm internal diameter tube using a blind technique. A capnograph is used to assess correct placement. A 24-gauge over-the-needle catheter has been placed in the cephalic vein for fluid administration. A pediatric stethoscope is being used to monitor heart rate.

(Decker et al. 1989). A reflectance pulse oximeter sensor is used in either the esophagus or the rectum or applied to the skin/fur surface on the ventral aspect of neck overlying the carotid artery (rat).

Hypothermia is common in anesthetized rodents because of the large surface area to volume ratio. Additionally, many anesthetics suppress normal thermoregulatory mechanisms. Furthermore, anesthetic gases are of low humidity and temperature. Body temperature is preferably measured continuously and the thermometer should be sufficiently small to be used in small patients. For measurement of core body temperature, it is necessary to use a temperature probe attached to an esophageal stethoscope.

Supportive Care

Vascular access is discussed above. The cephalic vein can be catheterized in medium to large rodents (Fig. 23.8). Small volume infusors are essential for accurate fluid infusion in small patients. Some can be preprogrammed to flow rates for emergency and other drugs, so that all that is necessary for administration is to enter the bodyweight of the animal. They also allow a continuous infusion, which is preferable to bolus injection.

General anesthetics usually produce a dose-dependent ventilatory depression. This effect may be either additive or synergistic with underlying disease resulting in marked hypercapnia and/or ventilatory arrest. High-inspired oxygen concentrations also decrease ventilatory drive. Ventilation is also affected by body position and compression of the respiratory exchange tissues by distended viscera and/or obesity. Inadvertent compression of the chest by surgeons is common in small exotic patients. Developing good hand position techniques, an attentive anesthetist, and the use of clear plastic drapes helps prevent this cause of hypoventilation.

Guinea pigs have relatively small diameter tracheas and are prone to airway obstruction because of regurgitation and profuse salivary secretions. Adequacy of ventilation is most accurately assessed using arterial partial pressure of carbon dioxide (P_aCO_2). Capnography provides an indirect estimate of P_aCO_2 (Fig. 23.6), but may be inaccurate in very small exotic patients. Visualization of chest wall movement is a deceptive guide to adequacy of ventilation. Consequently, the author recommends either assisted or controlled ventilation of intubated patients under general anesthesia. Doxapram is not recommended for use in hypoventilating patients unless intubation and mechanical ventilation is impossible or contraindicated.

Ventilation is either assisted or controlled by positive pressure manually or mechanically. Many of the ventilators used in small animal anesthesia can be modified to ventilate rodents. A commercially available combination ventilator and anesthesia machine (Anesthesia WorkStation, Halowell EMC, Pittsfield, MA, USA) has been designed for research rodents. It is both a circle system for delivery of inhalant anesthetic and an optional ventilator with an adjustable pressure safety limit. The advantage of mechanical ventilation is that it frees the anesthetist to concentrate on other tasks. The disadvantages are that mechanical ventilators require a thorough

theoretical and technical understanding for their safe use, endotracheal intubation, and produce positive intrathoracic pressures that interfere with venous return to the heart and may cause lung trauma.

Manual ventilation provides the advantage, with a skilled anesthetist, of rapidly adjusting ventilatory pressures and volumes, and responsiveness to the surgeon, who may require brief irregular periods of ventilatory arrest to safely complete a procedure. Further research is necessary to evaluate the efficacy and appropriateness of ventilation techniques in small mammal practice. There may be situations where some hypoventilation is preferable to the adverse effects of positive pressure ventilation.

Administration of elevated inspired oxygen concentrations (>40%) will often overcome mild to moderate hypoxemia, assuming no major pulmonary shunting is present. Although mammals are susceptible to pulmonary oxygen toxicity, this syndrome is unlikely to be observed in patients maintained on high-inspired oxygen concentrations for 24 hours.

Minimizing anesthesia time and the use of warm surgical preparation solutions, wrapping the body, increasing the room temperature, and the use external heat sources (i.e., circulating warm water blankets and forced air warmers) reduces hypothermia. Electric heat blankets are not used because they have the potential to cause severe burns. Similarly, heated fluid bags placed in contact with the skin may cause burns. If endotracheal intubation is not possible, an indirect ventilation technique using a bulb inflator placed over the nose has been used in small rodents (Ingall & Hasenpusch 1966).

Recovery

The patient is placed in a warm, quiet environment and monitored. Supportive care is continued until the patient is fully alert and physiologically stable. Vascular access is maintained to allow emergency administration of drugs and fluids. Drugs, procedure duration, and the magnitude of physiologic dysfunction incurred determine the duration and quality of recovery. Prolonged recovery is usually due to hypothermia, hypoglycemia, and anesthetic overdose and/or impaired drug elimination. Rewarming will exacerbate underlying hypovolemia and hypoglycemia.

Anesthetic Regimens for Small Domestic Rodents

Drug dosages are given in Tables 23.1, 23.2, 23.3, and 23.4. Most anesthetic regimens for clinical patients are based around an inhalant anesthetic (i.e., isoflurane or sevoflurane). Endotracheal intubation, as discussed previously, is difficult in many pet rodent species. Premedication with glycopyrrolate is recommended in guinea pigs and other rodents that have profuse salivary secretions. Although small rodents can be induced either in an anesthetic induction box or by mask using an inhalant, it is recommended the animals be premedicated.

Benzodiazepines (i.e., midazolam) are relatively safe, reduce response to handling, provide muscle relaxation, and decrease inhalant and other anesthetic requirements. They do not, however, provide any analgesia. Midazolam can be combined with a relatively low-dose ketamine. The ketamine provides some analgesia. Alpha-2 adrenergic agonists (i.e., xylazine, medetomidine, dexmedetomidine, and detomidine) have the advantage of being able to be reversed by yohimbine, tolazoline or atipamezole. They also improve analgesia, but produce sometimes severe cardiopulmonary depression.

Analgesics should always be included for painful procedures. Assuming good hydration this author will combine an NSAID (i.e., meloxicam) in the initial premedication, as well as an opioid. Analgesics work best when given before the onset of nocioception and pain. Although only a partial μ-opioid agonist, buprenorphine has the advantage of a relatively prolonged duration of effect (6–8 hours). Morphine or hydromorphone can also be used for severe pain. Tramadol and meloxicam be administered orally before and after a procedure, as well as at home.

Anesthetic Regimens for Free-living Rodents

Capture techniques for free-living, primarily small rodents are well described by Barnett and Dutton (1995). The anesthetic techniques described for small captive rodents based on inhalant anesthetics will also work for the wild species. Where inhalant anesthetics are not available or impractical, parenteral anesthetic protocols are required (Tables 23.3 and 23.4).

Capybara

The largest living rodent, the capybara, weighs approximately 35–65 kg. Their large size and robust incisors make them difficult and dangerous to immobilize. They are also well adapted to aquatic systems, and will retreat to water when threatened. They can hide immersed with just their nares breaking the surface under floating vegetation. It is imperative, therefore, to capture free-living animals away from water and prevent their escape. Capybaras have been captured by lassoing, as well as darting, from horseback (Salas et al. 2004). Alternatively, they can be trapped in baited traps or corrals. Both techniques require a dry area for capture.

In one study in capybaras, ketamine (10.0 mg/kg) and xylazine (0.5 mg/kg) provided the best immobilization and analgesia in comparison to tiletamine/zolazepam (5.0 mg/kg), and tiletamine/zolazepam (5.0 mg/kg) and levomepromazine (0.5 mg/kg) (Nishiyama et al. 2006). Drugs were administered intramuscularly using darts delivered by a blowgun. The tiletamine/zolazepam combination allowed approximately 1 hour immobilization for procedures where intense analgesia is not necessary. The addition of levomepromazine improved analgesia and muscular relaxation, as well as the duration of anesthesia and recovery time.

In another study in capybaras, an intramuscular combination of tiletamine/zolazepam (1.5 mg/kg), medetomidine (0.0075 mg/kg), and butorphanol (0.075 mg/kg) was preferable to tiletamine/zolazepam alone or combined with medetomidine (King et al. 2010) for immobilization. This combination provided adequate analgesia for intraperitoneal implantation of radio transmitters.

Beaver

The Eurasian (*Castor fiber*) and North American (*C. canadensis*) beavers are the second-largest rodents. Similar to capybaras, they are robust and potentially dangerous, and agile in water. Consequently, some form of physical or chemical immobilization is required for safe handling of these species.

Ketamine alone (10–15 mg/kg IM) successfully immobilized beaver for handling (Lancia et al. 1978). Inhalant anesthesia (halothane) following immobilization with a combination of ketamine (25 mg/kg IM) and diazepam (0.1 mg/kg IM) was safe and effective for handling and surgery for intraperitoneal implantation of radio transmitters in North American beavers (Greene et al. 1991). Anesthesia was maintained with halothane in oxygen via a semiclosed circle anesthetic circuit. Throughout the surgical procedure, all beavers had mean arterial pressure less than 60 mmHg and esophageal temperature less than 35°C. Respiratory acidemia was observed in spontaneously ventilating beavers, but not in beavers maintained with controlled ventilation.

In another study comparing anesthetic regimens for intraperitoneal implantation of radio transmitters in European beavers (*Castor fiber*), a combination of medetomidine (0.05 mg/kg), ketamine (5 mg/kg), butorphanol (0.1 mg/kg), and midazolam (0.25 mg/kg) was preferred (Ranheim et al. 2004).

Alternatively, isoflurane or sevoflurane alone was used for surgical anesthesia in North American beavers (Breck & Gaynor 2003). After placement in a burlap bag, a mask was placed over the nose of the beaver through the bag and the inhalant anesthetic administered at the highest vaporizer setting until the animals became relaxed. The animals were not intubated.

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24

Chiropterans (Bats)

Darryl Heard

Introduction

After rodents, bats are the most diverse and widely distributed mammal group (Wilson & Mittermeier 2019; Wilson & Reeder 2005). They are also the most abundant and form the biggest mammalian aggregations known (Nowak 1999). The order Chiroptera contains 18 recent families and ≥1116 bat species (Wilson & Reeder 2005). It is divided into suborders Microchiroptera and Megachiroptera. The latter comprises just one family, the Pteropodidae, with 42 genera and ≥186 species.

Bats inhabit most of the temperate and tropical areas of the world, except for some remote oceanic islands and beyond the tree growth line in the colder parts of either hemisphere. The Megachiroptera are confined to the tropical and subtropical regions of the Old World, east to Australia, and the Caroline and Cook Islands.

Physiology and Anatomy

"Chiroptera" is derived from the Greek *cheir* (hand) and *pteron* (wing). Skeletal adaptations for flight include a keeled sternum and elongated second to fifth metacarpals that form long rigid spokes for the wing membrane. The thumb (digit one) is an agile grasping tool and the only digit with a functional claw. The thoracic vertebrae are interconnected to form a rigid column that supports the flight muscles.

Compared to other mammals, the acetabular opening is rotated and shifted dorsally, and the legs are rotated 180° around their long axis so the knees face the rear. Since they usually perch inverted, their legs are adapted for pulling rather than pushing. At rest the entire bodyweight is suspended from the toes. Most have a locking mechanism that keeps the claws in a flexed position without muscular contraction (Fig. 24.1). Consequently, bats must be "unhooked" from a perch rather than pulled; excessive force will injure toes and in juveniles cause epiphyseal fractures. The hindlimb claws are compressed into hooked blades that will lacerate skin during restraint of larger bats.

The maximal aerobic capacities are the same as similar sized birds. The minimal metabolic requirement in level flight is 1.5 times greater than the maximal aerobic capacity of a similar sized nonflying mammal. Consequently, bats at rest are not likely to manifest overt clinical signs until respiratory dysfunction is well advanced.

Active bats are homeotherms, maintaining their body temperature between 35 and 39°C. They utilize a large amount of energy to compensate for heat loss due to a high body surface area to metabolically active tissue ratio. Additionally, large lungs and naked flight membranes result in heat loss from a surface area six times larger, and a thermal conductance 1.5–4 times greater, than wingless animals. Some bats compensate for this with heterothermy; temperate bats and tropical Vespertilionids and Molossids have a variable ability to lower body temperature and go into torpor (diurnal lethargy) or hibernation. This is based not only on temperature, but also food availability and reproductive condition. Lowered body temperature and metabolic rate in hibernating or torpid animals are assumed to reduce anesthetic requirement, and alter drug uptake and elimination. When possible, bats are not anesthetized while in torpor.

Bats consume large quantities of food relative to their body size. Gastrointestinal transit is also very rapid, possibly to minimize bodyweight for flight. Vomiting is therefore unlikely unless animals are anesthetized immediately after feeding. Bats usually feed at night when they are most active. Consequently, blood glucose and tissue glycogen levels are lowest at dusk before the animals begin feeding (Widmaier & Kunz 1993).

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Figure 24.1 Most bats possess a locking mechanism in the toes that allows them to hang without effort. Pulling downward causes the claws to turn inward. To remove bats from a perch the claws must be unhooked to prevent injury. Golden-mantled flying fox (*Pteropus pumilus*).

Zoonotic Diseases

Bat populations are known reservoirs for several infectious agents of significance to humans and other animals (e.g., Lyssaviruses, Henipaviruses, *Leptospira* spp.) (Calisher et al. 2006; Constantine 1970; Rupprecht et al. 2001). It is recommended all personnel working with bats should be vaccinated against rabies and other lyssaviruses (Rupprecht et al. 2001). Care is taken to minimize contact with blood, saliva, and other secretions or emissions that may contain infectious organisms. Although the teeth of many microchiropterans are very small, they can still penetrate human skin. Furthermore, saliva contact with skin is also a possible source of infection. It is recommended bats be anesthetized for procedures requiring close contact to reduce biting and transmission of secretions.

Physical Restraint

Techniques used for capturing free-living bats are described by Kunz and Kurta (1988). All restrained bats are capable of delivering a defensive bite. Most have jaws that are shortened, giving them a powerful bite. Neonatal bats possess needle-like, caudally directed milk teeth for gripping the nipple. The thumbs and associated claws of large bats will scratch an unprotected handler and are used to pull fingers in for a bite.

Bats are restrained with leather gloves (Fig. 24.2). Alternatively, a towel is used to cover the head and confine the limbs. In small bats nets can be used for initial capture, but are cumbersome in larger animals. However, they should always be available in case of an escape. The duration of manual restraint is minimized to reduce stress and prevent hyperthermia. Prolonged restraint



Figure 24.2 (a) Leather gloves are recommended for handling even small bats, such as this evening bat (*Nycticeius humeralis*), to protect from bites. (b) Physical restraint of a large flying fox (*Pteropus vampyrus*) for sample collection. Note the use of long-sleeved gloves to protect the holder from scratches, and the hold around the neck and feet.

induces marked elevations in cortisol and glucose (Widmaier & Kunz 1993). Carrying cages must be sufficiently tall to prevent the head of the bat from touching the floor.

Wimsatt et al. (2005) describe the use of a restraint device made of polyvinyl chloride tubing in big brown bats (*Eptesicus fuscus*). An attachment at one end is used to administer inhalant anesthesia. Morgan et al. (2022) similarly describe a device for blood collection in awake microchiropterans.

Blood Collection and Handling

The blood volume of active bats is approximately 9.0–11.0 mL/100 g. Blood is collected in bats ≥100 g from the median artery or vein on the medial aspect of the distal humerus with a 25-gauge needle and a 1- or 3-mL syringe (Fig. 24.3). If the collector is right-handed, the right wing of the supine bat is extended until the elbow joint forms a 90° angle. The left hand of the collector is then used to rotate the biceps muscle laterally while compressing the median veins to cause their distension. The right hand is supported on the table surface and the needle and syringe rest across the proximal radius as the needle enters the vessel. Once blood is identified in the needle hub, continued flow must be "finessed" with gentle alteration in suction, rotation of the needle, and patience. There are usually two or more veins and an artery in close contact at the insertion site. Although arterial blood can be used for sampling, care must be taken to ensure adequate hemostasis. Large hemotomas are common, even with venous puncture, and in small bats may result in death.



Figure 24.3 Venepuncture of the right median vein in an anesthetized large flying fox (*Pteropus vampyrus*). Note the positioning of the elbow at a right angle to facilitate access to the vessels on the ventral aspect of the distal humerus.

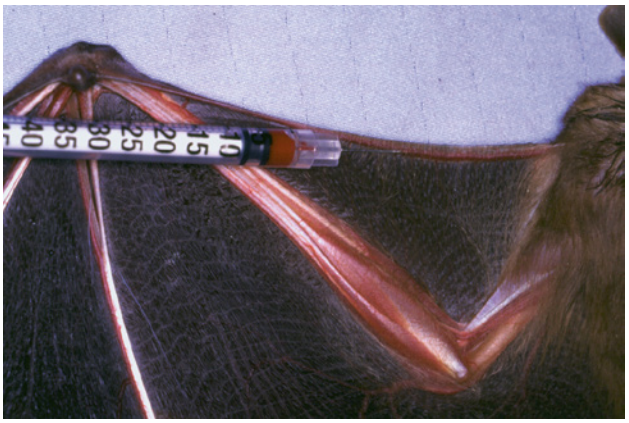


Figure 24.4 Venepuncture of the cephalic vein in an anesthetized Egyptian fruit bat (*Rousettus aegyptiacus*).

Since collection time may be prolonged, heparinization of the syringe is recommended when a plasma sample is appropriate (Heard et al. 2006a). However, if collection lasts >2 minutes and is traumatic, the anticoagulant effect of the heparin will be overcome by thromboplastin released from tissue. Further excessive pressures will result in hemolysis.

In small bats, blood samples are collected from the cephalic vein along the leading edge of the patagium (Fig. 24.4). A 25-gauge needle is used to make a hole in the vessel and blood is collected into a microhematocrit tube from the incision site. Alternatively, a 0.5-mL insulin syringe with attached 27-gauge needle is used. This technique is also used to collect blood from the interfemoral (Fig. 24.5) and saphenous (Fig. 24.6) vessels. In very small bats the uropatagial vessels can be dilated with the application of a warm pack (Wimsatt et al. 2005).

The external jugular veins are large in microchiropterans and may in some species be used for collection. Cranial vena caval collection has also been successful in some large bat species. The internal and external jugular veins of Megachiropterans are small and of similar size.

Bat blood is easily altered by inappropriate collection, handling, and storage. Even moderate hemolysis during sample collection will cause pseudo hyperkalemia, hyponatremia, hypochloremia, and elevated aspartate transaminases (Day et al. 2001). Hyperkalemia in otherwise healthy animals is usually an indication of sample collection error. If the plasma remains in contact with the red cells for ≥6 hours, there will be an elevation in phosphorus and decreases in chloride and glucose concentrations (Day et al. 2001). Heparinized blood samples allow centrifugation immediately after collection and the plasma to be removed from the blood cells and frozen until analysis (Day et al. 2001; Heard et al. 2006a).

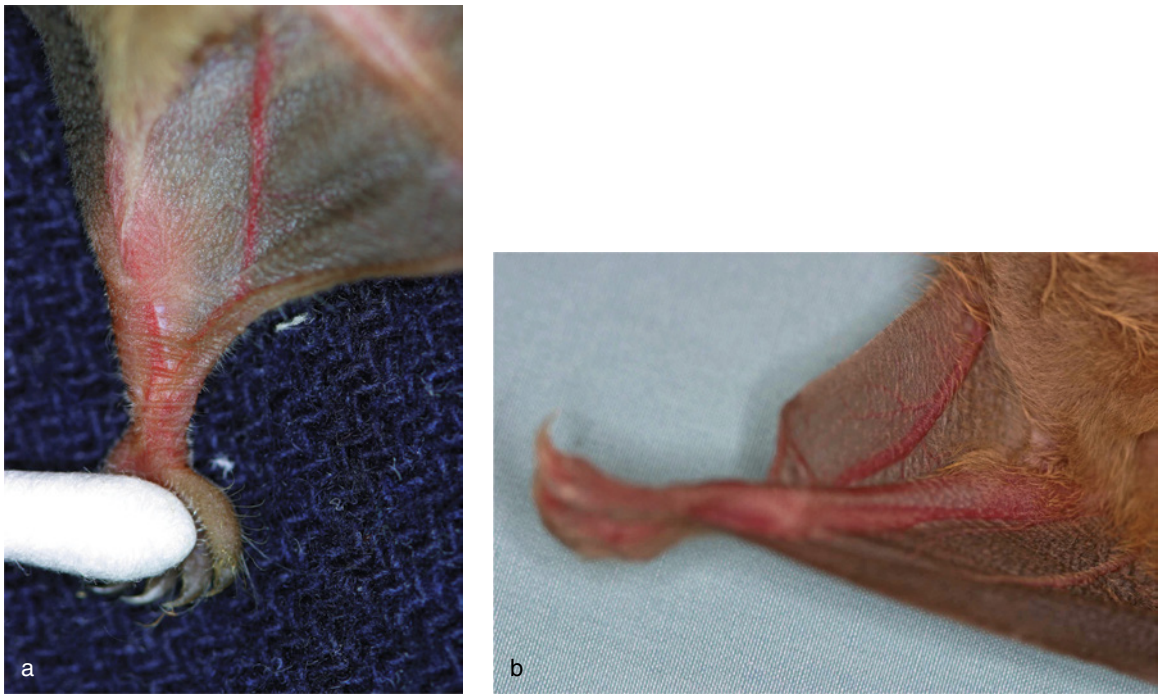


Figure 24.5 (a) The interfemoral vein in the uropatagium of a microchiropterans, a Mexican free-tail bat (*Tadarida brasiliensis*). This vessel can be used for small volume blood collection. (b) The interfemoral vein in the uropatagium of an Egyptian fruit bat (*Rousettus aegyptiacus*).



Figure 24.6 Blood collection from the saphenous vein of a Jamaican fruit bat (*Phyllostomus hastatus*) using a heparinized insulin syringe (27-gauge needle).

Parenteral Anesthesia

Inhalation anesthesia is preferred in bats. There are circumstances, however, where it is either not available or not appropriate to the situation (i.e., anesthesia of free-living animals in remote locations). Parenteral anesthetic regimens are summarized in Table 24.1.

Injection Sites

When possible, intramuscular injection in the flight muscles is avoided. However, in large aggressive bats it is easier to press them into sternal recumbency and administer drugs in the large triceps or thigh muscles. The sternum is relatively narrow and pectoral muscle injection may result in the needle passing between the ribs if the bat moves. Subcutaneous injection is appropriate, but not in the patagial membranes. The injection of tissue irritant drugs (e.g., ketamine HCl) in these areas may result in necrosis.

Intravenous injection sites are the same as those used for blood collection: cephalic (Fig. 24.4), median, and femoral or saphenous (Fig. 24.6). Small-gauge catheters are placed temporarily in the cephalic and median veins. Awake bats usually do not tolerate catheters. Intraosseous catheterization of the radius is an alternative route for administration of fluids. This route can be used in even the smallest bats. Spinal needles are used in megachiropterans, while regular hypodermic needles can be used in microchiropterans.

Microchiropterans

Although there are several examples of "big" little bats, most Microchiropterans are <50 g. Small body size is usually associated with a higher anesthetic dosage required for

Table 24.1 Anesthetic and analgesic drugs used in megachiropteran and microchiropteran bats.

		Dosage		
Drug	**Route**	**Megachiroptera**	**Microchiroptera**	**Comments**
Parenteral				
Ketamine	IM	40–50 mg/kg	≥100 mg/kg	Not recommended because of poor muscle relaxation and prolonged recovery with wing flapping
Xylazine/ ketamine	IM	Combine equal volumes of xylazine (20 mg/mL) and ketamine (100 mg/mL); 0.4 mL/kg		Variable flying fox (*Pteropus hypomelanus*) (Heard et al. 1996) Australian flying foxes (*Pteropus* spp.) (A. Olsson, pers. comm.)
Xylazine/ ketamine	IV	Xylazine 1 mg + ketamine 5 mg in 0.1 mL		Free-living variable flying foxes; provided safe short-term immobilization for collection of biological samples (Sohayati et al. 2008)
Medetomidine	IV	0.03 mg/kg		Free-living variable flying foxes (Epstein et al. 2011)
Medetomidine/ ketamine	IM	Combine equal volumes of medetomidine (1 mg/mL) with ketamine (100 mg/ml); 0.5 mg/ml		Captive variable flying foxes (Heard et al. 2006)
Medetomidine/ ketamine	IV	0.05/5.0 and 0.025/2.5 mg/kg		Free-living variable flying foxes (Epstein et al. 2011)
Tiletamine/ Zolazepam	PO	40 mg/kg		For immobilization of large bats when physical restraint is dangerous (i.e., suspect rabid bats or animals caught in barbed wire) Drug combination is squirted into the mouth of the animal (Vogelnest 1999) Recovery is prolonged – not recommended for routine anesthesia/ immobilization
Propofol	IV	6–8 mg/kg	8–10 mg/kg	Dilute 1:4 with saline to obtain injection volume in small bats (A. Olsson, pers. comm.)
Midazolam/ alfaxalone	SC	2/15 mg/kg		Egyptian fruit bats (*Rousettus aegyptiacus*) (Tuval et al. 2021) Sufficient anesthesia to perform routine diagnostic and therapeutic procedures for ~40 minutes. Twitching/tremors observed during induction in some Reverse with flumazenil (0.3 mg/kg) SC
Midazolam/ alfaxalone/ morphine	SC	1.5/15/1.5 mg/kg		Adequate anesthesia in several Egyptian fruit bats for castration and spays (Tal & Shilo-Benjamini 2023) Supplemental alfaxalone and sevoflurane in some Bupivicaine infiltration at surgical site
Inhalation				
Halothane	Inhalation	Induction 4–5%, maintenance 1–1.5%		
Isoflurane	Inhalation	Induction 5%, maintenance 2.5%		
Sevoflurane	Inhalation	Induction 6–7%, maintenance 3–4%		Expensive

(*Continued*)

Table 24.1 (Continued)

Drug	Route	Dosage		Comments
		Megachiroptera	Microchiroptera	
Analgesics				
Butorphanol	SC, IM	0.4 mg/kg q4h	2 mg/kg q4h	
Buprenorphine	SC, IM	0.03 mg/kg q6–12h	0.05–0.1 mg/kg q6–12h	
Morphine	SC, IM	0.5–1.0 mg/kg q4–6h	2–5 mg/kg q4h	
Carprofen	SC, IM, PO	1–4 mg/kg q24h (q12h PO)	3–5 mg/kg q12h	
Meloxicam	SC, IM, PO	0.1–0.3 mg/kg q12h	1–2 mg/kg q12h	
Tramadol	PO	0.5–2.0 mg/kg q24h		

IM, intramuscular; IV, intramuscular; PO, per os; SC, subcutaneous.

a given level of analgesia or anesthesia. Most reported studies of parenteral anesthetics in Microchiropterans investigate their effects on wing membrane capillary function; no mention is made of anesthetic effect (Harris et al. 1971; Longnecker & Harris 1972; Longnecker et al. 1974).

Megachiropterans

In variable flying foxes (*Pteropus hypomelanus*), ketamine alone (30–37.5 mg/kg intramuscular [IM]) produced short-term chemical restraint, but poor muscle relaxation and struggling during recovery (Heard et al. 1996). In the same species, xylazine (2 mg/kg IM)/ketamine (10 mg/kg IM) and medetomidine (50 μg/kg)/ketamine (5 mg/kg IM) combinations produce short-term immobilization (30 minutes) with good muscle relaxation and quiet recovery (Heard et al. 1996, 2006b). Similar dosages have been used in free-living variable flying foxes, both IM and intravenous (IV) (Epstein et al. 2011; Sohayati et al. 2008).

During induction with medetomidine/ketamine the palpebral response is lost first, followed by clinch and bite response (Heard et al. 2006b). These responses return in the reverse order during recovery. It is recommended xylazine or medetomidine not be reversed, except in an emergency, because the adverse effects of ketamine (wing flapping and struggling with associated hyperthermia) will be unmasked during recovery. In other bat species the dosages per kilogram are increased as the size of the animal decreases.

This author has used a combination of medetomidine (30–40 μg/kg), ketamine (3–4 mg/kg), and buprenorphine (0.03–0.04 mg/kg) administered subcutaneously with an insulin syringe in Egyptian fruit bats. This combination produced adequate short-term anesthesia for liver biopsy performed through a mid-abdominal incision. Bupivacaine was infiltrated into the surgical site for additional analgesia. No supplemental oxygen or inhalant anesthetic was provided. The medetomidine was reversed at the end of the procedures with atipamezole (five times the medetomidine dosage).

Tiletamine/zolazepam (20–40 mg/kg) produces immobilization, but prolonged recovery. However, it has been used to immobilize free-living animals suspected of being rabid or trapped in barbed wire (Vogelnest 1999; A. Olsson, pers. comm.). The drug combination is sprayed into the open mouth, preventing contact with people until anesthetized.

Propofol (8–10 mg/kg IV) provides 5–15 minutes of anesthesia in animals in which a vessel can be accessed for injection. Propofol may be diluted 1:4 with saline to facilitate administration (A. Olsson, pers. comm.). Rapid injection is associated with marked cardiopulmonary depression and possibly apnea; endotracheal tubes, laryngoscope, and a mechanism for providing assisted ventilation must be available.

A combination of midazolam (2 mg/kg subcutaneous [SC]) and alfaxalone (15 mg/kg SC) produced and sufficient anesthesia to perform routine diagnostic and therapeutic procedures for approximately 40 minutes in Egyptian fruit bats (*Rousettus aegyptiacus*) (Tuval et al. 2021). During induction, an excitation behavior consisting of twitching/tremors was observed in many of the bats. Despite this, the quality of induction and muscle relaxation were assessed as good. Flumazenil (0.3 mg/kg SC) reduced recovery time and improved quality of recovery.

A combination of alfaxalone (15 mg/kg), midazolam (1.5 mg/kg), and morphine (1.5 mg/kg) administered in an

insulin syringe subcutaneously between the scapulae produced adequate anesthesia in several Egyptian fruit bats for castration and spays (Tal & Shilo-Benjamini 2023). Additional alfaxalone (5 mg/kg SC) was added as needed. Furthermore, bupivacaine (0.5% diluted to 0.25%) with saline was infiltrated into the surgical incisions for analgesia. Isoflurane anesthetic supplementation was also available, but not used.

Inhalation Anesthesia

Inhalation anesthesia is very safe and effective in both captive and free-living bats (Wimsatt et al. 2005). An efficient respiratory system (Canals et al. 2005) makes induction and recovery times comparable to those of birds. Isoflurane (5% by mask, then maintenance at 2–2.5%) provides rapid (1–2 minutes) induction and recovery, as well as rapid response to changes in vaporizer setting. For prolonged anesthesia bats are attached to a nonrebreathing system with either an endotracheal tube or a mask (Fig. 24.7). Portable, lightweight inhalant anesthetic systems developed for avian anesthesia (Chapter 21) are ideal for field immobilization. In Jamaican fruit bats (*Artibeus jamaicensis*), isoflurane was associated with increases in white blood cell, lymphocyte, and monocyte counts compared with awake bats (Strumpf et al. 2020).

Endotracheal Intubation

Bats ≥150 g are intubated with a ≥2-mm internal diameter endotracheal tube. For intubation the author prefers to place the bat in dorsal recumbency to visualize the glottis (Fig. 24.8). The mouth is opened using gauze placed around the upper and lower jaws, and the tongue pulled forward and to the side. A laryngoscope with a small straight pediatric blade is used for illumination. Topical anesthetic applied to the glottal opening decreases reflex coughing.

Monitoring

Cardiovascular

Heart rates range from 100 beats per minute (bpm) in large Megachiropterans at rest to 1000 bpm in the smallest. Heart rates are influenced by restraint, anesthesia, environmental temperature, and size. The rate of the 5–10-g *Myotis lucifugus* ranges from around 350 bpm at thermoneutrality (33–38°C) to as low as 6 bpm during hibernation (rectal 6°C) (Kallen 1977). Although the electrocardiogram is typically mammalian (Mihova & Hechavarria 2016), its configuration in Microchiropterans varies with rate and there are species differences. In some Vespertilionids at high rates the T and R waves fuse, and the P wave is difficult to identify. Active and dormant bats may develop a functional bradycardia interrupted by transitory compensatory tachycardias. At low



Figure 24.7 Medium to large bats, like this Wahlberg's epauletted fruit bat (*Epomorphorus wahlbergi*), can be intubated with commercially available endotracheal tubes (≥2 mm internal diameter). The trachea is relatively short and the endotracheal tube should be premeasured before placement.



Figure 24.8 The oral cavity of a dorsally recumbent Wahlberg's epauletted fruit bat (*Epomorphorus wahlbergi*) before endotracheal intubation. The tongue is pulled dorsally. The epiglottis lies just beyond the opening in the soft palate.

body temperatures, supraventricular arrhythmias and second-degree heart block are common, but reverse with warming. However, bats appear resistant to hypothermia-associated ventricular fibrillation (Kallen 1977).

Heart rate and rhythm, and peripheral blood flow are assessed with a Doppler flow probe secured over the tibial artery behind the knee or the pedal artery on the palmar surface of the feet. In an anesthetized flying fox species (*Pteropus vampyrus*) a noninvasive oscillometric technique was shown to be unreliable for estimating systemic blood pressures (Paranjape et al. 2023). Conversely, an indirect Doppler technique using a size 2 and 3 cuff on the pectoral and pelvic limbs, respectively, produced acceptable estimations of mean systemic arterial pressure across a wide range (Paranjape et al. 2023).

Direct arterial catheterization for systemic blood pressure measurement has been described in variable (*Pteropus hypomelanus*) and Malaysian (*P. vampyrus*) flying foxes (Gatson et al. 2019). Arterial catheterization was performed using a 24-gauge, 1-inch over-the-needle catheter under aseptic technique. Percutaneous arterial access was obtainable in two locations in these species. In the wing, the median artery is the largest arterial branch of the subclavian artery that courses along the cranio-medial aspect of the humerus before continuing its course along the ulna in the antebrachium. The median artery can be easily palpated on the medial aspect of the distal two-thirds of the humerus. After puncturing the skin over the median artery, the catheter is directed towards the proximal head of the humerus hindlimb.

The posterior tibial artery, a branch of the ischiadic artery, courses along the dorsomedial aspect of the tibia and can be easily palpated at any point along its course down the length of the tibia (Gatson et al. 2019). The puncture site for the posterior tibial artery is anywhere between the proximal two-thirds to the midshaft of the dorsomedial tibia (Fig. 24.9). The catheter is then directed in a cranial direction along the length of the artery.

Normal arterial values, reported as a median (interquartile range) for systolic, diastolic, and mean arterial pressures (MAPs) for Malaysian flying foxes were 101 (94, 107), 69 (57, 80), and 86 (75, 93), respectively (Gatson et al. 2019). Normal MAP for clinically healthy variable flying foxes was 86 (67, 93) (Gatson et al. 2019). Placement of variable flying foxes in a vertical head-down position did not alter blood pressure in clinically healthy bats, but significantly increased MAP in two animals with cardiomyopathy (Gatson et al. 2019).

In another study of healthy adult Livingstone's fruit bats (*Pteropus livingstonii*), placing them in a roosting or upside-down position produced a mild bradycardia, but had no effect on right atrial systolic area and right ventricular velocity during atrial contraction (Drane et al. 2018). In bats with dilated cardiomyopathy, however, left ventricular ejection fraction appeared improved while roosting. All bats were anesthetized with sevoflurane in oxygen for echocardiography.



Figure 24.9 Arterial catheterization with a 25-gauge over-the-needle catheter for arterial blood pressure measurement in a large flying fox (*Pteropus vampyrus*).

Respiratory

Hemoglobin saturation and heart rate are monitored with a pulse oximeter probe placed on the tongue, foot (Fig. 24.10), or median artery, or with a rectal reflectance probe. Arterial blood samples for gas analysis can be collected from the median artery as described above.

A computed tomography lung volume study in isoflurane anesthetized Egyptian fruit bats showed an inverted or roosting position decreased lung volume associated with atelectasis (Hostnik et al. 2019). Consequently, vertical positioning is recommended during maintenance and recovery when possible.

Body Temperature

The thermoneutral zone can be used for setting environmental temperatures for captive bats. This is the ambient temperature range in which a resting, fasting animal consumes the least amount of oxygen. Within this range, an animal can maintain a constant body temperature without



Figure 24.10 Pulse oximeter probe placed on the foot of a flying fox for measurement of arterial oxygen saturation.

additional energy cost. For large flying foxes (500–1000 g), the thermoneutral zone lies between 24 and 35°C, whereas for a lightweight bat such as *Saccopteryx bilineata* (7 g) it is restricted to 30–35°C.

Bats die quickly if the ambient temperature is above body temperature, particularly if the humidity is high. Their only means of lowering body temperature are evaporative cooling and the creation of convection currents by air movement. Flying foxes roost in large trees, often in full sun. As the ambient temperature rises, they initially start fanning the air with bent wings. If the ambient temperature approaches body temperature, they wet their fur with saliva and urine and pant, but they cannot sweat. Microchiropterans and smaller Megachiropterans avoid intense heat through their choice of diurnal roosts. Caves, crevices, and hollow trees are ideal, thermally stable environments with temperatures in or near the thermoneutral zone. Because the bats only fly out at night, they never run the risk of overheating. Since most bats roost in sites with localized climates, preferred roost humidity is likely to be greater than 30% and may approach 100%. Humidity is an important influence on the elasticity of the patagium and very dry conditions will be associated with dry membranes.

A temperature probe is placed in either the rectum or esophagus; the latter is preferred because it reflects core body temperature. Rectal temperatures in healthy animals may be as low as 35°C.

Metabolic

Hypoglycemia is very likely to occur in the perianesthetic period, particularly in very small, anorectic animals (Widmaier & Kunz 1993). Blood glucose levels should be maintained above 80 mg/dL.

Supportive Care

To prevent hypothermia, the wings are folded to the body and the animal is placed on a circulating water blanket. When possible, the bat is wrapped in either a blanket or bubble-wrap. Alternatively, a commercial forced air warmer developed for human surgery is used. Electric and chemical heating pads, as well as heated water bottles, are avoided because they will cause severe burns to the wing membranes. The wing membrane is also very susceptible to damage from bandaging and taping.

IV over-the-needle catheters can be placed in anesthetized bats in the cephalic (Fig. 24.11), ulnar, and saphenous veins. The catheter needs to be removed before recovery or the animal will chew it out. Catheters are secured with glue or tape.

Recovery

For recovery, bats are wrapped in a towel and left in a quiet cage to prevent struggling and wing flapping; the animals are usually sufficiently recovered when they able to crawl out. Alternatively, once gripping returns the bat is suspended from its perch.



Figure 24.11 Cephalic vein catheterization in an anesthetized large flying fox (*Pteropus vampyrus*). Most bats are intolerant of catheters when awake. Care is taken to not compress the patagium (wing membrane) within constrictive bandages.

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25

Rabbits, Hares, and Pikas

Marta Romano

Introduction

The order lagomorpha includes Leporidae (rabbits and hares) and Ochotonidae (pikas). The concepts described in this chapter focus on anesthesia of the domestic rabbit (*Oryctolagus cuniculi*) because this species is most commonly encountered in clinical practice. The techniques described here are also applicable to hares and pikas.

Common breeds of domestic rabbits include Netherland Dwarfs, Lionhead, Dwarf Lop, and giant breeds, ranging in size from 1 to 10 kg. In general, monitoring, orotracheal intubation, intravenous (IV) catheterization, and effective mechanical ventilation are more difficult in smaller patients. Smaller breeds may therefore present the anesthetist with greater challenges than larger. Aggressive breeding for certain morphologies (e.g., lionhead) is also resulting in greater brachycephalism and skull anatomy, which may complicate intubation and respiration.

Behavior and Physiology

Perianesthetic mortality is more common in rabbits than any other domestic species (Brodbelt et al. 2008) and often remains unexplained. Rabbits are prey animals often exhibiting a flight response. When frightened, rabbits may emit loud screams. The inability to flee causes stress, resulting in catecholamine and cortisol release. In rabbits, overcrowding, inappropriate husbandry, and chronic pain due to dental disease may also be associated with cardiomyopathy (Weber & van der Walt 1975) and stress (Harcourt-Brown & Baker 2001). Much like any other species, chronic stress may cause reduced gastrointestinal motility, decreased renal blood flow, immunosuppression, and increased predisposition to infections. These factors may go largely unnoticed and become apparent once the animal is presented for veterinary care.

In rabbits, even more than in other domestic species, reducing the stress associated with anesthesia and surgery is paramount to maximize the chances of recovery. Several strategies can be adopted for this purpose. Rabbits should be housed in a quiet area separated from other animals and familiar objects should be placed in the enclosure whenever possible.

Although rabbits are not aggressive, they can bite and scratch when frightened. While being restrained, they can forcefully kick with their hindlimbs, which may result in vertebral fractures. As they jump away, rabbits may fall from examination tables and fracture limbs. Although manipulation should be gentle and minimal, care should be taken to minimize the risk of self-injury during restraint and sedation should be provided for more involved procedures.

Rabbits should be placed in cages when being moved across the hospital. Alternatively, they can be held with the head tucked between the elbow and the body of the handler, and supported with both arms. Following sedative administration, rabbits should be placed back in their enclosure in a quiet area, although they should be observed with care at all times to promptly detect signs of complications until the desired degree of sedation is achieved.

Cardiovascular System

The normal heart rate in rabbits ranges from 180 to 250 beats per minute. Given the rabbit's normal heart rate, it may be challenging to detect low-grade murmurs. Cardiac disease is uncommonly diagnosed in rabbit. Mitral and tricuspid valve disease have been reported in rabbits with bacterial endocarditis (Snyder et al. 1976). Hypertrophic cardiomyopathy may also occur, particularly in obese animals (Carroll et al. 1996). Multiple anesthetic episodes with ketamine xylazine has also been be associated with myocardial fibrosis in laboratory rabbits (Marini et al. 1999).

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The entire blood volume in rabbits ranges between 55 and 70 mL/kg (Benson & Paul-Murphy 1999; Donnelly 1997), therefore an acute loss of 11–14 mL/kg, corresponding to 20% of the total blood volume, warrants blood transfusion. Blood group antigens have been studied in laboratory rabbits and at least three antigens have been identified. The nomenclature of the identified antigens varies in different studies, although most commonly they are referred to as A, B, and H, with their combinations resulting in different blood groups. Blood typing is not commonly performed in rabbits. When the need for blood transfusion is anticipated during surgery, a healthy donor of an adequate size should be identified and cross-matched. A total volume of 9–10 mL/kg of blood can be removed from the healthy donor. The jugular vein is most commonly used for blood collection. Alternatively, a catheter can be inserted in the auricular artery for blood collection. Local anesthetic infiltration around the artery will inhibit reactive vasoconstriction and provide analgesia. Care must also be taken to ensure continued blood flow through the artery after catheter removal.

Respiratory System

Rabbits are obligate nasal breathers, and when the head is in a neutral position the soft palate is positioned ventral to the larynx, connecting it with the nasopharynx. This implies nasal edema and discharge may cause a complete airway obstruction. This scenario can occur during recovery after extubation, particularly following prolonged procedures in dorsal recumbency. Administration of topical phenylephrine may help reduce hyperemia and reduce the risk of airway obstruction during recovery.

Multiple aspects of anatomy render orotracheal intubation particularly challenging in rabbits. Their mouths are small and the oropharynx is elongated with a narrow intermandibular space. The base of the tongue, or *torus linguae*, is prominent and makes larynx visualization difficult. The orpharynx is particularly fleshy in overweight rabbits, rendering airway visualization even more difficult. Since the soft palate is elongated and covers the larynx completely in rabbits, the base of the tongue must be pushed ventrally to displace the soft palate and allow oral airway visualization (Fig. 25.1). When attempting direct laryngoscopy to achieve endotracheal intubation, a small stylet or guidewire can be used to gently displace the soft palate from the epiglottis. The epiglottis is relatively small and prone to laryngospasm. Topical application of lidocaine in the larynx may reduce the risks of laryngospasm during intubation.

The thoracic cavity is small in rabbits in comparison to their size (Fig. 25.2). Conscious rabbits breathe at a rate of 30–70 breaths per minute (bpm), although much higher

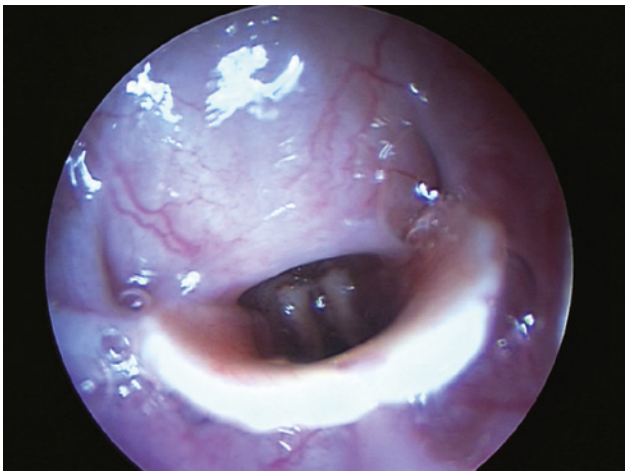


Figure 25.1 Endoscopic view of the glottal opening in an eastern cottontail rabbit (*Sylvilagus floridanus*). Lagomorphs are obligate nasal breathers. The soft palate has been displaced, allowing a view of the simple flat epiglottis and the arytenoid cartilages.



Figure 25.2 Lateral radiograph of a domestic rabbit. Note the small thoracic cavity relative to the large abdomen. The trachea is also relatively short compared with body length, and single bronchial intubation is common. Note also the angle of the oral cavity in relation to the trachea, emphasizing the need to hyperextend the head and neck to facilitate intubation.

respiratory rates might be observed in stressed rabbits. The small size of the thoracic cavity should be taken into account when performing lung auscultation. Given the large size of the abdomen, rabbits are likely prone to developing significant ventilatory depression when placed in dorsal recumbency under heavy sedation or general anesthesia. Mechanical or manual ventilation should be provided when possible, especially for long procedures. Elevating the chest and creating a slope between the thorax and the abdomen may alleviate some of the pressure on the diaphragm when rabbits are positioned in dorsal recumbency. At a minimum, a tight-fitting face mask should be placed for oxygen administration when rabbits are positioned in dorsal recumbency, even for very short periods of time, and pulse oximetry monitoring is highly recommended. Airway obstruction and cyanosis are common in anesthetized, dorsally recumbent rabbits breathing

spontaneously, despite oxygen administration via a facemask (Bateman et al. 2005).

Rabbits are prone to developing a number of respiratory diseases, including infectious and noninfectious etiologies (Deeb 2004). *Pasteurella multocida* infection may cause clinical or subclinical respiratory disease and is associated with pneumonia in pet rabbits. Careful physical examination should be performed prior to anesthesia to detect signs of preexisting respiratory disease which may result in increased morbidity and mortality during anesthesia. If respiratory disease is suspected, obtaining a thoracic radiograph under sedation is recommended prior to proceeding with general anesthesia.

Rabbits may become apneic and severely bradycardic in response to the pungent smell of isoflurane. Induction of general anesthesia using injectable agents is preferred in rabbits, similarly to other domestic animals. Mask induction (Fig. 25.3) should be considered exclusively when sedation is insufficient for catheter placement. There are also disadvantages associated with mask or chamber induction (Fig. 25.4) using either isoflurane or sevoflurane, including hypercapnia, apnea, and severe bradycardia (Flecknell et al. 1996). Sevoflurane is preferred for mask induction when available as it provides a quicker induction and has a less pungent smell compared to isoflurane. Induction of anesthesia using a facemask or chamber is not recommended in nonsedated animals, given the known associated complications and the stress this procedure may cause to the animals. Careful monitoring of respiration is recommended when performing mask induction, and IV access should be obtained as soon as the animals tolerates.

Nervous System

Head tilt is frequently caused by *Encephalitozoon cuniculi*, a microsporidial parasite that also causes renal disease in rabbits. If encephalitozoonosis is suspected, kidney function should be assessed prior to anesthesia so supportive therapy can be established if needed. Although liver,



Figure 25.3 Mask induction is recommended only in animals that have been premedicated or administered a parenteral induction agent to prevent struggling. Note the extension of the head and neck to reduce the possibility of airway obstruction.

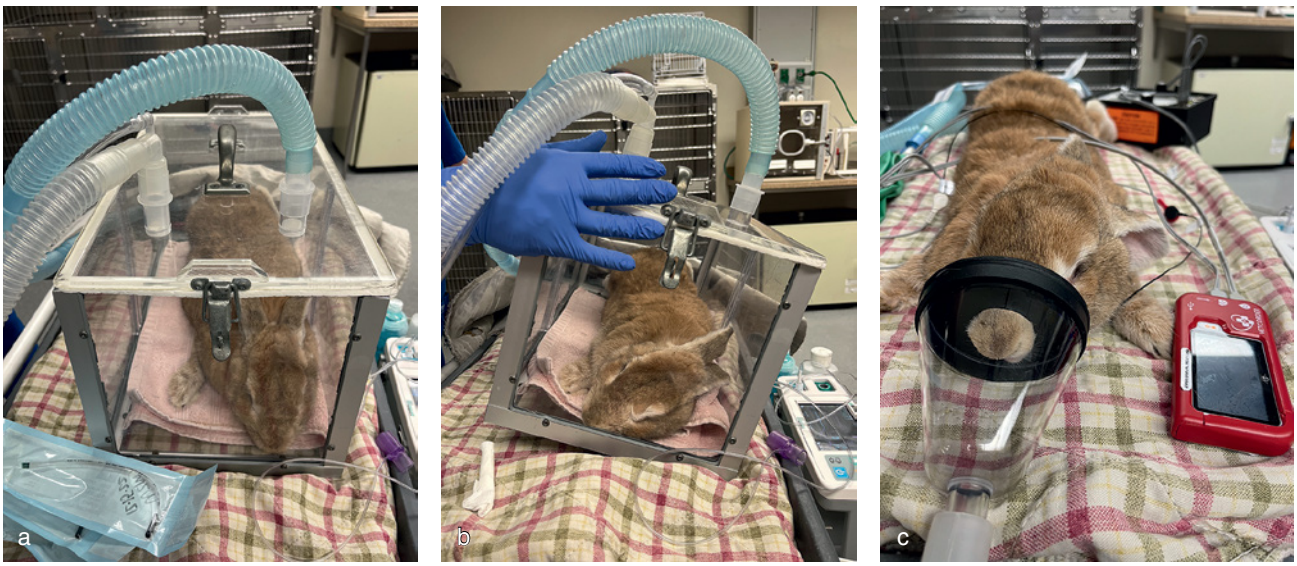


Figure 25.4 (a) Induction of a sedated rabbit with an inhalant anesthetic administered in oxygen. Note the clear chamber to allow visualization of the animal and the scavenging system. (b) Once the animal loses its righting reflex, it is removed from the chamber and maintained with a mask (c) until intubated. The disadvantages of using this technique include increased stress, breath-holding, and excessive anesthetic exposure to personnel.

cardiac, and respiratory diseases are rarely apparent in rabbits with encephalitozoon, studies have shown significant damage to these organs during postmortem examinations (Latney et al. 2014). *Encephalitozoon cuniculi* is also a potential zoonotic pathogen in humans, particularly immunocompromised individuals. Pasteurellosis may also cause head tilt associated with otitis interna or seizures due to encephalitis, and is often associated with respiratory disease.

A full preanesthetic assessment is critical in rabbits presenting with neurologic disease to detect possible systemic disease and organ injury.

Gastrointestinal System

Since rabbits cannot vomit, fasting is not normally recommended prior to anesthesia. Although prolonged periods of fasting may cause ileus and hepatic lipidosis, some anesthetists prefer to fast rabbits for 1–2 hours prior to anesthesia to limit the amount of food residues in the oral cavity that may be inhaled during general anesthesia, and to decrease the pressure of the gastrointestinal content on the diaphragm. Alternatively, the oral cavity of rabbits can be washed before induction.

Gastrointestinal dysfunction may occur after anesthesia, particularly following prolonged and invasive procedures, and may be due to stress and pain. Strategies to limit stress, such as housing in a quiet environment, avoidance of sudden diet changes, presence of familiar objects in the enclosure, as well as provision of analgesia when deemed appropriate, should be employed to limit the detrimental effects of perianesthetic ileus. If appetite cannot be restored within a few hours after anesthesia, syringe feeding should be initiated.

Preanesthetic Assessment

A full history should be obtained by the anesthetist prior to anesthesia. For the reasons described previously, a complete physical examination should be performed, with particular focus on the respiratory, cardiovascular, and nervous systems. Basic preanesthetic bloodwork, including packed red blood cells, total solids, blood glucose, and blood urea nitrogen, is sufficient for young, healthy individuals undergoing elective, short procedures. If venipuncture is not tolerated, it is acceptable to obtain blood after premedication in healthy young individuals. Older rabbits, those with preexisting conditions or undergoing invasive procedures should be assessed similarly to any other small animal patients. Full blood work, blood gas analysis, and additional diagnostics including thoracic radiographs and cardiology evaluation should be performed as deemed necessary. Obese rabbits are at increased risk of anesthetic complications as they may suffer from chronic hypertension, cardiac hypertrophy, and are more prone to developing hepatic lipidosis (Carroll et al. 1996). Similarly to obese animals of other species, obese rabbits may be more challenging to intubate due to the presence of a fleshy oropharynx, and can suffer from significant hypoventilation and lung atelectasis as a consequence of anesthesia.

Morbidity and Mortality in Rabbits Undergoing Anesthesia

Perianesthetic morbidity and mortality is substantially higher in rabbits than in other domestic species (Brodbelt 2009), ranging from 1.39% to 4.8% according to different retrospective studies (Brodbelt et al. 2008; Lee et al. 2018) compared to 0.17% and 0.24% in dogs and cats, respectively (Brodbelt 2009). Although the causes of such a high mortality rate remain largely unknown, many rabbits undergoing anesthesia are reported to carry *Pasteurella multocida* (Flecknell 1996), whose signs may go undetected yet cause a significant risk factor for perianesthetic death. Perianesthetic deaths have been often attributed to presumptive or confirmed cardiac or respiratory conditions (Brodbelt 2009; Lee et al. 2018). If finances allow, taking a thoracic radiograph as part of the preanesthetic assessment may help detect subclinical lung disease, and is advisable particularly if planning long duration of anesthesia and invasive procedures, or in older and sick rabbits.

Other factors that may contribute to high perianesthetic mortality in rabbits are the difficulty that may be encountered in obtaining venous access and achieving orotracheal intubation, as well as the more limited monitoring equipment reliability due to the small patient size. Moreover, most clinicians are less experienced in anesthetizing this species compared to dogs and cats.

One study identified the higher American Association of Anesthesiologists (ASA) status as a risk factor for perianesthetic mortality, with mortality rates being 0.73% and 7.37% in healthy (ASA 1 and 2) and sick (ASA 3–5) rabbits, respectively (Brodbelt 2009). A more recent study, however, did not identify the ASA status as a risk factor, and 80% of the fatalities encountered in this study were rabbits undergoing elective procedures (Lee et al. 2018).

Regarding the timing of death, two studies identified the majority of the fatalities occur after anesthesia, often after discharge (Brodbelt 2009; Lee et al. 2018). Only 6% and 30% of the fatalities occurred during induction and maintenance of general anesthesia, respectively (Lee et al. 2018).

Gastrointestinal complications are also common in rabbits undergoing anesthesia and surgery. Ileus may be caused by the stress and pain associated with anesthesia and surgical procedures, as well as by some anesthetic drugs, particularly alpha-2 adrenergic agonists and opioids. Studies comparing the effect on the gastrointestinal motility of opioid-based analgesic strategies with other analgesic protocols are lacking. The fear of causing drug-induced ileus should never, however, be a reason to withhold adequate analgesia for painful procedures. Additionally, the stress response associated with untreated pain can cause intense ileus. This may be harder to treat than drug induced ileus since both full μ opioids and alpha-2 adrenergic agonists are relatively short-acting and reversible. Reliance on multimodal analgesic strategies with less potential impact on the gastrointestinal motility, including the administration of ketamine, lidocaine, and nonsteroidal anti-inflammatory drugs (NSAIDs) and the use of regional anesthesia, are beneficial in rabbits.

Equipment and Monitoring

All the equipment and monitoring needed for rabbit anesthesia should be readily available prior to administering preanesthetic medication to ensure preparedness in case of an emergency.

These should include (Fig. 25.5):

- IV catheter placement supplies.
- Intubation equipment (tight-fitting face mask for preoxygenation and emergency ventilation, endotracheal tubes of multiple sizes, lubricant, local anesthetic for topical administration, laryngoscope/otoscope/endoscope, small size soft guide wire, gauze or tape to secure the tube).
- Previously pressure-checked anesthetic machine with either a nonrebreathing or a pediatric circle system, depending on the patient size. The machine should be checked for correct functioning prior to administration of anesthetic drugs. The vaporizer containing the agent of choice should be filled adequately.
- Emergency drugs available and their doses precalculated based on the animal's body weight.
- Heating devices (such as a warming blanket, Bair hugger® or hot dog®) available and functioning.
- Monitoring equipment.
  - Electrocardiogram (ECG).
  - Pulse oximeter.
  - Capnograph with low dead space (pediatric) adaptor, either sidestream microstream or mainstream.
  - Rectal thermometer or esophageal temperature probe.
  - Indirect blood pressure monitor (either doppler or oscillometric).



Figure 25.5 Anesthetized rabbit. Note the patient is intubated, has a cephalic catheter for vascular access, and has a sidestream capnograph, pulse oximeter probe, and ECG for monitoring.

- Anesthetic drugs and fluids.
- Anesthetic record.

Small-diameter endotracheal tubes are necessary when anesthetizing small rabbits. Usually, for animals weighing approximately 1–2.5 kg, uncuffed endotracheal tubes with an outer diameter of 2.0–2.5 mm are used. While positive pressure ventilation can be achieved with an adequately sized uncuffed endotracheal tube, some degree of anesthetic agent leaking should be expected. While this may be acceptable in most situations and in adequately ventilated rooms, the anesthetic protocol may need to be modified when using uncuffed endotracheal tubes in presence of susceptible individuals, and total IV anesthesia may be preferred in some cases.

Small-size endotracheal tubes are very prone to occlusion due to tube kinking or mucous secretions becoming lodged within the lumen. Endotracheal tube occlusion can be detected using capnography, and a partial obstruction should be suspected every time a shark fin waveform or failure to return to zero between breaths is seen. A complete obstruction results in rapid loss of the capnography waveform. Advanced respiratory monitoring, such as spirometry, can also be used to detect such complication.

If using mechanical ventilation, a sudden increase in the peak inspiratory pressure will trigger the maximum working pressure limit alarm, which will alert the anesthetist to

the possibility that there may be an occlusion. Whenever an obstruction is suspected, prompt troubleshooting should be performed. An obstructed endotracheal tube will make it hard to impossible to manually ventilate the patient, providing an additional clue when attempting to troubleshoot.

Complete orotracheal tube obstructions rapidly result in death and should therefore be addressed immediately and quickly. If the occlusion is due to endotracheal tube kinking, this is often visible in the extra oral portion of the tube, and more rarely it involves the intraoral and intratracheal portions. This problem can be easily resolved by correctly positioning the patient's head and the breathing circuit, and using supports to ensure the endotracheal tube sits straight and there is no weight applied to it that may cause kinking. When the occlusion is due to secretions lodged within the tracheal or endotracheal tube lumen, however, the problem may be harder to resolve. Soft suction tips of a diameter small enough that can be inserted within the lumen of the endotracheal tube can be used to remove soft secretions and should be available when anesthetizing rabbits. Suctioning, however, is often ineffective in removing very thick secretions such as thick mucous plugs. If suctioning is unsuccessful, an endotracheal tube exchanger or a small flexible metal wire can be introduced within the endotracheal tube lumen, prior to extubation, as a guide to quickly insert another endotracheal tube. If the secretion responsible for the airway occlusion is lodged within the tracheal lumen, changing the tube will not result in alleviation of the occlusion, and this scenario will likely result in death of the animal unless the material causing the occlusion can be suctioned out.

Nonrebreathing anesthetic circuits are best for very small patients as they are associated with minimal dead space and are lighter compared to circle systems. These circuits, however, rely on a relatively high fresh gas flow to ensure carbon dioxide removal. The best way to determine whether the fresh gas flow is adequate when using a nonrebreathing circuit is to use a capnograph and the inspired carbon dioxide should be zero.

Circle breathing systems can be used for larger rabbits. Although the dead space and resistance with these circuits are greater compared to nonrebreathing circuits, pediatric versions are available. These are associated with lower dead space and assisted ventilation will offset the increased resistance. Circle systems allow a reduction of the fresh gas flow, saving oxygen as well as anesthetic agent. As long as a capnograph is used to ensure there is no inspiration of carbon dioxide, either type of breathing circuit is adequate for use in rabbits.

If inspiration of carbon dioxide is detected while using a rebreathing circuit, adequate troubleshooting includes inspecting the inspiratory and expiratory valves, and ensuring the carbon dioxide absorbent is not exhausted. If these factors are not responsible for carbon dioxide inspiration, then an excessive dead space should be suspected. This could be addressed by cutting the extra oral portion of the endotracheal tube as close as possible to the patient's incisors and switching to a nonrebreathing anesthetic circuit.

ECG should always be monitored in anesthetized rabbits to ensure prompt detection of arrhythmias and sudden changes in heart rate. Placing the ECG leads prior to induction allows for prompt recognition of vagal responses that could be associated with intubation attempts. These may require prompt anticholinergic administration. Alligator ECG clips work best in rabbits, as there is no good way to use adhesive ECG patches without shaving their fur. Fur on the bottom of rabbit feet should not be shaved since it is important for preventing pododermatitis.

Pulse oximetry may be challenging to monitor, particularly for procedures involving the oral cavity. Pulse oximetry probes can be placed on the tongue, or on ears or paws in unpigmented animals, although they tend to slip or easily become displaced in rabbits. Surprisingly, the ears often make poor sites for the attachment of the probe. For invasive procedures or sick animals, it may be worth monitoring arterial blood gases periodically using an arterial catheter.

Oscillometric blood pressure readings may be inaccurate, particularly in hypotensive animals (Bellini et al. 2018). It appears mean blood pressure measurements are more accurate than systolic measurements using this method (Rodriguez et al. 2021). Some studies have shown systolic blood pressure measurements obtained with oscillometric devices or with Doppler might be subject to significant error (Barter & Epstein 2014), while others show good correlation between Doppler and direct blood pressure readings (Harvey et al. 2012). The accuracy of oscillometric blood pressure readings is improved by using high-definition devices and by placing the cuff distal to the elbow over the course of the brachial artery as opposed to distal to the tarsus (Calero-Rodriguez et al. 2021). The cuff width should be approximately 30% of the circumference of the limb.

Doppler probes for blood pressure measurement can be placed on the limbs, tail or ears. Arterial catheter placement may be warranted in sick animals or those undergoing long, invasive procedures. The most commonly used site for arterial catheterization in rabbits is the central auricular artery (Fig. 25.6). In small rabbits, 24- or 26-gauge catheters can be used for this purpose. Arterial catheterization allows for accurate blood pressure monitoring and arterial blood sampling. Since more accurate and real-time blood pressure changes can be assessed with this method,



Figure 25.6 (a) The ear of a domestic rabbit showing the relationship of the auricular artery (the large central vessel) and veins (the vessels along the edge of the ear). (b) Care should be taken to prevent injury of the auricular artery, which may lead to thrombosis and ischemic necrosis.

intervention is more prompt and better targeted to the changes observed. The catheter can be secured by using a roll of gauze or plastic syringe case inserted within the ear to support the tape. Significant hemorrhage may occur if the catheter and all the connections to the blood pressure transducer are not appropriately secured, tight, and frequently assessed. Arterial catheters can also be used for sampling purposes, which is particularly useful in long procedures and sick animals. Arterial blood gases not only allow assessment of the acid base, electrolyte, and ventilation status of the animal, but provide information on its oxygenation that can be used to adjust mechanical ventilation and establish whether the animal is likely to require oxygen support postoperatively.

In some cases of auricular arterial catheterization and monitoring, pinnal necrosis may ensue as a consequence of damage of the artery (Harcourt-Brown 2002) (Fig. 25.6b). One study in 18 Himalayan rabbits where arterial catheters were used identified three cases of necrosis of the pinna which occurred within 1 week after surgery (Hedenqvist et al. 2015). Two of these rabbits had also developed transient neurological signs during recovery from general anesthesia, and one showed a head tilt for 5 days postoperatively. These rabbits recovered from anesthesia, but necropsy was performed as part of the terminal study, which revealed a necrotic area in the cerebral cortex in the rabbit with head tilt (Hedenqvist et al. 2015). The authors suggested the use of saline as opposed to heparinized saline to flush the arterial lines in this study may have been a contributing factor to this problem. Although this study was not designed to evaluate the effects of arterial catheterization in rabbits, it highlights the importance of evaluating the risk/benefit ratio when performing arterial catheterization, particularly in small size rabbits.

Drug and Fluid Administration

Subcutaneous administration in the skin fold dorsal to the thorax or abdomen can be used to administer fluids and drugs. However, this route is not recommended for administration of anesthetic drugs as the absorption is slow and the onset time is unreliable.

The lumbar epaxial and quadriceps muscles can be used for intramuscular (IM) injections in rabbits. Good restraint is mandatory when performing IM injections in rabbits to minimize the risk of injury resulting from sudden movements. This route is preferred for sedative and hypnotic drugs administration, as it provides fast absorption and more reliable onset of the effects.

Vessels that can be used for venipuncture include the cephalic, saphenous, and lateral auricular veins (Fig. 25.6). Other vessels, including the jugular and femoral veins, can also be accessed if needed. Access to the jugular vein in

rabbits, however, is complicated because their necks are comparably short, redundant skin may impair visualization, and they have an inability to overextend their necks compared to other species. The presence of skin folds (dewlaps) on the neck of overweight animals, especially females, make palpation of the vessel virtually impossible. Ultrasound guidance or surgical cut-downs can be employed if needed in sick animals under heavy sedation or general anesthesia when jugular access is desired for blood draws or central line placement.

Moderate to profound sedation is generally necessary in healthy rabbits to successfully place IV catheters. The most commonly accessed vessels for indwelling catheter placement are the cephalic vein (Fig. 25.7), the lateral saphenous vein, and the lateral auricular vein (Fig. 25.6). The size of the catheters used varies in relation to the size of the animal, but a 24–26-gauge catheter is typically used in small rabbits, whereas a 22–24-gauge catheter is appropriate for larger rabbits. The cephalic and lateral saphenous veins are very superficial and short in small rabbits, which may make catheterization challenging. The lateral saphenous vein is usually visible, but fairly mobile, similar to other species. Catheters placed in the lateral auricular vein can be secured in place using a small roll of gauze placed inside the pinna with tape.

Postoperatively, conscious rabbits might be negatively affected by the weight of the catheter and bandage placed for auricular catheters, which might lead the animal to refuse to eat. Careful assessment of the risk/benefit ratio of maintaining the catheter in place versus removing it should be performed in such cases. The catheterized ear can be bandaged to the other ear if it is to be maintained in recovery.



Figure 25.7 The cephalic vein is readily catheterized with a 24-gauge over-the-needle catheter in a sedated or anesthetized rabbit.

The application of EMLA cream, a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine, to the catheter site might facilitate catheter placement in conscious or lightly sedated rabbits. This cream should be applied 30–60 minutes prior to attempting catheter placement, on clipped skin. Following the application, an occlusive bandage should be applied on the site. Rabbits can be subject to skin tears during clipping and care should be taken to avoid this occurrence. The application of scrub solution may sometimes lead to significant skin irritation in this species.

Intraosseous catheter placement can be performed either on the femur or tibia. The greater trochanter of the femur or the tibial crest should be used as landmarks during placement, and the catheter should be advanced in line with the medullary cavity of the bone. An 18–22-gauge intraosseous needle (spinal needle) can be used for this purpose in rabbits when IV catheter placement is unsuccessful. A stylet should always be used to prevent occlusion of the catheter lumen during placement. Intraosseous catheter placement requires heavy sedation or general anesthesia, and should be performed using a sterile technique. The application of a lidocaine bleb to the periosteum 5 minutes prior to intraosseous catheter placement is recommended. A small injection of saline should be used to test correct placement and little to no resistance to injection should be encountered. Correct intraosseous catheter placement can also be confirmed with a radiograph.

Preanesthetic Medication

Sedation prior to induction of general anesthesia is necessary in most rabbits to minimize stress and fear during handling, allow effective preoxygenation via a tight-fitting facemask, and facilitate a smooth induction of general anesthesia.

IV catheter placement is possible in most sedated rabbits, but occasionally heavily sedated animals continue to respond to attempts at catheter placement. In such cases, induction of general anesthesia using inhalants delivered with a facemask followed by orotracheal intubation might be a safer choice than adding higher dose sedative drugs. Catheter placement can then be performed after induction of general anesthesia. Apnea can occur following premedication, particularly in heavily sedated animals. Close monitoring of the breathing movement and readily available equipment for airway management and ventilation are imperative to control such complications.

Table 25.1 Drugs and dosages used for premedication in rabbits.

Class	Drug	Dose	Route	Comments
Alpha-2 adrenergic agonists	Dexmedetomidine Medetomidine Xylazine	15–30 μg/kg 30–60 μg/kg 0.5–5 mg/kg	IM, IV IM, IV IM, IV	Cause significant cardiovascular side effects. Use should be limited to healthy rabbits. Lower doses should be used IV. Higher doses are associated with more significant side effects.
Benzodiazepines	Diazepam Midazolam	0.5–1 mg/kg 0.5–1 mg/kg	IV IM, IV	Minimal cardiovascular side effects. Provide good sedation when associated with opioids, ketamine or alfaxalone. Diazepam results in erratic absorption following IM administration.
Dissociative anesthetics	Ketamine	5–40 mg/kg	IM, IV	Lower doses can be administered IV. Increases sympathetic tone. Association with alpha-2 adrenergic agonists or benzodiazepines is recommended for muscle relaxation.
Neurosteroids	Alfaxalone	2–6 mg/kg	IM, IV	May cause apnea, close respiratory monitoring is advised.
Phenothiazines	Acepromazine	0.1–1 mg/kg	IM, IV	Causes dose-dependent peripheral vasodilation. Do not use in animals with uncorrected hypovolemia.
Opioids	Butorphanol Buprenorphine	0.1–0.5 mg/kg 0.01–0.06 mg/kg	IM, IV, SQ IM, IV, IN	Full μ agonists are not commonly used in clinical practice due to concerns for gastrointestinal effects.

IM, intramuscular; IN, intranasal; IV, intravenous; SQ, subcutaneous.

Doses of commonly used premedication drugs in rabbits are summarized in Table 25.1.

Alpha-2 Adrenergic Agonists

These drugs provide reliable sedation, muscle relaxation, and analgesia as well as having minimum alveolar concentration (MAC) sparing properties. The most commonly used agent in small animal practice is dexmedetomidine. Alpha-2 adrenergic agonists may be used alone or in various combinations with opioids, ketamine, alfaxalone, and benzodiazepines. Although these drugs do not cause significant respiratory depression per se, their use in combination with other respiratory depressant drugs may exacerbate this effect. Cardiovascular side effects include significant reduction in cardiac output and bradycardia. There is also a biphasic effect on systemic vascular resistances, with an initial vasoconstriction followed by vasodilation. For this reason, the use of alpha-2 adrenergic agonists should be limited to healthy (ASA 1 or 2) animals.

IV catheter placement might be rendered more difficult following the administration of these agents due to marked vasoconstriction. Peripheral tissue perfusion can be impaired, making pulse oximetry challenging. Mucous membrane may assume a blue purple hue due to hypoperfusion. It is hard to differentiate from hypoxemia given the poor performance of pulse oximetry when alpha-2 adrenergic agonists are used. Gastrointestinal motility might be reduced following the administration of these agents.

Reversal of dexmedetomidine with atipamezole is effective at reversing its sedative effects. The cardiovascular side effects, however, might not be reversed and could even be exacerbated by the administration of alpha-2 adrenergic antagonists. The analgesic effects will also be reversed when administering antagonists, and when dissociative analgesics are administered in conjunction with alpha-2 adrenergic agonists, muscle stiffness and significant dysphoria might be triggered by reversal administration.

Benzodiazepines

Rabbits respond well to benzodiazepines and they provide good sedation, particularly when combined with other agents such as opioids, ketamine, and alfaxalone. They are

considered safe for compromised rabbits since they are not known to have marked cardiovascular side effects. Although inadequate sedation and excitation have been described in other species, these effects are not usually observed in rabbits. In addition to sedation, these agents provide muscle relaxation and antiepileptic effects, but are not analgesics.

Dissociative Anesthetics

These agents are commonly used as part of the premedication. When combined with other drugs, such as benzodiazepines or alpha-2 adrenergic agonists, they provide reliable sedation and facilitate handling and general anesthesia induction. These agents have sympathomimetic effects that might cause an indirect, dose-dependent increase in heart rate and blood pressure. Direct myocardial depressant effects, however, are also present, although they are usually masked by sympathetic stimulation. Dissociative anesthetics provide good analgesia mainly via antagonist effects on the NMDA receptors and have significant MAC sparing properties. Muscle stiffness may occur if these agents are administered alone. To offset this effect, they should be combined with drugs that have muscle relaxant properties, such as benzodiazepines or alpha-2 adrenergic agonists. High doses of ketamine cause a significant increase in intracranial and intraocular pressures, and their use should be avoided in patients with intracranial or intraocular disease.

Ketamine is the most commonly used dissociative anesthetic. Its duration is typically 15–30 minutes after a single injection. For prolonged analgesic effects, a constant rate infusion (CRI) should be used. A combination of ketamine and a benzodiazepine administered intramuscularly provides good sedation. As compared to combinations involving alpha-2 adrenergic agonists, it does not usually impair peripheral perfusion and thus facilitates IV catheter placement. Minor surgical procedures can be performed when this combination is used, although an alternative plan should be in place if the anesthetic plain is insufficient.

Telazol®, a combination of tiletamine and zolazepam, is not commonly used in rabbits. Reports of severe central tubular necrosis following administration of very high doses of tiletamine in New Zealand white rabbits exist (Brammer et al. 1991; Doerning et al. 1992). This concern is probably not applicable to the doses commonly used in clinical practice, although specific studies are lacking. Prolonged recoveries are common when Telazol® is used in other species.

Alfaxalone

This synthetic neuroactive steroid can be administered intramuscularly and provides good sedation, particularly when combined with other premedication drugs. It is typically administered at doses between 2 and 6 mg/kg IM, and can also be used intravenously as an induction agent.

Alfaxalone administration might cause mild hypotension. Its cardiovascular effects, however, are less significant than those observed with alpha-2 adrenergic agonists, making it a more suitable agent for use in sick rabbits. Apnea can occur following alfaxalone administration. Close monitoring of respiratory movements and the availability of equipment for airway management and ventilation equipment are essential when using this agent. To reduce adverse physiological effects alfaxalone, like propofol, should be given slowly IV to effect.

Acepromazine

As a phenothiazine tranquilizer, acepromazine usually provides less reliable sedation compared to alpha-2 adrenergic agonists, although a moderate sedative effect can be achieved when this agent is combined with opioids. Side effects include dose-dependent vasodilation and hypotension, therefore acepromazine should not be used in hypovolemic patients. Hypothermia, resulting from peripheral vasodilation, is also a common complication following acepromazine administration.

The doses of acepromazine reported in the literature for use in rabbits are generally very high. Due to concerns for dose-dependent side effects, the use of such doses is not recommended for clinical cases. A dose of 0.1 mg/kg in combination with butorphanol provides mild to moderate sedation in most rabbits. Acepromazine takes more than 15 minutes to reach peak effect, even when given intravenously. It also has its most profound effect if the patient is placed in a quiet and dark area for the onset of the drug's effects.

Opioids

Opioids provide good analgesia and some sedation, the latter effect being more evident when these agents are combined to sedatives or tranquilizers. Side effects include bradycardia, hypoventilation, and reduced gastrointestinal motility. Full μ-opioid agonists are more likely to cause side effects compared to partial agonists or agonist/antagonists. Due to significant concerns for perioperative ileus in rabbits, full μ agonists are seldom used in this species. A combination of fentanyl and fluanisone (hypnorm®) can be used for premedication, although this was more commonly used in the past. The administration of the opioid antagonists naloxone or naltrexone can be used to reverse such effects, but analgesia will also be reversed.

Butorphanol, a κ agonist and μ antagonist, or buprenorphine, a partial μ agonist, are most commonly used in this species, and their administration is less likely to be associated with gastrointestinal side effects. Their analgesic effect

is less profound compared to full μ agonists, and they should be used in conjunction with other pain management strategies for very painful procedures. Butorphanol also has a very short duration of effect (<3–4 hours) compared to buprenorphine (6–8 hours).

Anticholinergics

The routine use of anticholinergics as part of the premedication is no longer recommended. In the past these drugs were often incorporated in the premedication to prevent bradycardia and reduce airway secretion. However, tachycardia may result from routine administration of these agents, which could predispose the myocardium to hypoxia-induced arrhythmias. Moreover, although secretions are reduced when these agents are used, they are also thicker and more likely to cause airway obstruction. Anticholinergics also cause significant reduction in gastrointestinal motility, which might contribute to ileus in rabbits. For these reasons the routine use of anticholinergics as part of the premedication should be avoided.

These drugs, however, should be used promptly to treat bradycardia. Severe vagal responses are commonly observed in rabbits during induction of general anesthesia and intubation attempts. In such a scenario, the use of anticholinergics can be life saving.

Atropinase is present in some but not all rabbits, making atropine administration less effective. Although glycopyrrolate has a slower time to peak effect compared to atropine, the use of this agent might be more reliable in rabbits with high circulating levels of atropinase.

Induction

Drug combinations used for sedation and induction of general anesthesia frequently cause significant respiratory depression and hypoxemia, therefore oxygen supplementation via a tight-fitting facemask is necessary to reduce the risk of complications. It should be performed for at least 5 minutes prior to induction of general anesthesia. This is particularly important in rabbits, which often have difficult orotracheal intubations.

Heavily sedated animals, or those where hypnotics were used as part of the premedication protocol, may allow orotracheal intubation without any additional drug. Most frequently, however, additional drugs must be used to achieve induction of general anesthesia. Animals that despite being heavily sedated do not tolerate IV catheter placement might benefit from mask induction using inhalant anesthetics. This procedure may result in personnel exposure to halogenated agents, and precautions such as adequate room ventilation and use of a tight-fitting mask connected to a breathing circuit should be used to minimize personnel exposure when performing mask inductions. Rabbits frequently stop breathing when exposed to the pungent smell of isoflurane. Close monitoring of the respiration should be performed when using this agent for mask induction. Discontinuation of the administration and stimulation of the animal can work to encourage the animal to resume breathing, but quick airway control and manual ventilation might be necessary. Sevoflurane has a less pungent smell and is typically better tolerated for mask inductions. Being less soluble than isoflurane, it also provides a quicker induction, making it a more appealing choice for use in this species.

Chamber induction of unsedated animals is not recommended as it may result in significant stress for the animal. Moreover, inhalant administration is harder to titrate based on the patient's response, and monitoring equipment cannot be used during chamber induction.

Vagal responses are frequent and can be profound in rabbits during induction of general anesthesia. For this reason, close monitoring is advised in this phase. An ECG can be easily placed and is well tolerated in sedated rabbits. Sudden drops in the heart rate should be address promptly by administering an anticholinergic and discontinuing any anesthetic drug administration, if applicable.

Injectable anesthetics provide a more controlled induction and can be titrated to effect when administered intravenously, provided they are injected slowly. All induction agents (Table 25.2) have the potential to cause apnea, therefore airway management and ventilation equipment should be readily available. Combinations of ketamine (5–10 mg/kg IV) with a benzodiazepine (0.5–1 mg/kg IV), propofol (1–6 mg/kg IV) with or without ketamine (3–6 mg/kg IV), or alfaxalone (3–6 mg/kg IV) are most commonly used for induction of general anesthesia in rabbits.

Propofol and alfaxalone provide a smooth induction and good muscle relaxation, facilitating orotracheal intubation. However, they can cause hypotension and apnea, particularly when large doses are administered quickly. Slow administration of any induction agent minimizes cardiovascular and respiratory side effects and allows adequate titration and discontinuation of the administration when the desired effect is reached.

Airway Management

Obtaining and maintaining a safe airway for spontaneous and/or assisted ventilation is essential for general anesthesia in rabbits. Orotracheal intubation, however, is challenging. Their narrow oral cavity, limited mouth opening, big incisors, and prominent torus linguae impair visualization

Table 25.2 Induction agents and combinations used in rabbits.

Drug	Dose	Comments
Propofol	6–10 mg/kg IV	Administer slowly to effect. Higher doses might be needed in lightly sedated rabbits. May cause vasodilation and apnea if given too fast. Administer increments of 1–2 mg/kg at a time.
Propofol + ketamine	3–6 mg/kg of each, IV	Administer slowly to effect. Higher doses might be needed in lightly sedated rabbits. Less likely to cause hypotension than propofol alone.
Ketamine + midazolam or diazepam	5–10 mg/kg + 0.5–1 mg/kg IV	Administer to effect. Less likely to cause hypotension compared to propofol. May be harder to titrate to effect.
Alfaxalone	3–6 mg/kg IV	Administer to effect. Similar side effects to propofol. Can be combined with ketamine or a benzodiazepine.

IV, intravenous.

of the larynx. Many techniques have been described to intubate rabbits. They include blind and assisted methods for direct laryngeal visualization. Other strategies, such as the use of tight-fitting facemasks and laryngeal mask airways, are also sometimes employed for oxygen and anesthetic gas administration.

Rabbits have relatively small tracheas. Most dwarf species can be intubated with 2.0–2.5-mm uncuffed endotracheal tubes, while giant breeds can fit up to a 5-mm cuffed tube. Rabbit anatomy also puts them at high risk of bronchial intubation (Fig. 25.3). Their trachea is short and care should be taken to premeasure the endotracheal tube and advance it only 1–2 cm past the larynx, particularly in dwarf species. Reliance on thoracic auscultation to rule out bronchial intubation is often inaccurate, particularly in very small species. Referred respiratory noises can be heard on either side of the chest even when one lung is not being ventilated. Similarly, observation of symmetric chest movement during breathing may also be misinterpreted. Bronchial intubation (Fig. 25.2) should be suspected in animals showing signs of hypoxemia (low hemoglobin oxygen saturation despite assisted ventilation with a high fraction of inspired oxygen, increased respiratory rate, and abnormal breathing pattern) as well as high peak inspiratory pressure during volume-controlled mechanical ventilation. If bronchial intubation is suspected, the tube should be retracted slightly. To prevent accidental extubation during tube retraction, a guide wire can be introduced within the endotracheal tube lumen for use as an introducer should the endotracheal tube be accidentally removed.

Given the challenges with orotracheal tube intubation in rabbits, administration of oxygen via a tight-fitting facemask prior to induction and in between intubation attempts is strongly advised to mitigate the risks associated with hypoxemia. In emergency situations, tight-fitting face masks can be used to provide manual ventilation.

Rabbits are also prone to laryngospasm, particularly following multiple intubation attempts. The application of topical lidocaine 1–2 minutes prior to attempting intubation is advised in this species.

Capnography is essential to confirm correct orotracheal intubation (Fig. 25.8). Remarkably, a small amount of carbon dioxide can be present in the stomach and can be detected by the capnograph immediately after esophageal intubation. This may lead the operator to incorrectly assume orotracheal intubation was successful. In such cases, the carbon dioxide detected by the capnograph is usually lower than a normal $EtCO_2$, and tends to decrease quickly.

Endotracheal tube introducers/exchangers can be used to facilitate orotracheal intubation or replacement of a tube when tube obstruction is suspected. Due to the small size of the rabbit oral cavity and trachea, a flexible guide wire, such as those used for central line placement in small animals, or a small polypropylene urinary catheter are usually adequate for use in rabbit. It is important to keep in mind that although such guide wires and catheters are flexible, they are not designed as endotracheal tube introducers and carry the risk of airway injury. They, therefore, should be inserted gently and with care.

When attempting direct laryngeal visualization to achieve orotracheal intubation, the endotracheal tube itself may impair visualization in such a narrow oral cavity. Using a guide wire or catheter as tube introducer allows

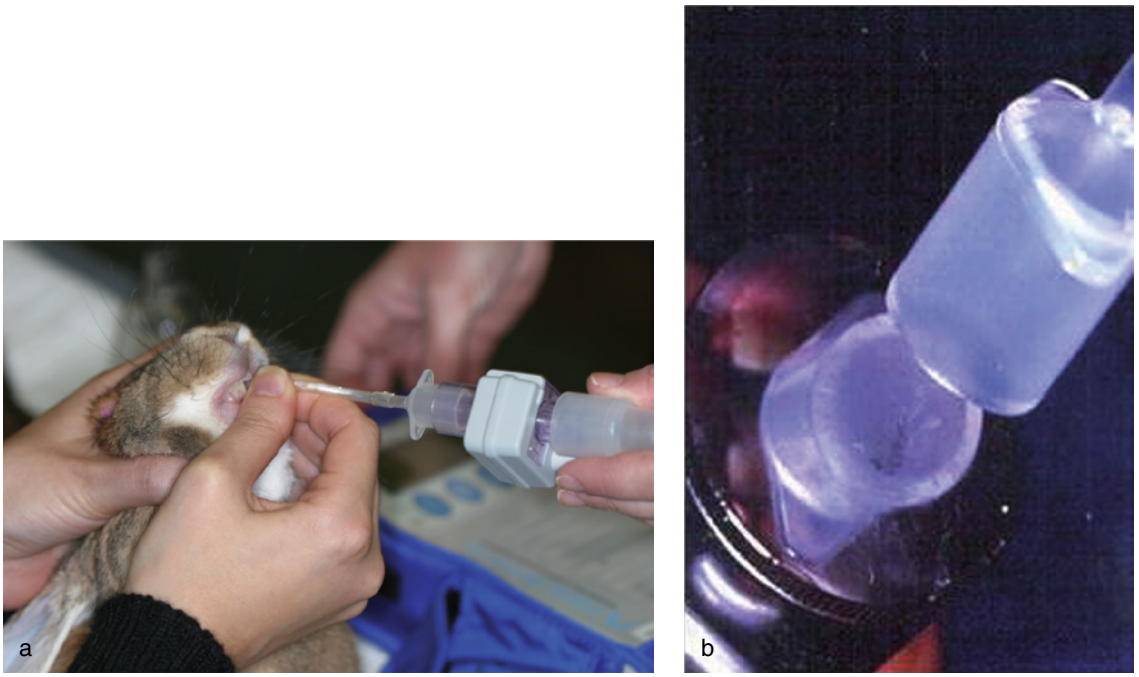


Figure 25.8 (a) Assessment of the correct positioning of the endotracheal tube in the trachea can be done either by visualizing condensation within the clear tube on exhalation or with the use of a capnograph. (b) Assessment of correct positioning of the endotracheal tube in the trachea can also be done by observing condensation on a metal surface, such as the bottom of a laryngoscope. Rabbit hair can also be placed over the end of the endotracheal tube to observe subtle air movement associated with breathing.

better visualization during insertion between the arytenoids, thus improving success rates. Gently extending the neck maximizes alignment between the oral cavity and the larynx, and is recommended when attempting orotracheal intubation. While overextension is often unnecessary, the operator attempting direct visualization should direct the helper holding the rabbit's head to a position that allows visualization. Due to the small size of the rabbit's oral cavity, a thin tie or string of folded tape should be used to open the mouth while direct laryngeal visualization and intubation are attempted, as the helper's fingers holding the mouth open will inevitably impair visualization. The tongue should be pulled gently outside of the mouth to displace it and maximize visualization of the larynx. Some operators prefer dorsal recumbency when incubating rabbits and claim it provides better airway visualization.

Orotracheal tube obstruction as a result of airway secretion may occur in rabbits, particularly given the small size of the endotracheal tubes employed. This complication can be suspected when a shark fin capnograph waveform is observed. With complete obstructions there will be an absence of an expired carbon dioxide wave. If an obstruction is suspected, prompt suctioning within the endotracheal tube should be performed. Flexible suction catheters of small enough diameter to fit within the lumen of the endotracheal tube should be readily available when anesthetizing rabbits. If the obstruction cannot be resolved with suctioning, the endotracheal tube should be promptly replaced using a tube exchanger.

Techniques for Tracheal Intubation in Rabbits

Blind Technique

This relies on the subjective assessment of the operator, who listens to breathing sounds while advancing the tube within the airways. It is performed by gently extending the neck and slowly advancing the tube in the oral cavity while listening to breathing sounds at the connector end of the endotracheal tube (Figs 25.9, 25.10, and 25.11). Breathing sounds are loudest when the tube is in proximity of the larynx. If breathing sounds can no longer be heard while the tube is advanced, this indicates that the tube is placed in the esophagus, and it can be often palpated in the ventral neck. If the tube is advanced within the trachea, breathing sounds keep being heard at the connector end. Rabbits sometimes cough as the tube is advanced within the trachea. Some operators use a small amount of fur and hold it in front of the tube to observe its movements in correspondence with inspiration and expiration. Condensation within the tube, on a glass slide, or on the bottom of the laryngoscope handle can also be used as an indirect assessment of correct tube placement. Synchronized movement



Figure 25.9 For blind intubation it is unnecessary to open the jaws. Once the rabbit is unconscious and relaxed, the endotracheal tube is introduced through the space between the incisors and first premolars, and passed over the base of the tongue.



Figure 25.10 For endotracheal intubation it is usually necessary to alter the normal angle between the oral cavity and trachea (Fig. 25.1). Regardless of technique used, the head and neck need to be hyperextended. Heard (pers. comm.) prefers the animal to be in sternal recumbency for this positioning. Others either extend the head neck out along the table or intubate the dorsally recumbent rabbit.



Figure 25.11 Blind intubation requires listening for respiratory noise to identify the positioning of the endotracheal tube. The loudest noise indicates the tube is aligned and close to the laryngeal opening. If the noise goes away during positioning, it indicates the tube is likely in the esophagus and it should be gently pulled back until respiratory sounds are again identified. When peak respiratory noise is attained, a small volume of local anesthetic (2% lidocaine) can be introduced into the tube and blown down into the glottis to further facilitate intubation.

of the reservoir bag with respiration can normally be seen. A capnograph is the best and most reliable indicator of correct endotracheal tube placement.

Some well-trained operators have good success rates at blind intubation in rabbits. However, because this is a blind, subjective technique, it is inherently prone to errors and should be performed with care, particularly by inexperienced operators.

Multiple intubation attempts carry a significant risk of laryngeal or tracheal trauma and might trigger laryngospasm. Accidental aspiration of the endotracheal tube has been reported in many species, including rabbits (Yan et al. 2021). This complication is more likely to result in death of the animal in rabbits due to the difficulty in retrieving the tube, given the small size of the oral cavity and airways. Care should be taken to ensure orotracheal tubes are well secured at all times. Ties should be applied directly to the tube as opposed to the connector (Yan et al. 2021).

Laryngoscope

A size 0 or 1 Wisconsin or Miller laryngoscope blade is typically used for intubation (Fig. 25.12a). Alternatively, a specifically designed Flecknell laryngoscope can be

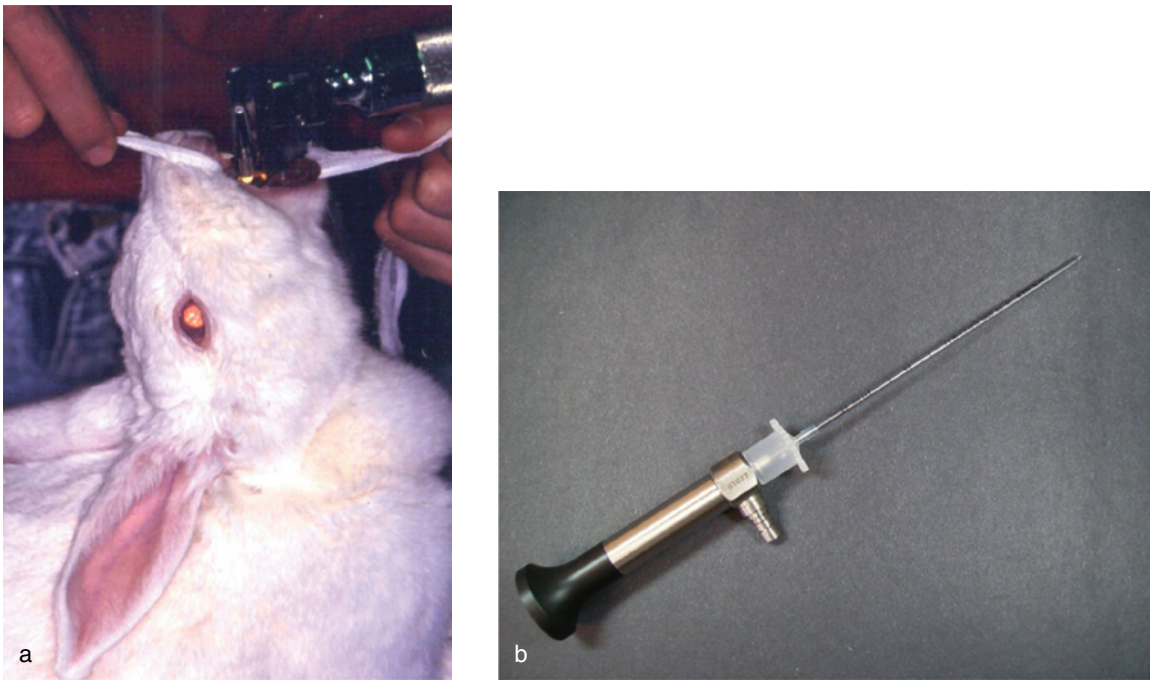


Figure 25.12 (a) Direct visualization techniques require the head and neck to be hyperextended, as for the blind technique. In this animal, a small pediatric straight laryngoscope is being used to visualize the glottis. A guide wire or catheter will facilitate tube placement using this technique. (b) An alternative direct visualization technique for orotracheal intubation uses an endoscope. The tube is placed on the outside of the semirigid endoscope, then guided into the larynx once the glottis is visualized. This is an example of a relatively inexpensive semiflexible 1.9-mm scope with a 2-mm uncuffed endotracheal tube. A small amount of water-soluble lubricant placed on the scope will facilitate pushing the tube off the scope once in the correct position. Antifogging liquid can be placed on the lens to improve visualization. In general, always direct the scope towards the "dark" areas at the back of the throat to displace the soft palate and visualize the glottis (Fig. 25.8).

employed. Even these very small blades can sometimes be too large compared to the rabbit's small oral cavity, particularly in dwarf breeds. A tube introducer can facilitate orotracheal intubation in cases when the larynx is barely visible. Attempting direct placement of the endotracheal tube in such cases is challenging as the tube itself may impair visualization of the larynx. Several flexible stylets or guide wires can be used to facilitate intubation in rabbits. The characteristics of a tube introducer should be: (1) diameter small enough to fit within the lumen of the endotracheal tube and allow for easy threading of the tube; (2) material flexible enough to minimize the risk of airway and oral cavity damage; and (3) material rigid enough that the introducer can be guided through a small airway opening. The author routinely uses guide wires obtained with a small animal central line kit. Alternatively, thin polypropylene urinary catheters can be used.

Otoscope

The advantage of using an otoscope for direct laryngeal visualization in rabbits is that it is suitable even for smaller patients, provided a small enough cone is used. Due to the small visual field afforded by an otoscope, it is sometimes difficult to identify the anatomical landmarks to perform intubation. However, by slowly moving the otoscope it is easy to visualize the glottis, which is most commonly seen covered by the soft palate. The arytenoids become visible by gently displacing the soft palate. A tube introducer (small flexible guide wire or catheter) can be gently guided within the trachea under direct visualization. Once the introducer is correctly positioned, the otoscope can be removed and the endotracheal tube can be introduced within the trachea. The introducer can be threaded either within the lumen of the tube or within its Murphy eye, when present. Slight resistance is normally encountered when advancing the tube through the larynx. Sometimes small changes of the position of the head facilitate tube insertion. A smaller tube should be used if resistance continues to be encountered, while keeping the previously inserted introducer in place.

Endoscope

An endoscopic-guided technique has been described to facilitate intubation in rabbits (Fig. 25.12b) (Tran et al. 2001). Size 1.9-mm semirigid endoscopes are available and suitable for use in small rabbits. The endoscope itself is small enough to be used as a stylet, and the tube

can be inserted under direct endoscopic visualization. One big limitation of this tool, beyond the elevated cost, is its rigidity, which may cause significant airway injury if used inappropriately, therefore maximum caution and gentle movement should be employed when using this equipment. The advantage is that this endoscope allows airway visualization even in very hard to intubate rabbits, making it a very desirable option to have available as back-up when other techniques fail. Condensation obscuring visualization can be reduced using antifogging liquid or soap.

Smartphone-operated Endoscope

These inexpensive and widely available devices have been used to allow direct airway visualization in rabbits. Although some practitioners anecdotally report good success rates when using this technique, a study comparing it to blind intubation performed by veterinarians experienced in rabbit intubation could not identify a benefit of using it (Saldanha et al. 2020). These devices are typically hard to maneuver and subject to condensation and clouding. Their diameter does not allow for use as tube introducer, therefore the tube has to be inserted laterally to the endoscope, making this technique technically challenging. Introducing both the endoscope and the endotracheal tube within the oral cavity may not be possible in small rabbits (Saldanha et al. 2020).

Retrograde

Retrograde endotracheal intubation is performed in small animal practice when orotracheal intubation is impossible or unsuccessful. This technique has been described in rabbits and performed via a small cervical incision to allow visualization of the trachea (Corleta et al. 1992). A needle can be used to puncture the trachea and insert a guide wire, which is then gently threaded towards the mouth. When the guidewire exits the oral cavity, it can be used as a tube introducer to guide the tube in the trachea. Although no complications were identified with this technique in one study (Corleta et al. 1992), preference should be given to less invasive techniques in routine cases.

Nasotracheal Intubation

Nasotracheal intubation is possible in rabbits and might be useful in cases requiring full access to the oral cavity, such as dentistry procedures. However, this technique requires a much smaller endotracheal tube, which is more prone to obstruction. Nasal hemorrhage due to turbinate damage is also common with this technique.

Laryngeal Mask Airways (V-gel®)

Specifically designed supraglottic airway devices (SADs) called V-gel® are available for use in rabbits (Fig. 25.13).

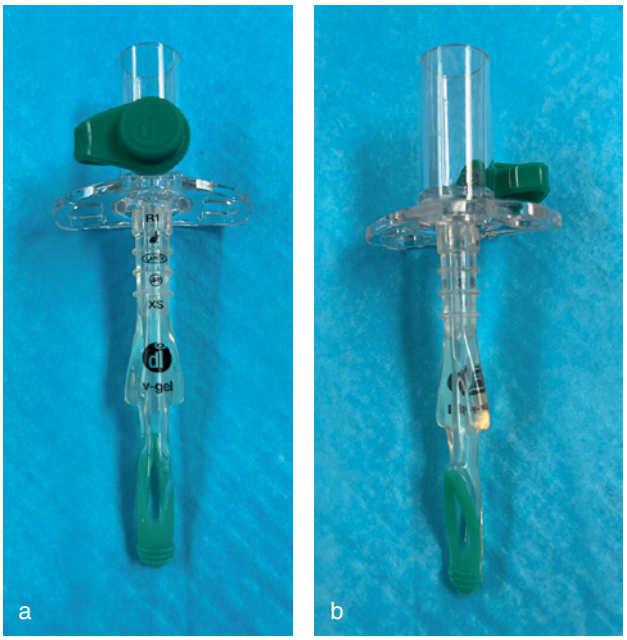


Figure 25.13 (a) and (b) A commercially available laryngeal mask (V-gel®). These can be used to rapidly obtain an airway, but can be dislodged. It is essential that a capnograph be used with these artificial airways to ensure there is no occlusion.

These devices are easy to place, are available in different sizes, and can be used to provide oxygen and anesthetic gases and positive pressure ventilation (Engbers et al. 2017). When compared to blind or endoscopy guided orotracheal intubation, SADs take less time to place and are associated with less orotracheal damage (Engbers et al. 2017; Comolli et al. 2020). However, they are prone to displacement and can cause complete airway obstruction when that occurs. Displacement is more likely to occur when the rabbit is moved during anesthesia. For this reason, SADs should always be used in conjunction with a capnograph. Should the capnograph show any sign of partial airway obstruction, visible as a shark fin waveform, or total obstruction, visible as sudden loss of expired carbon dioxide, the V-gel® should immediately be repositioned or removed. Although SADs can be used for positive pressure ventilation, gastric distension may occur due to incomplete seal of the esophagus, particularly when high peak inspiratory pressures are reached (Bateman et al. 2005). Migration of the V-gel® tip in the laryngeal vestibulum can occur and cause reduction of the airway cross-sectional area (Engbers et al. 2017; Wenger et al. 2017).

One study evaluated the feasibility of using a V-gel® to facilitate orotracheal intubation in rabbits (Fusco et al. 2021). This was achieved by using a polypropylene urinary catheter as a guide or by inserting the endotracheal tube directly in the lumen of the V-gel®, and resulted in good success rates. It is worth noticing that the studies

evaluating the safety of V-gel® devices were performed in New Zealand white rabbits. Care should be taken when extrapolating the results obtained in giant breeds to the population of rabbits typically seen in practice, which most commonly includes dwarf, brachycephalic breeds. In the author's opinion, these devices are useful as an emergency back-up when endotracheal intubation cannot be achieved, and are better suited for short procedures and uncomplicated cases that do not require any changes in positioning of the animal.

Nasal Catheters

Nasal catheters can be used to provide oxygen supplementation when a face mask is unpractical, for example for brief oral examinations or uncomplicated dentistry procedures. They may also be used to provide oxygen postoperatively to compromised animals. Soft nasogastric tubes (3–4 French) can be used for this purpose and introduced in sedated animals. The application of a small amount of topical lidocaine gel will facilitate placement and reduce discomfort.

Maintenance of General Anesthesia

Maintenance of general anesthesia in rabbits can be achieved with a multitude of drugs and combinations. Intubated rabbits can be given inhalant anesthetics and although uncuffed endotracheal tubes are typically used in rabbits, contamination of the environment and personnel exposure is usually minimal. A correctly sized V-gel® also provides good seal and can be used for inhalant administration during brief and uncomplicated procedures. Inhalant administration for prolonged periods of time using a face mask, although common practice, should be avoided because a perfect seal is hard to achieve, which inevitably results in personnel exposure to anesthetic agents.

Isoflurane is the most commonly used inhalant anesthetic in small animal practice. The MAC of this agent in rabbits is in the range of 2–2.4% (Drummond 1985; Valverde et al. 2003; Turner et al. 2006a; Gianotti et al. 2012), which is significantly higher than the MAC reported in most other species. Isoflurane has a pungent smell that frequently triggers apnea in rabbits. Sevoflurane, on the other hand, has a less pungent smell and is usually better tolerated in sedated animals for mask induction. The MAC of sevoflurane in rabbits is between 3.7 and 4.1% (Scheller et al. 1988; Yin et al. 2012), which is also significantly higher than most other species. Sevoflurane has a lower blood:gas partition coefficient than isoflurane, which promotes a faster onset and clearance. This characteristic makes sevoflurane a more desirable choice for mask induction, and allows for easier titration of the anesthetic depth and faster recoveries, which are desirable in compromised animals.

Common side effects observed with halogenate anesthetics include vasodilation, reduction in cardiac contractility, and subsequent hypotension. The administration of sympathomimetics is often necessary to offset these effects. The addition of premedication drugs, opioids, or CRIs typically has a MAC sparing effect on the inhalants, which contributes to reducing side effects.

Total or partial IV anesthesia is possible in rabbits and can be achieved with a variety of drug combinations. Propofol CRI can be used alone or in combination with other injectable agents at a dose of 20–80 mg/kg/h. It is important to notice that accumulation will occur over time if the dose is not adjusted, which may lead to prolonged recoveries. Alfaxalone CRI can also be used, but recoveries with this drug tend to be poorer compared to propofol. A protocol involving the use of midazolam and sulfentanil for total IV anesthesia has also been investigated and provided good-quality anesthesia in rabbits undergoing ovariohysterectomy and premedicated with medetomidine (Hedenqvist et al. 2015).

Analgesia

The addition of analgesics as part of the premedication or during maintenance of general anesthesia allows for reduction of the doses of anesthetic drugs, thus limiting their side effects. Because full μ-opioid agonists may cause gastrointestinal ileus in rabbits, other strategies are usually preferred in this species. It is important to notice that while ileus is a significant concern in rabbits, it should never be a reason to withhold the administration of analgesics, as uncontrolled pain and subsequent stress response have the potential to cause even more significant and harder to treat ileus.

Drugs commonly used for pain management in rabbits are listed in Table 25.3.

Pain evaluation in rabbits is challenging. As pray species, rabbits evolved to hide pain. Subjective pain evaluation is prone to errors, and the lack of a gold standard and objective methods to measure pain may lead to under- or overdosing of analgesics. Physiologic changes occurring in relation to pain, such as tachycardia and tachypnea, are commonly observed with stress, fear or disease, such as infection. Most rabbits will show tachycardia and tachypnea when being handled, making the assessment based on these parameters extremely challenging. Loss of body

Table 25.3 Analgesic drugs for use in rabbits.

Drug	Dose	Route	Duration	Comments
Butorphanol	0.1–0.5 mg/kg	IV, IM	2–4 hours	Questionable analgesic effect
Buprenorphine	0.01–0.06 mg/kg	IV, IM, IN	6–8 hours	Use in conjunction with other strategies for very painful procedures.
Lidocaine	2 mg/kg bolus followed by 3–6 mg/kg/h CRI	IV	10–20 minutes after a single bolus	Reduce doses during prolonged CRIs.
Ketamine	1 mg/kg bolus followed by 2–5 mg/kg/h CRI	IV	10–20 minutes after a single bolus	Reduce doses during prolonged CRIs. Discontinue or reduce doses 20–30 minutes prior to recovery to avoid dysphoria.
Dexmedetomidine	3.5 μg/kg/h	IV	20–40 minutes after a single bolus	Loading dose may not be needed in rabbits premedicated with dexmedetomidine. Can cause ileus.
Carprofen	2–4 mg/kg	IV, SC, PO	12–24 hours in other species	PK/PD studies are lacking in rabbits.
Meloxicam	0.6–1 mg/kg	IM, SC, PO	24 hours	Chronic administration is well tolerated.

CRI, constant rate infusion; IM, intramuscular; IN, intranasal; IV, intravenous; PD, pharmacodynamic; PK, pharmacokinetic; PO, per os; SC, subcutaneous.

weight as a consequence of decreased appetite is commonly seen in rabbits with chronic pain (Cooper et al. 2009; Goldschlager et al. 2013). Although this sign is common in rabbits as a consequence of disease, possible untreated pain should be suspected in rabbits showing weight loss in association with a painful condition. Behavioral changes are considered a more reliable indicator of pain in nonverbal species. Rabbits commonly show decreased movements and activity, unwillingness to explore the environment, as well as decreased fecal output after surgery (Weaver et al. 2010; Farnworth et al. 2011). Increased grooming on the surgical area and flinching may also be observed (Farnworth et al. 2011). Pain scales have been developed in several species to provide a more objective tool for pain evaluation. A grimace scale, using changes in facial expression as a tool to assess pain, has been developed for rabbits (Keating et al. 2012; Hampshire & Robertson 2015). Although pain scales can provide a more objective tool for pain assessment in rabbits and other animals, surveys indicate they are seldom used as part of the pain assessment in veterinary practice (Weber et al. 2012; Hunt et al. 2015) and laboratory settings (Bradbury et al. 2016).

Butorphanol, a κ agonist and μ antagonist, as well as buprenorphine, a partial μ agonist, are most commonly used in this species. Among full μ agonists, a fentanyl and fluanisone combination is used for research rabbits (Hexeberg et al. 1995). However, clinical studies regarding the analgesic effects of this combination and the effects on the gastrointestinal motility are lacking. Although other full μ opioid agonists have been anecdotally used in clinical practice (Benato et al. 2019), studies evaluating their safety, recommended dosing regimen, and analgesic effects in this species are lacking. It is unknown if and to what extent clinical doses of full μ-opioid agonists affect the gastrointestinal motility in rabbits, and the gastrointestinal effects associated with the administration of full μ opioids can be reversed with opioid antagonists in other species (Yuan et al. 1997). However, most practitioners tend to err on the side of caution and these agents are seldom used for rabbits in clinical practice.

Although butorphanol has been shown to have MAC sparing effects in rabbits (Turner et al. 2006a), its analgesic properties are questionable (Hedenqvist et al. 2002). It is most commonly used at a dose of 0.1–0.5 mg/kg and it lasts 2–4 hours (Benato et al. 2019). Generally speaking, butorphanol is considered appropriate for mildly painful procedures, but other strategies should be preferred for animals undergoing invasive surgery.

Buprenorphine, a partial μ-opioid agonist, provides better analgesia compared to butorphanol in other species. It is used at a dose of 0.01–0.06 mg/kg in rabbits and lasts 6–10 hours (Benato et al. 2019). It is most commonly used IV or IM, as well as intranasally (Lindhardt et al. 2001). Subcutaneous and oral transmucosal routes of administration are considered less reliable (Freijs & Kannin 2016). Its analgesic effects in rabbits are questionable.

While buprenorphine, administered in combination with meloxicam, appeared appropriate to provide analgesia in rabbits undergoing surgical cut-down of the femoral artery (Goldschlager et al. 2013), it was inadequate to control pain following orthopedic surgery (DiVincenti et al. 2016; Hedenqvist et al. 2016). Preemptive buprenorphine administration attenuated the cardiovascular response to a visceral noxious stimulus in conscious rabbits (Shafford & Schadt 2008). Some evidence suggests that buprenorphine does not alter the gastrointestinal motility in rabbits (Cooper et al. 2009; Goldschlager et al. 2013; Deflers et al. 2018). However, one study showed that buprenorphine decreased the gastrointestinal transit time, and this effect could not be reversed with the administration of methylnaltrexone (Martin-Flores et al. 2017).

The addition of drugs other than opioids to the pain management strategy is particularly beneficial in rabbits given theoretical concerns with opioid administration. Drugs that provide alternative mechanisms of action may be combined and used to achieve multimodal analgesia.

Lidocaine is a local anesthetic that can also be administered intravenously, contributing to systemic analgesia. It works by blocking the sodium channels, leading to reversable blockade of action potential propagation. Lidocaine lasts 10–20 minutes following administration of a single IV bolus, therefore a CRI is needed for prolonged analgesic effect. Lidocaine is also an IV class 1B antiarrhythmic, frequently used to treat ventricular arrhythmias. However, high doses of lidocaine can lead to cardiac and neurotoxicity, and care should be taken when this drug is administered as a CRI for prolonged periods of time because this may lead to significant accumulation. Possible anti-inflammatory and prokinetic effects of lidocaine administration have been investigated in other species (Cook et al. 2009; Torfs et al. 2009), although the existing evidence in this regard is conflicting (Salem et al. 2016). In rabbits undergoing ovariohisterectomy, lidocaine CRI provided comparable postoperative analgesia to buprenorphine and better outcomes in terms of fecal output and food intake (Schnellbacher et al. 2017). In this study, lidocaine was administered at a dose of 6 mg/kg/h for 2 days with no reported complications. Lower doses may be sufficient to provide analgesia, although specific studies are still lacking. A 20–21% reduction in the MAC of isoflurane was documented with the use of 2 mg/kg lidocaine bolus followed by a 3–6 mg/kg/h CRI in rabbits, with the higher dose resulting in a larger MAC sparing effect (Schnellbacher et al. 2013).

Ketamine is a widely used anesthetic and analgesic drug in small animal practice. Although it has several mechanisms of action, it appears to achieve most of its analgesic effects via blockage of the NMDA receptors, which are upregulated in association with chronic and neuropathic pain. Ketamine has no known effects on the gastrointestinal motility in other species (Fass et al. 1995). Studies assessing the analgesic effects and optimal dosing regimen of this agent in rabbits are lacking. However, the author routinely uses ketamine CRI at a dose of 2–5 mg/kg/h as part of a multimodal anesthetic regimen in rabbits. To prevent dysphoria during recovery, ketamine administration should be discontinued or the dose drastically reduced at least 30 minutes prior to recovery. A ketamine bolus of 1 mg/kg IV followed by 2.4 mg/kg/h CRI decreased the MAC of isoflurane from 2.1% to 1.6% (Gianotti et al. 2012).

Dexmedetomidine can also be used as a CRI to provide analgesia and MAC sparing effects. In dogs, the analgesia achieved with the administration of a dexmedetomidine CRI was comparable to that achieved with the administration of morphine for the management of pain associated with invasive surgery (Valtolina et al. 2009). Although the analgesic effects of dexmedetomidine administration were not evaluated in rabbits, when this drug was administered as an infusion (30 μg/kg/h for 10 minutes followed by a CRI of 3.5 μg/kg/h) it was associated with a 33% MAC reduction (Terada et al. 2014). Dexmedetomidine is associated with well-documented reduction in the gastrointestinal motility in mice and other species, even following a single bolus given for sedation (Chang et al. 2020). For this reason, this drug should be administered judiciously in rabbits, particularly those with preexisting ileus. The effects of alpha-2 adrenergic agonists on gastrointestinal motility can be reversed with the administration of alpha-2 adrenergic antagonists (Heikki et al. 1993). However, the analgesic and sedative effects will also be reversed.

NSAIDs have analgesic, antipyretic, and anti-inflammatory properties. They should not be used in rabbits with conditions associated with compromised organ perfusion, gastrointestinal ulceration, hepatic or renal disease. Meloxicam and carprofen are the most commonly employed NSAIDs in rabbits. Carprofen is administered subcutaneously, intravenously, and orally at doses of 2–4 mg/kg in rabbits, although specific pharmacokinetic studies are lacking. One study showed that when carprofen was administered at a dose of 5 mg/kg in conjunction with buprenorphine for postoperative pain in rabbits, grimace pain scale scores were not improved compared with the use of buprenorphine alone (Hedenqvist et al. 2016). Several studies have been performed evaluating the pharmacokinetic and pharmacodynamic profiles of meloxicam in rabbits (Turner et al. 2006b; Leach et al. 2009; Goldschlager et al. 2013; Fredholm et al. 2013). Meloxicam can be administered intramuscularly, subcutaneously, and orally at a dose of 0.6–1 mg/kg (Benato et al. 2019). Chronic administration of 1 mg/kg for up to 29 days was well tolerated and resulted in no obvious side effects (Delk et al. 2014).

Selected Regional Anesthesia Techniques in Rabbits

Regional anesthesia consists of the administration of local anesthetics, with or without additives, to block the conduction of pain stimuli from a specific area of the body. Although regional anesthesia is widely used to provide perioperative analgesia in small animal practice, only a few techniques have been published in rabbits. The difficulty with pain assessment in this species, combined with the concerns related to possible effects on gastrointestinal motility with some analgesic drugs, make the addition of regional anesthesia particularly appealing in this species. When performed correctly, regional anesthesia is safe and very effective at eliminating the sensation of pain. In contrast with systemic analgesics, which act by modulating the transmission of the painful stimulus, regional anesthesia works by completely interrupting the nerve conduction from the affected area of the body. As such, regional anesthesia is typically more effective at controlling pain compared to systemic analgesics. Additionally, systemic side effects associated with analgesics, including sedation and decreased gastrointestinal motility, can be eliminated by the use of regional anesthesia. Long-lasting local anesthetics, such as bupivacaine and ropivacaine, are most commonly used in small animal practice and can provide up to 10–12 hours of analgesia. Even after the effect of the block is gone, pain is typically easier to control than when a block is not used. Although some simple blocks can be performed blindly (i.e., by relying on anatomical landmarks), objective methods to approach specific nerves, such as nerve stimulator or ultrasound guidance, are preferred for most techniques and are commonly implemented in small animal practice. Blind techniques are prone to error and have a lower accuracy and success rate compared to those relying on ultrasound or nerve stimulator guidance. High-frequency (13 mHz) linear transducers are needed for most regional anesthesia techniques.

Clinicians should be familiar with signs of local anesthetic toxicity when implementing these techniques in clinical practice. Treatment of possible local anesthetic toxicity with lipid solution should be available.

Specific studies evaluating the toxic doses of local anesthetic in rabbits are lacking. Clonic seizures and tremors were triggered by subcutaneous administrations of 9 mg/kg of bupivacaine in rabbits (Richard et al. 2011). A maximum bupivacaine dose of 3 mg/kg is commonly used in small animal practice. It is important to notice that systemic administration of lidocaine in animals that received a block may trigger local anesthetic toxicity and should be avoided.

Dexmedetomidine is commonly combined with bupivacaine at a dose of 1 μg/mL and it is thought to increase block duration and effectiveness. While epinephrine is sometimes used to prolong block duration when lidocaine is used, this strategy is more rarely used with long duration regional anesthetics (i.e., bupivacaine and ropivacaine), which are more commonly used in practice. Although onset time is quicker with lidocaine compared to bupivacaine, this difference is in the order of a few minutes and is therefore unlikely to be clinically relevant in most clinical scenarios. Cardiotoxicity may occur when bupivacaine (and to a lesser extent ropivacaine) are injected intravenously. For this reason, the extravascular position of the tip of the needle should always be confirmed with a negative aspiration test prior to injecting a local anesthetic. No resistance should be encountered when injecting local anesthetics because a high resistance to injection may indicate that the tip of the needle is positioned within the nerve. If resistance to injection is encountered, the injection should be immediately discontinued and the needle should be repositioned.

Sharp hypodermic needles carry significant risk to cause nerve damage and should never be used to perform nerve blocks. Insulated and/or echogenic regional anesthesia needles, or spinal or Tuohy needles should be used for regional anesthesia. Being short beveled, they are blunter compared to hypodermic needles, making them a safer choice for injections around nerve structures. All regional anesthesia techniques should be performed aseptically.

Maxillary and Mandibular Blocks in Rabbits

Maxillary Nerve Block Guided by Anatomical Landmarks

This block is performed by introducing the needle ventral to the zygomatic arch in line with the lateral canthus of the eye (Otero & Portela 2019) or 2–3 mm caudal to the facial tuber (Pena et al. 2020) and advancing it towards the pterygopalatine fossa until bone contact with the alveolar bulla can be perceived. The needle should then be slightly withdrawn. The recommended volume of local anesthetic is 0.05–0.1 mL/kg administered using a 24-gauge spinal needle. The expected area of anesthesia includes the maxilla and associated soft tissue, hard and soft palate, upper dental arch, upper lip, and nostril.

Mandibular Nerve Block Guided by Anatomical Landmarks

This approach is performed by inserting the needle medially to the mandible, on the ventral aspect of the mandibular notch, and advancing it cranially while directing it towards the medial aspect of the mandible (Otero & Portela 2019). The recommended volume of local anesthetic

is 0.05–0.1 mL/kg administered using a 22-gauge, 1.5-inch spinal needle. The expected area of anesthesia is the mandible and associated soft tissue, lower dental arch, and lower lip.

Infraorbital Nerve Block

Neuropraxia was described in a rabbit following infraorbital nerve block using a hypodermic needle (d'Ovidio & Adami 2021). This nerve occupies most of the infraorbital canal in rabbits (Pena et al. 2020), making it prone to nerve damage when a needle is introduced within the canal. For this reason, the subzygomatic approach to block the maxillary nerve should be preferred in this species.

Ultrasound-guided Periconal Ocular Block

This technique has been described in rabbits (Najman et al. 2015; Otero & Portela 2019) and is performed by injecting local anesthetic in the extraconal space. It is suitable for use in animals undergoing enucleation. A linear ultrasound transducer is positioned on the supraorbital rim to visualize the globe of the eye, the muscular cone, the optic nerve, and the periconal space. A 22-gauge, 1.5-inch spinal needle is then introduced in the plane (i.e., parallel to the long axis of the transducer) on the lateral aspect of the inferior orbital rim, and visualized as its tip is advanced in the periconal space, until it is positioned outside, but in proximity to the muscular cone. After a negative aspiration test, the local anesthetic is injected and is visualized as it distributes in the periconal space. The recommended volume of local anesthetic is 0.05–0.1 mL/kg. The expected area of anesthesia is the globe of the eye, cornea, conjunctiva, and eyelids. This technique requires a high-frequency (13 mHz) linear transducer.

Auricular Nerve Blocks

Blocks of the greater auricular and auriculotemporal nerves have been described in rabbits and can be used for total ear canal ablation and lateral or ventral bulla osteotomy.

The greater auricular nerve provides innervation to the pinna and vertical ear canal, whereas the auriculotemporal nerve provides innervation to the medial horizontal ear canal. Both blind and nerve stimulator-guided techniques to block these nerves have been described in rabbits (Otero & Portela 2019; de Miguel Garcia et al. 2020a).

Greater Auricular Nerve Block Guided by Anatomical Landmarks

This technique is performed by inserting the needle subcutaneously, caudal to the transverse process of C1, in a cranial direction, and advancing it 1–2 cm subcutaneously. The local anesthetic is then injected while the needle is withdrawn (de Miguel Garcia et al. 2020a). The recommended volume of local anesthetic is 0.1 mL/kg through a 22-gauge, 1.5-inch spinal needle.

Auriculotemporal Nerve Block Guided by Anatomical Landmarks

The needle is introduced perpendicular to the skin over the caudal aspect of the zygomatic arch at the level of the lateral canthus of the eye. The needle is then walked off the caudal aspect of the zygomatic arch until it contacts the mandibular ramus, and walked off this structure until its tip is positioned between the ramus and the auditory bulla, at a depth of approximately 0.5–1 cm. The needle is then tilted at a 45°degree angle, with the tip directed towards the mandibular body and parallel to the mandibular ramus (de Miguel Garcia et al. 2020a). The recommended volume of local anesthetic is 0.075 mL/kg administered through a 22-gauge, 1.5-inch spinal needle.

A study evaluating the effects of this approach in live rabbits following an injection of bupivacaine showed rather disappointing results. The auriculotemporal nerve could only be blocked in 1 out of 16 ears, whereas the greater auricular nerve was blocked in 75% of the ears, but for a short amount of time (88 minutes) given that bupivacaine was used. The study also showed that the auriculopalpebral nerve was accidentally blocked in 3 out of 16 cases (de Miguel Garcia et al. 2020b), which is clinically relevant as blocking this nerve will result in inability to blink, thus care should be taken to adequately lubricate the eye in this scenario. Collectively, the results of this study indicate the need to refine this technique, possibly involving more objective methods such as ultrasound guidance. The author of this chapter advises caution in performing this approach until more information is available.

Transversus Abdominis Plane Block

The transversus abdominis plane block aims to block the ventral branches of the spinal nerves T9–L2, innervating the abdominal wall and the underlying parietal peritoneum. This block is performed under ultrasound guidance exclusively. Unlike other approaches, where the target nerve is directly visible under ultrasound, the nerves are too small to be seen with this approach. However, these nerves run in the fascial plane between the internal oblique and the transversus abdominis muscle on the lateral aspect of the abdomen, and between the rectus abdominis muscle and the transversus abdominis muscle on the medial aspect of the abdomen, and these fascial planes can be seen with an ultrasound. An ultrasound-guided injection of local anesthetic in this plane results in distribution around the

target nerves. Due to the broad area that needs to be blocked, two to three injections per side are recommended, one subcostal (between the rectus abdominis and the transversus abdominis muscles) and one or two on the lateral aspect of the abdomen (between the internal oblique and the transversus abdominis muscles). The lateral approach has been described in rabbits (Di Bella et al. 2021). The injections are performed by driving the needle in plane (i.e., parallel to the long axis of the transducer) to the target planes.

The recommended volume of local anesthetic is 1–1.2 mL/kg, divided in two or three injection points per hemiabdomen. Diluted bupivacaine (0.25%) can be administered to avoid exceeding the recommended dose. One subcostal injection and one or two lateral injections are performed on both sides of the abdomen. It is recommended to use a 22-gauge, 1.5-inch spinal needle connected to a prefilled T port.

The expected area of anesthesia is the abdominal wall and underlying parietal peritoneum. This technique requires a high-frequency (13 mHz) linear transducer.

Proximal Radial, Ulnar, Median, and Musculocutaneous Block

This approach aims at blocking the radial, ulnar, median and musculocutaneous (RUMM) nerves. The area of regional anesthesia achieved with this approach includes the distal humerus, elbow, radius-ulna, carpus, metacarpus, and phalanges. The proximal RUMM block can be performed with nerve stimulator or ultrasound guidance, or with a combination of both. The latter approach provides maximum accuracy. In rabbits, the ultrasound-guided proximal RUMM block can be performed with a lateral approach (Otero & Portela 2019). The transducer should be placed on the lateral aspect of the humerus, perpendicular to its long axis, on the proximal epiphysis of the humerus. Ultrasonographic landmarks include the humerus, the axillary artery and vein, the biceps brachialis, and the triceps brachii muscles. Color Doppler facilitates visualization of the blood vessels. The needle should be visualized by the transducer until it is advanced in proximity to the target nerves. A positive muscular response should be elicited with 0.5 mA (1 Hz, 0.1 ms) using a nerve stimulator consisting of flexion of the elbow (musculocutaneous nerve), flexion of carpus and digits, pronation of the antebrachium (median and ulnar nerves), and extension of the elbow (radial). Muscular response should be absent with 0.3 mA, as a positive muscular response with 0.3 mA may indicate that the needle is too close to the nerve.

The recommended volume of local anesthetic is 0.4–0.5 mL/kg administered through a 22-gauge, 1.5-inch insulated needle. The expected area of anesthesia is the thoracic limb distal to the distal humerus. This technique requires a high-frequency (13 mHz) linear transducer and nerve stimulator.

Lumbosacral Plexus Block

Block of the lumbosacral plexus can be achieved by combining a lateral pre-iliac approach to the femoral nerve with a parasacral approach to the sciatic nerve. Anesthesia of the entire pelvic limb, including the coxofemoral joint, can be achieved with this approach, making it a suitable alternative to provide analgesia in animals undergoing hindlimb amputation or femur fracture repairs. Both these approaches can be performed with nerve stimulator or ultrasound guidance. Nerve stimulator-guided approaches are described here.

Block of the Femoral Nerve with a Lateral Pre-iliac Approach (Otero & Portela 2019)

Landmarks for this approach include the iliac crest and the spinous process of L6. An imaginary line is traced starting from the spinous process of L6 in a ventral direction, perpendicular to the spine. A second line is traced parallel to the spine, starting from the most cranial point of iliac crest. The injection point is the intersection of these two lines. The needle is introduced with a 30–45°degree angle in a caudo-medial direction towards the greater trochanter of the femur. The nerve stimulator should initially be set at 1 mA (1 Hz, 0.1 ms). When the target muscular response is elicited, consisting of extension of the stifle, the nerve stimulator setting should be reduced to 0.5 mA. A positive muscular response should be present with 0.5 mA but absent with 0.3 mA. A positive muscular response with 0.3 mA may indicate that the needle is too close to the nerve.

Block of the Lumbosacral Trunk with a Parasacral Approach (Otero & Portela 2019)

This approach is performed by tracing an imaginary line connecting the ischiatic tuberosity to the dorsal aspect of the iliac crest. This line is then divided into three equal segments. The point between the cranial and middle third of this line is the injection point. The needle is introduced perpendicular to the skin with an initial nerve stimulator setting of 1 mA (1 Hz, 0.1 ms). When the correct muscular response is elicited, consisting of flexion of the stifle, or flexion or extension of the tarsus, the nerve stimulator setting should be reduced to 0.5 mA. A positive muscular response should be present with 0.5 mA but absent with 0.3 mA. A positive muscular response with 0.3 mA may indicate that the needle is too close to the nerve.

The recommended volume of local anesthetic is 0.4–0.5 mL/kg, equally divided between the lateral preiliac and the parasacral injection points using a 22-gauge, 1.5-inch insulated needle. The expected area of anesthesia is the entire pelvic limb, including the coxofemoral joint. This technique requires a nerve stimulator.

Sacrococcygeal Epidural Injections

Epidural anesthesia consists of administration of either local anesthetic or other analgesics within the epidural space. In small animals, epidural injections are commonly performed using a lumbosacral approach to the epidural space. However, this approach frequently results in a subarachnoid injection in rabbits (Otero et al. 2012) due to their small size and to the extension of the spinal cord into the sacrum in this species (Greenway et al. 2001). For this reason, lumbosacral epidural injections should not be attempted in rabbits. The sacrococcygeal space is a safer location to perform epidural injections in this species. A nerve stimulator can be used to improve the accuracy of this technique and should be set at 0.5 mA (1 Hz, 0.1 ms). The needle is advanced towards the sacrococcygeal space. Piercing of the yellow ligament, which is sometimes perceived as a pop sensation when performing lumbosacral epidural injections in small animals, is not normally perceived with the sacrococcygeal approach. When the tip of the needle enters the epidural space, the muscles of the distal part, but not the base of the tail, are expected to contract. Epidural administration of local anesthetics is contraindicated in animals with uncorrected hypovolemia, coagulopathy, and sepsis.

The recommended volume of local anesthetic is 0.1–0.3 mL/kg of sterile local anesthetic solution, depending on the extension of the block desired, using a 22-gauge, 1.5-inch insulated needle. The anesthesia can be limited to the perineum or extended to the pelvic limbs or even abdomen, depending on the volume of local anesthetic selected.

Recovery from General Anesthesia

A number of complications can arise during the recovery phase from general anesthesia. Being obligate nasal breathers, rabbits may experience airway obstruction on removal of the endotracheal tube as a consequence of nasal hyperemia. For this reason, administration of topical phenylephrine is advised in rabbits recovering from general anesthesia, particularly after long procedures. Assessment of the airflow can be performed by observing breathing movements and using a stethoscope positioned in front of the nose to listen for air movement.

Prolonged recovery is a common complication following anesthesia, particularly in compromised animals. Adequate troubleshooting includes assessment of body temperature, and of cardiovascular and respiratory status. If excessive sedation is suspected, reversal agents can be administered as needed.

Hypothermia is a common cause of prolonged recoveries, particularly in rabbits, given that their small size predisposes them to losing heat during anesthesia. Heat support should be provided until normothermia is achieved.

The residual effect of anesthetic drugs can induce significant hypoventilation. Significant hypercapnia can prevent arousal and should be corrected by providing manual or mechanical ventilation until the residual effects of the anesthetic drugs subside or are reversed (if applicable). The presence of hypoxemia should also be ruled out, using either a pulse oximeter or arterial blood gas, and corrected as needed with the administration of oxygen.

Lastly, electrolyte and acid-base imbalances should be assessed, particularly in sick animals or those who have undergone long and invasive procedures. An IV catheter should be left in place until the animal regains consciousness or longer for sick individuals requiring supportive care. It is important to provide a calm environment to minimize stress for rabbits recovering from general anesthesia.

Perioperative gastrointestinal complications, defined as decreased food intake, decreased or increased fecal output, diarrhea or the need for syringe feeding, were documented in 38% of the rabbits following general anesthesia in one study (Lee et al. 2018). The administration of prokinetics can be considered to prevent and treat gastrointestinal stasis. Metoclopramide can be administered at a dose of 0.5–1 mg/kg IV, SC or PO every 8–12 hours. A metoclopramide CRI can also be considered in severe cases, at a dose of 2 mg/kg per day. Ranitidine may have intestinal prokinetic effects and can be administered at a dose of 2–5 mg/kg IV, SC or PO, every 12–24 hours. Alternatively, compounded liquid formulations of cisapride can be administered orally at a dose of 0.5 mg/kg every 8 hours (Oglesbee & Lord 2020).

Blood Pressure Support and Emergency Drugs in Rabbits

The effects of anesthesia on the cardiovascular system commonly result in hypotension as a result of decreased myocardial contractility and vasodilation. A multitude of drugs can be used to counteract these effects in anesthetized animals (Table 25.4). The choice between drugs is based on what is thought to be the cause of hypotension in

Table 25.4 Drugs used for blood pressure support in rabbits.

Drug	Dose	Route	Mechanism of action	Comments
Ephedrine	0.05–0.1 mg/kg	IV	Stimulation of the postsynaptic alpha and beta receptors by increasing the activity of endogenous norepinephrine	Given as a single bolus, lasts 10–15 minutes. Subsequent boluses are less effective.
Dopamine	2–10 μg/kg/min	IV	Acts on D1 and D2 receptors at low doses, and on alpha and beta receptors at higher doses.	Positive inotropic effect and vasoconstriction may occur with high doses.
Dobutamine	2–10 μg/kg	IV	Mainly beta-1 agonist	Positive inotropic effect. May induce tachycardia and ventricular arrhythmias
Norpepinephrine	0.1–1 μg/kg/min	IV	Alpha-1 and beta-1 agonist	Positive inotropic effect and more marked vasoconstriction compared to dopamine.
Phenylephrine	0.1–1 μg/kg/min	IV	Alpha-1 agonist	Vasoconstriction

IV, intravenous.

a specific animal as well as clinician preference. Indices such as pulse pressure variation with mechanical ventilation and other parameters correlated with peripheral perfusion can be used to establish the best course of treatment for specific patients. Norepinephrine was effective at increasing the blood pressure in anesthetized rabbits when administered at doses of 0.5 and 1 μg/kg/min (Uccello et al. 2020).

Given the high mortality rate in rabbits undergoing general anesthesia, the need for emergency intervention when anesthetizing rabbits should be expected. Preparedness is pivotal when dealing with life-threatening situations. Emergency drugs should be precalculated and even predrawn in syringes, particularly when anesthetizing sick animals. Current guidelines regarding dosing regimens for emergency drugs in rabbits are lacking. In this context, the extrapolation of dosing regimens used for small animals is considered acceptable (Table 25.5). Attaining to the RECOVER guidelines formulated for dogs and cats when performing CPR in rabbits is acceptable in the absence of specific guidelines (Hopper et al. 2012). Return of spontaneous circulation in rabbit was achieved in seven out of 15 cases in one retrospective study in hospitalized rabbits (Buckley et al. 2011). A tight-fitting face mask can be used to provide manual ventilation in emergency situations when endotracheal intubation is not feasible and would result in detrimental interruption of basic life support (Buckley et al. 2011). Alternatively, V-gel® devices can be quickly inserted and used for this purpose in animals that do not have an endotracheal tube in place.

Atropinesterase has been documented in 62% of New Zealand white rabbits, more commonly in males than females (Liebenberg & Linn 1980). Rabbits given high doses of atropine (0.2–2 mg/kg) exhibited only brief increases in heart rates (Olson et al. 1994). Because it is impossible to predict which rabbits have this enzyme, glycopyrrolate should be preferred for treatment of bradycardia in this species.

Table 25.5 Emergency drugs and doses for use in rabbits.

Drug	Dose	Route	Indication/comments
Epinephrine	0.01–0.1 mg/kg	IV, IO, intratracheal	Higher dose should be used for intratracheal administration and as a last resort for unsuccessful CPR
Atropine	0.02–0.04 mg/kg	IV, IM, SC, IO, intratracheal	Atropinesterase is present in some rabbits
Glycopyrrolate	0.01–0.02 mg/kg	IV, IM, SC, IO, intratracheal	Bradycardia
Lidocaine	1–2 mg/kg	IV	Ventricular arrhythmias. May induce profound vasodilation and suppress idioventricular rhythms

CPR, Cardiopulmonary resuscitation; IM, intramuscular; IO, intraosseous; IV, intravenous; SC, subcutaneous.

Mechanical Ventilation in Rabbits

Severe hypoventilation and hypoxemia are common in anesthetized rabbits (Bateman et al. 2005) and if left untreated can lead to significant complications and even increased mortality. Monitoring of the expired carbon dioxide alone can sometimes give the false impression that the animal is normocapnic, particularly when nonrebreathing circuits are used or in the presence of dead-space ventilation, as ~30% of the tidal volume consists of anatomical dead space in rabbits (Tolnai et al. 2018). Venous or arterial blood gases can be used to assess ventilation, while arterial blood gas is needed to assess oxygenation. Pulse oximetry should always be monitored in anesthetized animals.

Mechanical ventilation is challenging in very small animals. The use of precision ventilators capable of delivering small tidal volumes should be preferred for use in rabbits. A normal respiratory rate for rabbits is in the range of 30–40 bpm. While it is normal for the respiratory rate to decrease some during anesthesia, a rate of 25–30 bpm is preferred when mechanically ventilating a rabbit. The exact tidal volume has not been determined in rabbits. Clinically, adequate ventilation can be achieved using 10–12 mL/kg in this species. Pressure-controlled ventilation may also be employed, and a setting between 10 and 12 mmHg peak pressure is usually a good starting point. The ventilation settings should be adjusted based on assessment of capnography and pulse oximetry, or based on venous or arterial blood gases, when available. The addition of a positive end expiratory pressure of 3–7 mmHg may help prevent anesthesia-induced atelectasis, and an inspiratory pause (about 30% of the duration of the inspiration) may be added to decrease the anatomical dead space.

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26

Marsupials

Peter Holz

Introduction

Marsupials are a diverse group of mammals comprising approximately 350 species located predominantly in Australasia, with representatives in North and South America (Van Dyck & Strahan 2008). The infraclass Marsupialia is divided into seven orders: Dasyuromorphia (carnivorous marsupials), Peramelemorphia (bandicoots and greater bilby (*Macrotis lagotis*)), Diprotodontia (koala (*Phascolarctos cinereus*), wombats, possums, and macropods), Notoryctemorphia (marsupial moles), Didelphimorphia (opossums), Paucituberculata (shrew opossums), and Microbiotheria (monito del monte (*Dromiciops gleroides*)).

Anatomy and Physiology

The physiology of marsupials is well described by Tyndale-Biscoe (2005). Marsupials have a lower metabolic rate and a lower body temperature than eutherians. Instead of a separate anus and urogenital opening they combine the two into a single cloaca. To effectively measure a marsupial's temperature the thermometer needs to be inserted into the dorsal part of the cloaca, leading to the rectum. Thermoregulatory ability does not develop until about halfway through pouch life. Consequently, it is important to provide supplemental heat if young animals, particularly unfurred, are anesthetised. Marsupials combat cold by shivering. They do not have brown adipose tissue, which is used by some eutherians to generate heat. They cope with excessive heat by panting and licking. Kangaroos, in particular, will lick their forelegs to keep cool (Vogelnest 2015).

Most marsupials weigh less than 10 kg (see Table 26.1) and can be manually restrained with minimal risk to the handler. Consequently, where possible, mask induction with isoflurane is the anesthetic technique of choice. Standard analgesics and anti-inflammatory agents have been used at small animal dosages with no adverse effects (see Table 26.2). Venepuncture sites are listed in Table 26.3. Reference ranges for heart rate, respiratory rate, and body temperature for a variety of marsupials are given in Table 26.4.

Dasyuromorphia

Physical Restraint

Physical restraint is only used for minor procedures or to induce general anesthesia because restrained animals will struggle and attempt to bite. Antechinus or dunnart bites are only mildly painful but larger members of the group, such as the Tasmanian devil (*Sarcophilus harrisii*), can inflict severe injuries (Fig. 26.2).

Small dasyurids are gripped by the scruff of the neck or held around the body and placed in a bag. Do not clasp them too firmly, as suffocation is possible. Larger dasyurids, such as quolls and devils, can be caught in a net or restrained by the tail and then lowered into a bag or box (Fig. 26.3). They should not be carried long distances held only by the tail. Devils must be closely monitored while in the bag as they can chew their way out.

Smaller dasyurids, such as antechinus, dunnarts, and phascogales, should not be restrained by the tail as severe degloving injuries and tail fractures can occur. If quolls are held by the tail care is required as they are agile enough to turn and potentially bite the handler.

Bags are a convenient way of transporting dasyurids short distances. They can range in size from a pillowcase for smaller animals up to a large hessian (burlap) sack for

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Table 26.1 Body weights of selected marsupial species (Van Dyck & Strahan 2008).

Species	Body Weight	Species	Body Weight
Tasmanian devil	5–14 kg	Common ringtail possum	700–900 g
Eastern quoll	0.7–1.9 kg	Feathertail glider	10–15 g
Spotted-tailed quoll	0.9–5.0 kg	Sugar glider	95–160 g
Brown antechinus	17–71 g	Eastern grey kangaroo	17–85 kg
Fat-tailed dunnart	10–20 g	Western grey kangaroo	17–72 kg
Kowari	70–175 g	Red kangaroo	17–92 kg
Brush-tailed phascogale	106–311 g	Red-necked wallaby	12–24 kg
Southern brown bandicoot	0.4–1.8 kg	Swamp wallaby	10–20 kg
Greater bilby	0.8–2.5 kg	Tasmanian pademelon	2–12 kg
Koala	4–15 kg	Parma wallaby	3–6 kg
Common wombat	22–39 kg	Tammar wallaby	4–10 kg
Southern hairy-nosed wombat	18–36 kg	Marsupial mole	40–70 g
Common brushtail possum	1.2–4.5 kg	Virginia opossum	2–5 kg

Table 26.2 Dosages of analgesics and anti-inflammatory drugs used in marsupials (Johnson-Delaney 2006; Brust & Mans 2018; Bodley 2019).

Drug	Dose	Species
Butorphanol	0.1–0.5 mg/kg SC/IM/IV	Wombats, possums, gliders, opossums
Buprenorphine	0.01–0.05 mg/kg SC/IM/IV BID-TID	All
Fentanyl	0.5–3 µg/kg/h IV infusion	Koalas
Methadone	0.1 mg/kg IV 0.15–0.40 SC q4–6h	Macropods, bilbies Koalas, possums, gliders
Tramadol	5–10 mg/kg PO/IM BID	Macropods, possums, gliders
Paracetamol ± codeine	15 mg/kg PO BID-TID	Macropods, koalas, possums, gliders
Flunixin meglumine	1 mg/kg IM/IV SID 3 days	Macropods, opossums
Carprofen	2–4 mg/kg PO/SC SID	All
Firocoxib	5 mg/kg PO SID 3–5 days	Koalas
Meloxicam	0.1–0.2 mg/kg PO/SC SID	Macropods, wombats, sugar gliders, dasyurids, bandicoots, bilbies, opossums
Tolfenamic acid	4 mg/kg SC SID	All

BID, twice a day; IM, intramuscular; IV, intravenous; PO, per os; q4–6h, every 4–6 hours; SC, subcutaneous; SID, once a day; TID, three times a day.
There are very few marsupial drug kinetic studies and doses are generally extrapolated from domestic animals. A study of meloxicam in koalas found it unlikely to be effective due to poor absorption and low blood levels (Kimble et al. 2013).

Tasmanian devils. Animals in bags tend to relax as outside stimuli and visual threats are removed. The chance of injury is also decreased, as they cannot lash out against solid objects.

Most wild dasyurids are small enough to be caught in pit-fall traps or Elliott traps baited with meat.

Anesthesia

While most dasyurids are not prone to regurgitation under anesthesia, regurgitation can occur on occasion in Tasmanian devils. Consequently, preanesthetic fasting for 1–2 hours for smaller dasyurid species and 6–8 hours for larger species is recommended (Vogelnest 2019a).

Table 26.3 Accessible veins in marsupials (Portas 2019).

Ventral tail vein (Fig. 26.1a): Insert the needle perpendicular to the tail in the ventral midline and advance it until the vertebrae are felt. Withdraw the needle slightly and blood should enter the hub. This vein is useful for smaller dasyurids, possums, gliders, and opossums.
Lateral tail vein: A large vein is present on both dorso-lateral aspects of the tail. Applying pressure or a tourniquet to the tail base will raise the vessel. This vein is useful for macropods, larger possums, and opossums.
Femoral vein/artery (Fig. 26.1b): Direct the needle at the pulse felt in the inguinal region. Arterial blood is often obtained and digital pressure is required for up to 5 minutes to prevent haematoma formation. This vein is useful for dasyurids, bandicoots, bilbies, koalas, wombats, possums, gliders, and opossums.
Medial metatarsal (saphenous) vein (Fig. 26.1c): This is a small vein coursing over the medial aspect of the hind leg. It is useful for small dasyurids, wombats, possums, gliders, opossums, and macropods.
Cephalic vein (Fig. 26.1d): This vein is present on the dorsal surface of either foreleg. It is useful for Tasmanian devils, quolls, bandicoots, bilbies, koalas, wombats, larger possums, gliders, macropods, and opossums.
Caudal tibial vein: This vein is present on the caudal aspect of the hind leg, distal to the stifle. It is useful for Tasmanian devils, wombats, and koalas.
Jugular vein (Fig. 26.1e,f): This vein is useful for dasyurids, bandicoots, bilbies, koalas, wombats, possums, gliders, and macropods, but can be difficult to access in wombats and possums due to their short necks.



Figure 26.1 (a) Blood collection from the ventral coccygeal vessels of a mountain pygmy possum (*Burramys parvus*). Note the use of a tuberculin syringe and a 25-gauge needle. An insulin syringe can also be used for small volume blood collection. (b) Blood collection from the femoral vein (artery) of a spot-tailed quoll (*Dasyurus maculatus*). (c) Blood collection from the medial metatarsal (saphenous vein) of an Eastern barred bandicoot (*Perameles gunnii*). (d) Blood collection from the cephalic vein of a juvenile common wombat (*Vombatus ursinus*). (e) Blood collection from the jugular vein of a ringtail possum (*Pseudocheirus peregrinus*). (f) Blood collection from the jugular vein of a Tasmanian devil (*Sarcophilus harrisii*).





Figure 26.1 (Continued)

Table 26.4 Heart rate, respiratory rate and body temperature of selected marsupials (Johnson-Delaney 2006; Vogelnest & Woods 2008; Brust & Mans 2018).

Species	Heart Rate/Minute	Respiratory Rate/Minute	Temperature (°C)
Tasmanian devil	85–120	20	31–38
Bandicoot		31–37	34.6–36.4
Sugar glider	200–300	16–40	35–36
Koala	65–90	10–15	35.5–36.5
Wombat	60–120	12–30	32.0–36.5
Macropod[a]	60–150	10–30	35–36
Virginia opossum	180–240	25–40	32.2–35.0

[a] Heart rate and respiratory rate vary with the species, the rate decreases with increasing body size.

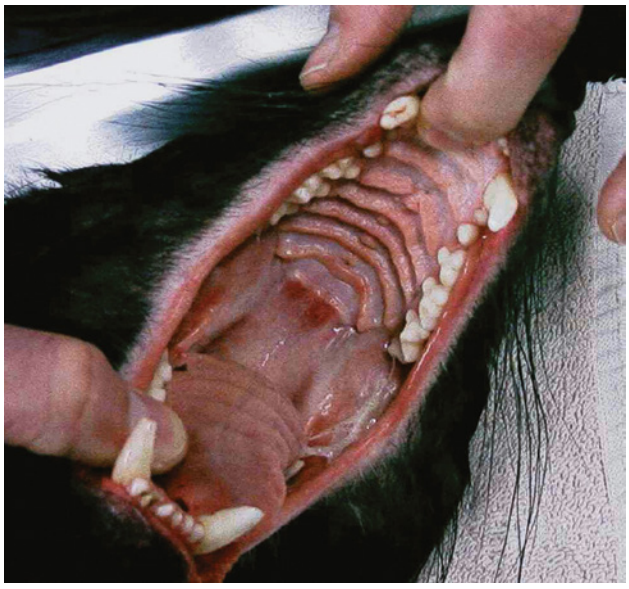


Figure 26.2 A Tasmanian devil (*Sarcophilus harrisii*) demonstrating its large gape and powerful jaws.



Figure 26.3 Physical restraint of an eastern quoll (*Dasyurus viverrinus*), a small carnivorous marsupial.

Inhalation anesthesia via mask induction is the method of choice. For animals in bags, anesthesia can be induced by extracting the head and placing it in the mask. It is important to grasp quolls and devils very firmly behind the head as they will attempt to pull back out of the mask to bite the handler. An alternative to mask induction is to place larger dasyurids in an induction box, which is flooded with isoflurane. This can result in considerable environmental anesthetic gas pollution and wastage when the animal is removed from the chamber. Once sedated the animal can then be maintained either on a mask or intubated. Tasmanian devils and quolls have a wide gape and are easily intubated for more prolonged procedures; a 4.5–5.0-mm internal diameter (ID) cuffed endotracheal tube is suitable for adult Tasmanian devils. Laryngospasm can occur and is prevented with the use of lignocaine (lidocaine) spray.

If inhalant anesthesia is not available an injectable induction is required. Dosages are given in Table 26.5. Tiletamine/zolazepam (TZ) is a useful drug combination because of its low volume and rapid effect. However, relaxation is variable, constant limb movement and salivation occur in Tasmanian devils, and recoveries can be prolonged. Alfaxalone is an effective alternative, but a larger volume is required and transient apnea can occur in Tasmanian devils. Medetomidine (0.05 mg/kg) and ketamine (5 mg/kg) (Portas, pers. comm.) or medetomidine (0.08 mg/kg), ketamine (5 mg/kg), and butorphanol (0.1 mg/kg), reversed with atipamezole (0.4 mg/kg intramuscular [IM]), have also been used in Tasmanian devils) (Vogelnest 2019b). Caution is advised with this drug combination as third-degree atrioventricular blocks have been diagnosed in aged Tasmanian devils and medetomidine is generally contraindicated in cases of cardiovascular disease.

Peramelemorphia

Physical Restraint

Bandicoots and bilbies are nervous animals. Care is required with physical restraint as they attempt to kick and can struggle so vigorously spinal damage results. They have sharp teeth and will bite if provoked. To restrain a bandicoot grasp it firmly behind the neck between the first two fingers of one hand and support the rump with the palm of the other. This form of restraint should only be used for minor procedures or to transfer the bandicoot into a bag. Greater bilbies can be grasped by the base of the tail and then transferred to a bag.

Anesthesia

Preanesthetic fasting is not necessary. Both bandicoots and bilbies can be mask induced and maintained on isoflurane and oxygen. Their wide gape makes visualization of the glottis and intubation easy. A 2.0-mm ID uncuffed endotracheal tube can be used for bandicoots and a 3.0–3.5-mm ID tube is suitable for bilbies.

Koalas (Diprotodontia)

Physical Restraint

Depending on the temperament of the koala, manual restraint may be sufficient for blood sampling, examination, or minor treatments. However, care is required as agitated koalas can deliver serious bites and painful scratches.

If the koala is in a tree and within reach, it can be coaxed down using a pole with a hessian (burlap) sack or piece of material tied to the end. Waving the sack just above the

Table 26.5 Dosages (mg/kg) of diazepam, tiletamine/zolazepam (TZ), medetomidine/ketamine (M/K), and alfaxalone for sedation/immobilization of marsupials (Vogelnest 2019b).

Species	Diazepam	TZ	M/K	Alfaxalone
Dasyurids	1–2	3–6	0.05/5	2–3
Koalas	0.5–1	5–10		1.5 IV or 3.0 IM
Wombats	0.5–1	3–8	0.125/2	3–5
Possums & Gliders	0.5–1	4–10	0.02–0.1/1–3	5–8
Macropods	1–2	4–10	0.1/5	1.5–3.0 IV
Opossums	0.5–2	15	0.05–0.1/2–3	5 IV

IM, intramuscular; IV, intravenous.
Administration is by IM injection unless otherwise indicated.

koala's head will encourage it to descend. When it is close enough a bag is placed over the koala's head, back, and rump. With the koala's body contained within the sack the claws are disengaged from the tree and the koala should tumble into the bag. It is important to keep the bag over the koala's head and detach the animal from the top down, otherwise it will attempt to climb back up the tree. One person can catch docile koalas. However, agitated animals need at least two people, one to cover the koala with the sack and one to detach its claws.

Once in the bag a foreleg can be extended for blood sampling (Fig. 26.4). Detailed examination and treatment should be performed under general anesthesia. When transporting the koala in the bag it is important to hold the bag away from the body and not sling it over the shoulder, as the koala can bite and scratch through the bag. Koalas can also be transported short distances by grasping the upper forelimbs from behind, either directly or through a towel (Fig. 26.5a).



Figure 26.4 Blood collection from the cephalic vein of an awake koala restrained in a large bag.







Figure 26.5 Physical restraint of (a) a koala (*Phascolarctos cinereus*), (b) a hand-raised juvenile wombat (*Vombatus ursinus*), and (c) a common brushtail possum (*Trichosurus vulpecula*). These animals are still capable of injuring an unwary handler with their claws and teeth.

Young hand-raised koalas can be carried on the handler's body, like a human child, with one hand supporting the rump. Make sure there is enough padding between the koala and the handler's skin, as claws will readily penetrate a shirt. Quiet adult koalas can be held with one hand on the scruff and the other supporting the rump (Vogelnest 2019a).

Anesthesia

Preanesthetic fasting is not necessary. For inhalant induction the koala's head is extracted from the bag and placed into the anesthetic mask. Koalas are very strong and the head must be firmly grasped as it is placed into the mask.

For prolonged procedures koalas should be intubated. Intubation is difficult as they have a narrow oral cavity and small gape. However, if the neck is extended and a long straight bladed laryngoscope is used it is possible to visualize the glottis. Alternatively, the tube can be placed over a rigid 2.7-mm endoscope for visualization and intubation. An endotracheal tube of approximately 3.0–5.0-mm ID can then be used.

If the koala cannot be restrained for inhalation anesthesia, it will require an injectable induction (see Table 26.5). Alfaxalone can be administered either intravenous (IV) or IM and provides a smooth, rapid induction and recovery with good muscle relaxation. TZ results in variable relaxation, moderate salivation, and potentially prolonged recoveries (up to 3–4 hours) (Vogelnest 2019a).

Koalas high up in trees have been darted with a combination of TZ (3.5 mg/kg) and medetomidine (0.055 mg/kg), and reversed with 2.0 mg atipamezole IV (Lynch & Martin 2003). Care is required with this method as koalas have a small hind-leg muscle mass and perch in trees with their hind legs tucked forwards, over their abdomen. The author has necropsied koalas with gastrointestinal perforations and peritonitis caused by darts penetrating the abdomen. Koalas have also been successfully immobilized in the field using either 3.5 mg/kg alfaxalone IM or a combination of 2.0 mg/kg alfaxalone and 0.04 mg/kg medetomidine, the latter reversed with 0.16 mg/kg atipamezole IM (Downey et al. 2020).

Wombats (Diprotodontia)

Physical Restraint

Wild wombats are extremely strong and can be aggressive, potentially inflicting painful bites on unwary handlers. Manual restraint should not be attempted. Hand-raised or docile wombats may permit themselves to be carried. One or both arms should be placed under the axilla, behind the forelegs, then the wombat picked up and held firmly

Bags or pillowcases are preferable. If presented in a trap, a towel should be used to cover the possum. Thick gloves can be worn, but large possums are able to bite through them and they decrease tactile discrimination. Once under the towel the possum is grasped firmly behind the head. If the grip is too lax the possum will pull its head back and bite the handler. It is also necessary to grasp the base of the tail with the other hand to prevent the possum swinging its hind legs forward to scratch (Fig. 26.5c). It can then be examined or anesthetized (Vogelnest 2019a).

Anesthesia

Regurgitation is unlikely, but 1–2 hours preanesthetic fasting has been recommended. If the possum is presented in a bag the material is rolled back and the face placed in an anesthetic mask for induction.

If the animal cannot be extracted from a trap or otherwise restrained to induce inhalant anesthesia, it will require an injectable induction (see Table 26.5). Alfaxalone inductions are smooth and recoveries rapid. It can be used on its own or in a combination of 8 mg/kg alfaxalone and 0.12 mg/kg medetomidine, reversed with 0.48 mg/kg atipamezole IM. Induction with TZ is rapid, but tachycardia, apnoea, muscle rigidity, and prolonged recoveries have been reported in several species (Vogelnest 2019b), and three deaths occurred when it was used in squirrel gliders (*Petaurus norfolcensis)* (Holz 1992).

Macropods (Diprotodontia)

Physical Restraint

Macropods have powerful hind legs, with a large claw on digit four, which can cause serious injury to individuals attempting to restrain them. They will also bite and can inflict painful injuries with their teeth. Manual restraint of smaller macropods is only used for minor procedures or prior to the induction of general anesthesia. Large kangaroos cannot be manually restrained. Chemical restraint is necessary.

Smaller macropods can be forced along a fence line and caught in a hand net. The inside wall of the pen must be smooth with no protuberances as macropods will run close to the fence. All poles and supporting structures must be on the outside. Patience and quiet are required. Many species panic easily and may collide with the fence, resulting in soft tissue trauma and cervical fractures. Macropods are also prone to capture myopathy if pursued in hot weather or for an extended period of time (Vogelnest 2019a).

Once caught in a net the macropod can be grasped by the base of the tail and lowered into a hessian (burlap) sack or pillowcase, depending on the size of the animal. If the tail is held too distally coccygeal fractures can occur, particularly in smaller species such as bettongs and potoroos. The handler should not hold the bag against their body while the animal is being transported as they can still kick or bite through the bag.

Once in the bag minor procedures, such as blood sampling, can be performed by restraining the wallaby within the bag and extracting the relevant body part. It is important to emphasize that animals restrained in this way, unless they are tame or hand-raised, will be extremely stressed and struggle vigorously against the restraint. It should only be used for short-term procedures or as a prelude to chemical restraint.

Anesthesia

Sedation suitable for transport will occur 5–20 minutes after 1–2 mg/kg diazepam IM. Duration of effect is approximately 2–4 hours. Midazolam (0.3–0.4 mg/kg IM or IV) is a shorter-acting alternative, lasting 1–2 hours. If necessary, the benzodiazepines can be antagonized with flumazenil (1 mg of flumazenil per 25 mg of benzodiazepine). Azaperone (1–2 mg/kg IM) may also be used. Effects appear after 15–20 minutes and last for 6–8 hours (Vogelnest 2019b).

For animals in bags isoflurane anesthesia is the method of choice and induced by extracting the macropod's head and placing it in the mask. The handler is protected to some extent from the powerful hind limbs as they are contained within the bag.

If the animal cannot be restrained to induce inhalation anesthesia it will require an injectable induction (see Table 26.5). TZ inductions are swift and the low volume required makes it an ideal combination for immobilization by dart. However, recoveries can be prolonged (1–5 hours). Ketamine combined with medetomidine provides superior relaxation to TZ and, if concentrated medetomidine (10 or 20 mg/mL) is used, is also suitable for remote immobilizations. It is, however, more expensive. Induction times are longer than with TZ (up to 20 minutes). It is important not to stimulate the animal during induction, as this will extend the time to recumbency or result in inadequate immobilization.

The author has successfully used a combination of ketamine (5 mg/kg) and medetomidine (0.1 mg/kg) for immobilization of docile red kangaroos (*Macropus rufus*) and western grey kangaroos (*Macropus fuliginosus*). This combination was also used to successfully immobilize Bennett's wallabies (*Macropus rufogriseus*) (Bouts et al. 2010, 2011). A slightly lower dose (4.5 mg/kg ketamine/0.08 mg/kg medetomidine) successfully immobilized bridled nailtail wallabies (*Onychogalea fraenata*) (Boardman et al. 2014).

However, in the author's experience, this combination at this dose failed to effectively immobilize the more nervous species such as eastern grey kangaroos (*Macropus giganteus*) or smaller macropods such as pademelons (*Thylogale* spp.) and parma wallabies (*Macropus parma*).

Bennett's wallabies have also been immobilized using combinations of ketamine (15 mg/kg) and xylazine (2 mg/kg), ketamine (5 mg/kg) and dexmedetomidine (0.05 mg/kg) (Bouts et al. 2010), alfaxalone (4 mg/kg) and medetomidine (0.1 mg/kg) (Bouts et al. 2011), and butorphanol (0.5 mg/kg), azaperone (0.2 mg/kg), and medetomidine (0.15 mg/kg) (BAM) (Watson et al. 2016). The ketamine/xylazine mix resulted in a shorter duration of anesthesia and poorer muscle relaxation than the other combinations. The alfaxalone/medetomidine combination is not suitable to immobilize larger macropods due to the large volume required. The BAM combination resulted in a very light plane of anesthesia and is not recommended as animals were aroused by any form of environmental stimulation.

Ketamine/medetomidine and ketamine/dexmedetomidine anesthesia was reversed using atipamezole (given either entirely IM or half IM and half IV) at five times the dose of medetomidine or dexmedetomidine (Bouts et al. 2010, 2011; Boardman et al. 2014; Watson et al. 2016). The author has used this dosage IV with no adverse effects. Animals are standing, but still ataxic, approximately 10–20 minutes after reversal. Animals given BAM were reversed with atipamezole 0.75 mg/kg IM and naltrexone 1 mg/kg IM (Watson et al. 2016).

Red kangaroos have been immobilized with a mix of ketamine (5 mg/kg), medetomidine (0.1 mg/kg), and butorphanol (0.1 mg/kg), and reversed with atipamezole (0.3 mg/kg IM and 0.15 mg/kg IV) and naltrexone (0.55 mg/kg IV). This combination was reported to provide a smooth induction, good muscle relaxation, and rapid recovery (Vogelnest 2019b). Red kangaroos have also been immobilized with TZ (0.5–1.0 mg/kg) combined with either medetomidine (0.03–0.04 mg/kg) or dexmedetomidine (0.03–0.04 mg/kg) (Heard, pers. comm.). This combination allows a small volume (when using concentrated medetomidine), relatively rapid induction, and a relatively shorter recovery period after reversal (~60 minutes or more). Higher doses (5–8 mg/kg TZ and 0.02–0.05 mg/kg medetomidine) have been used in other macropod species. However, this combination is unreliable for eastern grey kangaroo immobilizations (Vogelnest 2019b).

For wild macropods the TZ combination is preferred. A dose of 4.7–4.9 mg/kg in wild eastern grey kangaroos resulted in a mean induction time of 7–10 minutes with a recovery time of 116–130 minutes (Roberts et al. 2010). Free-ranging eastern grey kangaroos and red kangaroos have also been immobilized remotely using a combination of 1.3–5.1 mg/kg TZ, 0.01–0.02 mg/kg medetomidine, and 0.03 mg/kg acepromazine (Colgan & Green 2018).

For prolonged procedures macropods should be intubated as they may regurgitate. If possible, fasting for 12–24 hours is recommended. Intubation is difficult as macropods have a narrow oral cavity and small gape. However, if the neck is extended and a long straight bladed laryngoscope is used it is possible to visualize the larynx. An endotracheal tube can then be passed. A stylet within the endotracheal tube may facilitate this process (Watson et al. 2016). An alternative method is to place the animal in dorsal recumbency with its head and neck hanging vertically over the front of the table and an endotracheal tube passed in a blind fashion (Colgan & Green 2018). Lignocaine (lidocaine)sprayed on the glottis may assist passage of the tube. Successful nasotracheal intubation of a red kangaroo has also been reported. A 60-cm, 7-mm endotracheal tube was positioned ventrally in the right nostril and blindly directed into the trachea through the ventral meatus (Bauquier & Golder 2010).

Long-acting Tranquilizers

Many macropod species are naturally nervous and may benefit from the use of long-acting tranquilizers when settling into new exhibits. Recommendations include perphenazine enathate (5 mg/kg IM), which lasts up to 7n days, and haloperidol decanoate (4–6 mg/kg IM), which can last up to 30 days. Zuclopenthixol acetate (5–10 mg/kg IM) has a peak effect at 24 hours and duration of 48–72 hours. Species vary in their sensitivity to this drug. Deaths have been reported in bridled nailtail wallabies and agile wallabies (*Macropus agilis*) (Vogelnest 2019b). Historically, fluphenazine decanoate (2.5 mg/kg IM) was also used but the drug was discontinued in 2018.

Notoryctemorphia

Marsupial moles are rarely found in captivity. They can be held in the hand and do not attempt to bite, but may struggle when restrained. They can be mask-induced and maintained with isoflurane.

Didelphimorphia, Paucituberculata, and Microbiotheria

Physical Restraint

Opossums defend themselves by biting, but they may also feign death. It is important to remain vigilant if this happens as the opossum may suddenly become active and

either bite or attempt to escape. To restrain the opossum a towel should be placed over the animal, which can then be firmly grasped behind the head. They can also be lifted by grasping the base of the tail. However, some animals may be able to turn and bite, requiring additional restraint around the nape of the neck.

Anesthesia

This group of marsupials can all be mask-induced with isoflurane. A plastic induction chamber, connected to an isoflurane machine, can also be used. If inhalation anesthesia is not possible, an injectable induction is required. Dosages are given in Table 26.5.

Tractable Virginia opossums (*Didelphis virginiana*) can be immobilized with 5 mg/kg alfaxalone IV, injected into the ventral tail vein (Gardner, pers. comm.). IM combinations used include medetomidine (0.05–0.1 mg/kg IM) and ketamine (2–3 mg/kg IM), reversed with 0.05–0.4 mg/kg atipamezole IV (Johnson-Delaney 2006), or medetomidine (0.07 mg/kg IM) and ketamine (10 mg/kg IM), combined with butorphanol (0.5 mg/kg SC) (Capello 2007). TZ (15 mg/kg) has also been used and was reported to give a rapid, smooth induction (Stoskopf et al. 1999). Adult opossums can be intubated using a laryngoscope and a 3.5–4.5-mm cuffed endotracheal tube (Gardner, pers. comm.).

Six different drug combinations were tested in gray short-tailed opossums (*Monodelphis domestica*) (Barnett et al. 2017). The only combination resulting in a surgical plane of anesthesia in all opossums was a combination of ketamine (100 mg/kg intraperitoneal) and dexmedetomidine (0.1 mg/kg IP). However, this mix also resulted in bradycardia and bradypnea, and the authors commented all injectable combinations were inferior to isoflurane.

Patagonian opossums (*Lestodelphys halli*), weighing approximately 50 g, were immobilized with 4 mg of ketamine for intra-abdominal transmitter placement (Geiser & Martin 2013).

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27

Echidnas and Platypus

Peter Holz

Introduction

The monotremes are unique among mammals because they lay shell-covered eggs, but nurse their young. There are five species: the short-beaked echidna (*Tachyglossus aculeatus*), found throughout Australia and New Guinea, three species of long-beaked echidna (*Zaglossus attenboroughi*, *Zaglossus bartoni*, and *Zaglossus bruijnii*), found in New Guinea only, and the platypus (*Ornithorhynchus anatinus*), found in Tasmania and along the east coast of mainland Australia (Van Dyck et al. 2013).

Echidnas

Short-beaked echidnas weigh between 2 and 7 kg, while long-beaked echidnas can weigh up to 10 kg. Their dorsal surface is completely covered in spines, which are firmly attached to the skin and do not pull out the way porcupine spines do.

Capture and Physical Restraint

Echidnas have strong front feet and large pectoral muscles adapted for digging. When approached, the echidna will attempt to bury itself in the ground, rolling into a partial ball with its head tucked under its body, leaving only its spine-covered dorsum exposed. Although they do not contain venom, the spines are sharp and can injure the unwary handler. Male echidnas have spurs on their hind legs which connect to a crural gland, similar to the platypus (Koh 2010). Unlike platypus, echidnas do not attempt to strike with their spurs. The crural gland produces a milky substance during the breeding season. This substance does not contain many of the toxins found in platypus venom and is likely related to chemical communication during the breeding season (Wong et al. 2013).

To dislodge a semiburied echidna it may be possible to slip something underneath it, such as a spade. However, extreme care is required to not injure the echidna in the process. If the echidna is on a flat surface it should be possible to slide a hand under the rear of the body and grasp a hind foot. Alternatively, the entire echidna can be picked up either with a thick towel to protect the hands or while wearing sturdy leather gloves. If picking the echidna up by the leg, it is important to be wary of the cloaca, as stressed echidnas frequently spray urine and feces.

Suitable receptacles for transport and holding should have smooth solid walls and include plastic garbage cans and sturdy cardboard boxes. If placed in a wire cage echidnas tend to rub their beaks resulting in lacerations and bleeding. Bags are also not suitable for transporting echidnas.

Anesthesia

General anesthesia is required for examination because of the echidna's tendency to roll into a ball. As the echidna usually tucks its beak quite tightly into its body it is often not possible to access the beak for mask induction. Consequently, the echidna should be placed in an induction chamber connected to an anesthetic machine and flooded with a mixture of isoflurane and oxygen. Once sufficiently sedated the animal is removed, a mask is placed over its beak, and it is maintained with the inhalant anesthetic. Intubation is not possible because of the narrow oral cavity, inability to visualize the larynx, and the presence of a keratinous pad on the dorsal surface of the base of the tongue.

Occasionally echidnas are presented wedged into the luggage compartment of automobiles or other areas where they cannot be physically removed. Injectable agents will be required to anesthetize the echidna and extract it. A combination of medetomidine (0.3 mg/kg intramuscular [IM])

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Table 27.1 Analgesics and anti-inflammatories that have been used in echidnas (Middleton 2008; Bodley 2019).

Buprenorphine	0.01–0.03 mg/kg SC, IM BID-TID
Methadone	0.2 mg/kg SC QID
Meloxicam	0.2–0.5 mg/kg SC, IV SID
Carprofen	2 mg/kg PO BID
Flunixin	0.5 mg/kg SC, IM, IV SID
Ketoprofen	1 mg/kg SC, IM, IV SID

BID, Twice a day; BID-TID, Twice a day-Thrice a day; IM, intramuscular; IV, intravenous; PO, orally; QID, four times a day; SC, subcutaneous; SID, one a day.

and ketamine (5 mg/kg IM) works well. This can be reversed with atipamezole (five times the medetomidine dose IM). Alternatively, tiletamine/zolazepam (3–10 mg/kg IM) can be used. Induction and recovery are smoother with the medetomidine/ketamine combination (Vogelnest 2019a). IM injections can be administered into the hind leg or longissimus dorsi and sacrospinalis muscles.

Vascular Access

On the dorsal surface of the beak, just caudal to the nostrils, a soft swelling marks the presence of a vascular sinus (Fig. 27.1). This sinus is suitable for blood collection using a 25-gauge needle and 1–3-mL syringe. A heparinized winged infusion set (butterfly catheter) will reduce the likelihood of the needle coming out of the sinus if the echidna moves. Too much pressure on the syringe will collapse the sinus. A catheter can be inserted into a nostril and connected to an anesthetic machine to maintain anesthesia during the procedure (Fig. 27.1). The jugular vein can also be used, but is more difficult to access because of the echidna's short neck (Fig. 27.2) (Johnston et al. 2006; Holz 2015).



Figure 27.1 Blood collection from the beak sinus of a short-beaked echidna (*Tachyglossus aculeatus*).



Figure 27.2 A dorsally recumbent, anesthetized echidna (*Tachyglossus aculeatus*), demonstrating the technique for blood collection from the jugular vein.

Table 27.2 Selected physiological parameters for short-beaked echidnas (Holz 2015/with permission from Elsevier).

Heart rate	50–68 beats/minute
Respiratory rate	5–6 breaths/minute
Body temperature	28–33°C
Blood pressure	123/96 mmHg

Physiology

Table 27.2 lists some physiological variable ranges for short-beaked echidnas.

Platypus

Capture and Physical Restraint

Platypuses weigh from 0.6 to 3.0 kg. Males possess a sharp spur on each hind leg that is connected to a venom gland located in the upper thigh region. Venom is only produced by sexually mature males from about 4 years of age. Spurring and envenomation usually occurs on the hand and arm during restraint. While spurring is not fatal for humans, it has killed mice, dogs, and other platypuses, and is extremely painful. The subsequent pain and swelling can take up to 3 weeks to subside, with weakness and loss of function of the affected part persisting for up to 3 months (Vogelnest 2019b).

Platypuses are more aggressive and their venom more potent during the breeding season (August to October). The venom gland increases in weight from less than 5 g to almost 10 g. Consequently, extra care is required when handling them during this time (Holz 2015).



Figure 27.3 A manually restrained adult platypus (*Ornithorhynchus anatinus*), demonstrating the correct position of the hand at the base of the tail to avoid the spurs in adult males.

Platypuses are restrained by holding them by the tail base (Fig. 27.3). This keeps the spurs out of reach. Docile or hand-raised platypuses can be cradled in the hands. Platypuses are easily transported in bags such as pillowcases.

Anesthesia

Platypuses are anesthetized using a mask placed over the bill and induced with isoflurane and oxygen (Fig. 27.4). They are impossible to intubate because of their small gape, inability to visualize the larynx, and bulbous structure (torus linguae) at the base of the tongue. Transient bradycardia may occasionally occur. This usually resolves spontaneously or with a temporary reduction in anesthetic concentration. Injectable agents have rarely been used (Booth & Connolly 2008; Holz 2015).



Figure 27.4 An anesthetized platypus (*Ornithorhynchus anatinus*) induced and maintained with isoflurane in oxygen administered through a mask.

Vascular Access

A vascular sinus suitable for blood collection runs transversely along the rostral border of the bill (Fig. 27.5). A 25-gauge needle, attached to a 2–3-mL syringe, is inserted either side of the midline. Alternatively, a heparinized winged infusion set can be used as the needle is less likely to come out of the sinus if the platypus moves. Gentle pressure on the syringe is required to avoid collapsing the sinus. Blood can also be collected with greater difficulty from the ventral coccygeal vein or jugular vein.

Physiology

Table 27.3 lists some physiological variable ranges for platypus.



Figure 27.5 Venipuncture can be achieved in platypuses (*Ornithorhynchus anatinus*) by introducing a small-gauge needle into the sinus at the edge of the bill.

Table 27.3 Selected physiological variable ranges for platypus (Booth & Connolly 2008; Holz 2015).

Heart rate	140–230 beats/minute This can drop to 10–12 beats/minute during anesthesia
Respiratory rate	20–50 breaths/minute This can drop to 4–12 breaths/minute during anesthesia
Body temperature	29–34°C

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28

African Pygmy Hedgehog and Other Insectivores

Darryl Heard

Introduction

The most commonly encountered insectivore in clinical practice in North America is the African pygmy or white-bellied (*Atelerix albiventris*) hedgehog. In Europe the larger native hedgehog (*Erinaceus europaeus*) may be seen in rehabilitation facilities for trauma, primarily automotive. Consequently, this chapter will focus on the anesthesia of these hedgehogs.

The Order Insectivora has traditionally been used to unite several disparate mammalian groups (i.e., hedgehogs, moles, tenrecs, shrews, and solenodons) based on size and "primitive characters" (Nowak 1999). Recent revisions based on molecular evidence have redistributed insectivores into several orders: Afrosoricida (tenrecs and golden moles) and Eulipotyphala (hedgehogs, shrews, moles, and solenodons) (Wilson & Mittermeier 2018). For this discussion, however, these animals are grouped together. The tree shrews appear more closely related to primates and are classified within their own order Scandentia (Helgen 2005).

The biology, anatomy, and physiology of hedgehogs are well described by Reeve (1994). Their major anatomical characteristic is their spines, which are erected by a muscle originating in the deeper layers (Reeve 1994). When threatened and unable to flee, hedgehogs usually roll into a ball using several specialized muscles. All spiny hedgehogs appear able to hibernate during adverse conditions. Hibernation is associated with polycythemia and relative hypoglycemia (Reeve 1994). The "normal" body temperature of nonhibernating European hedgehogs is 35 ± 2°C (Reeve 1994). Heart rate is approximately 200–280 beats per minute (bpm), declining to ≤25 bpm during hibernation.

Moles and shrews are occasionally encountered as injured wildlife. Torpor occurs in shrews, some golden moles, and tenrecs (Reeve 1994). Shrews have some of the highest metabolic rates, oxygen consumption rates, water turnover, and heart and respiration rates of any mammal (Ishii et al. 2002; Ochocinska & Taylor 2005). Although moles are adapted to low-oxygen environments and can tolerate prolonged hypoxemia, that is no reason to allow this to occur during the perianesthetic period.

Physical Restraint

All insectivores can bite. In addition to the trauma that may be inflicted, shrews have venom, blarina toxin, within their saliva (Kita et al. 2004).

Reeve (1994) describes several techniques for unrolling a hedgehog. Leather gloves are worn to protect from the spines, as well as bites. If you are right-handed, gently lift the hedgehog's hind end in your right palm. Use your left hand under its front, head turned away from you. Gently bounce it up and down in your hands. The hedgehog will extend its feet and unroll its snout. Without hurrying, keep bouncing it gently and allow the snout to poke between the thumb and index finger of the left hand. Place the thumb on the back of its neck using gentle, firm pressure. This prevents it from tucking its head back down. Gently gripping the rear underside of the animal with your right fingers, put your right thumb in the small of its back and gently open out the animal by flexing it backwards. Alternatively, the rolled-up animal is held head down over a table. It then usually unrolls cautiously and tries to reach the surface. The back legs can then be grasped gently and the animal held by them. Alternatively, the animal can be transferred directly to an inhalant anesthetic induction chamber.

Preanesthetic Preparation

Fasting is not recommended since most insectivores are very small, have high metabolic rates and small glucose reserves, and are prone to develop hypoglycemia.

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Cardiomyopathy is a relatively common postmortem finding in African pygmy hedgehogs (Black et al. 2011; Raymond & Garner 2000). Orbits in hedgehogs are shallow and the palpebral fissures are large. This may predispose them to proptosis during the perianesthetic period, especially if the periocular area is damaged and inflamed (Wheler et al. 2001).

House musk shrews (*Suncus murinus*), and perhaps other shrew species, are very sensitive to inhalant and parenteral anesthetic-induced emesis (Gardner & Perren 1998; Horn et al. 2012). Conversely, morphine alone appears not to produce emesis in musk shrews (Selve et al. 1994). The neurokinin-1 antagonist GR205171 (1–3 mg/kg subcutaneous [SC]) and the 5-hydroxytryptamine antagonist ondansetron (3 mg/kg SC) both inhibited inhalant anesthetic-induced emesis in house shrews (Gardner & Perren 1998).

Parenteral Anesthesia

A summary of parenteral anesthetic/sedative/analgesic drugs is given in Table 28.1. Description of parenteral anesthesia in insectivores is scant; Doss and de Miguel Garcia (2022) give a summary of known publications. Although inhalation (isoflurane, sevoflurane) is preferred, parenteral anesthesia may be indicated for remote fieldwork or physical examination and imaging.

Xylazine (3 mg/kg SC) and ketamine alone (20–30 mg/kg intramuscular [IM]) or in combination with midazolam (1–2 mg/kg IM) will cause a hedgehog to unroll and allow examination (Reeve 1994). A combination of alfaxalone (3 mg/kg) and midazolam (1 mg/kg) administered SC into the mantle produced heavy sedation in hedgehogs (Hawkins et al. 2020). Doss and de Miguel Garcia (2021) recommend higher dosages of alfaxalone (5 mg/kg) and midazolam (1 mg/kg) SC for more reliable immobilization. Reversal of the midazolam with flumazenil (0.05 mg/kg or equal volume SC) usually hastens recovery.

Ketamine (30 mg/kg) and midazolam (1 mg/kg) SC provide a similar depth of immobilization to alfaxalone-midazolam, but recoveries were rougher and earlier premature. In addition, hedgehogs sedated with ketamine-midazolam had a significant decrease (>50%) in food intake for 2 days post sedation (Hawkins et al. 2020).

Subcutaneous tiletamine-zolazepam (Telazol) induces dose-dependent heavy sedation to light anesthesia in hedgehogs (Hausmann et al. 2021). However, recovery

Table 28.1 Anesthetic and analgesic drugs used in African pygmy hedgehogs and other insectivores (Doss & de Miguel Garcia 2022).

Parenteral Anesthetics/Sedatives	Dosage (mg/kg)	Comments
Midazolam	1–2 intranasal	Mild sedation, requires concentrated midazolam to reduce volume.
Midazolam/butorphanol	0.5/0.5 SC	Mild sedation, preanesthetic.
Midazolam/buprenorphine	0.5–1.0/0.03–0.05 SC or IM	Mild sedation, preanesthetic for mild-moderately painful procedures.
Ketamine	20 IM or SC	Poor relaxation, hypersalivation, but will allow hedgehog to unroll.
Ketamine/midazolam	30/1 SC	Heavy sedation to light anesthesia. Premature and hyperactive recoveries and drops in food intake. May need to double each of the dosages to get complete immobilization.
Ketamine/xylazine	20–40/3–5 SC or IV	Good immobilization with profound cardiopulmonary depression.
Ketamine/medetomidine	5/0.06 IM or SC	Good short-term immobilization.
Midazolam/butorphanol/ketamine	0.5/0.5/3–5 SC	Moderate sedation.
Alfaxalone/midazolam	3/1 IM	Heavy sedation to light anesthesia. Increase dosage for longer more profound sedation.
Tiletamine/zolazepam	10–30 SC	Heavy sedation to light anesthesia depending on dosage. As expected, prolonged recoveries marginally shortened by flumazenil.
Propofol	6–8 IV	Requires vascular access (cephalic vein). Administer slowly to effect – apnea/respiratory depression and hypotension can be an issue.

IM, intramuscular; IV, intravenous; PO, per os; SC, subcutaneous.
These drugs can be combined with the inhalant anesthetics isoflurane (induction 5%, maintenance 2–5%) or sevoflurane (induction 7–8%, maintenance 3–4%). The addition of parenteral sedatives/anesthetics can markedly reduce the maintenance anesthetic requirement or even supplant its use. Oxygen administration (occasionally respiratory support) is still recommended for parenteral anesthetic combinations. Additional analgesic drugs include meloxicam (0.2–1.0 mg/kg SC, IM, PO), tramadol (1–10 mg/kg PO), and gabapentin (15–20 mg/kg PO).

length was significantly increased and dose-dependent. Flumazenil (0.05 mg/kg) administration did not have a significant effect on reversal of the zolazepam, but recovery times were slightly faster for the lower dose (10 mg/kg) studied.

Injection Sites

For SC injections in hedgehogs, forceps are used to grasp a small fold of the spiny skin over the rump. Injection is made into the connective tissue at the base of the pleat formed with the needle parallel to the animal's body (Reeve 1994). A skin fold can also be raised by pulling upward on a spine.

Alternatively, an injection is made in the flank while a gloved helper pins the animal on a table. Intramuscular injections are made in the large muscles of the thigh, not the back. This route is avoided in most other insectivores because of the potential to cause irritation and self-trauma. Intraperitoneal injection is as described for rodents.

Intravenous injection is difficult or impossible in most cases. Potential sites include cephalic (over the forearm) and intraosseous injection into the femur, tibia, and possibly the humerus. A 24-gauge over-the-needle catheter can be placed in the cephalic vein of most hedgehogs.

Inhalation Anesthesia

Inhalation anesthesia provides rapid induction and recovery. An induction chamber can be constructed from a plastic container with an attachment for administration of the inhalant and another for removal of waste gases. Alternatively, a mask is held over the nose or used to completely enclose a small insectivore (Fig. 28.1). Animals caught in traps are either dropped into the induction chamber or the trap enclosed in a plastic bag for anesthetic administration.

Most insectivores are too small for endotracheal intubation. A large adult white-bellied hedgehog may be intubated with a 2-mm uncuffed endotracheal tube. Alternatively, an endotracheal tube made from an over-the-needle catheter can be used. A semirigid 1.9-mm endoscope can be used to facilitate intubation.

A laryngeal mask (V-gel®) designed for use in small rabbits has been successfully used in hedgehogs (Doss & de Miguel Garcia 2022; Huckins et al. 2021). Care must be taken, however, to ensure the tube is not dislodged and blocks the airway. Capnography (with or without pulse oximetry) is essential to monitor for a clear airway when using this technique.



Figure 28.1 Inhalation anesthesia is preferred for anesthesia in all insectivores. This white-bellied or African pygmy hedgehog (*Atelerix albiventris*) is being induced with isoflurane in oxygen administered into a commercial dog mask connected to a nonrebreathing system.

Analgesia

Analgesia is discussed in Chapter 2. Given the scant information available this author uses drugs and dosages based on information of other mammals of a similar size. This author has used buprenorphine (0.03 mg/kg SC every 12 hours) for analgesia.

Monitoring and Supportive Care

Monitoring and supportive care are as for rodents (Chapter 23). The high metabolic rate, oxygen requirement, and water turnover of many insectivores (especially shrews) make them very susceptible to hypothermia, hypoglycemia, hypoxemia, and dehydration. All effort should be made to minimize the duration of anesthesia. As described above, vascular access is difficult or impossible to attain in the smallest species. Intraosseous catheterization of the humerus, tibia, or femur is a possible alternative. The cephalic and

saphenous veins can be accessed using 24-gauge over-the-needle catheters. Monitoring can and should include pulse oximeter, Doppler flow detection, or electrocardiogram. When intubated or using a laryngeal airway, capnography is essential to monitor for possible airway occlusion.

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29

Xenarthrans

Gianmarco Rojas Moreno

Body Weight

The species of this superorder have very varied morphological and physiological characteristics, and include species as small as the pygmy anteater (*Cyclopes didactylus*) and the lesser fairy armadillo (*Chlamyphorus truncatus*) with weights that do not exceed 400 g, and others as large as the giant armadillo (*Priodontes maximus*) and the giant anteater (*Myrmecophaga tetradactyla*) that easily exceed 50 kg in adulthood.

Although there are currently many records of weights of the different species of xenarthra, it is important to know the exact weights of the animals as much as possible, since this will significantly improve anesthetic quality. Determining an accurate body weight will allow more precise dosing of anesthetic drugs. This may reduce the risks associated with anesthesia and may improve postanesthetic recovery.

Physical Restraint

The method of physical restraint of Xenarthra varies depending on the species.

Armadillos

Small armadillos can be contained manually, but the use of leather gloves is recommended to reduce the possibility of scratches and bites. The animal should be restrained from both sides of the shell. Animals should be prevented from being grabbed by the tail due to the high risk of dislocation or fracture of coccygeal vertebrae. Armadillos of large species (e.g., Priodontes) require the use of traps or mesh to facilitate their capture.

Anteaters

The capture technique will vary depending on the Genus and age of the animal. Pygmy anteaters (Cyclopes) can be contained with the help of leather gloves or towels that allow them to be covered during the procedure as, despite their small size, like their larger relatives, they have very strong and penetrating claws. The lesser anteaters (*Tamandua* spp.) can be held by the tail and pressed on its back, making the chest stick to the ground, thus preventing the animal from defending itself with its claws. The use of mesh or traps can be used in free-living animals. Giant anteaters (*Myrmecophaga* sp.) can be captured using large meshes or snares, but due to their size and strength, as well as their rapid, aggressive, and fierce response, physical restraint is not recommended for this species.

Sloths

Physical restraint in these animals is very simple in captivity under human care because they are constantly used for handling and contact. However, with free-living sloths, mainly those of the genus *Choloepus* spp., handling must be done with extreme care since these animals are quite strong and, despite not appearing to be quick, can make quick defense movements with their powerful arms. As well as very powerful claws, they have can give serious bites with modified teeth that are like canines, capable of generating very deep wounds in handlers. The recommended containment technique in these animals is to place a hand on their back and press them against the ground or a wall, making it impossible for them to scratch or bite (Rojas Moreno 2019).

Drug-delivery Method

In pygmy and medium anteaters (Cyclopes and Tamandua), drugs can be applied immediately after physical restraint using syringes and injecting mainly into the

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pelvic musculature. In giant anteaters (*Myrmecophaga* sp.), the use of remote injection methods is recommended, the most effective being the use of darts projected by blowpipes or pistols. The greatest difficulty in using this technique is that the animal's hair is so long and dense that it can decrease the accuracy of the firing point (Fig. 29.1).

Armadillos and sloths can be injected in the musculature of the pelvic limbs once adequate physical restraint has been applied.

Vascular Access

Venous access is a huge challenge when it comes to xenarthrans. All species have a peripheral vascular modification known as vascular cords or "rede mirabilis", which are vascular complexes made up of small microvessels. Multiple small vessels may be contained in a singular vascular sheath. This system improves venous return because xenarthrans normally have a small heart with a low heart rate and low cardiac output. Apart from in pregnancy, there are some vascular access points that can be used easily. In armadillos, the ventral coccygeal vein, the saphenous vein, and the jugular vein are recommended for blood sampling as well as for the administration of anesthetics or intravenous fluids. In sloths, the venous access points are limited to the femoral and brachial veins, and in the case of hypovolemic or shock patients, a phlebotomy is required to adequately access these veins. In anteaters, the venous accesses are the jugular vein (Fig. 29.2) and the facial vein in giant anteaters, and the ventral coccygeal vein in pygmy and lesser anteaters (Fig. 29.3).



Figure 29.1 Darting a giant anteater.



Figure 29.2 Jugular vein access in a giant anteater.



Figure 29.3 Ventral coccygeal vein access in a lesser anteater.

Endotracheal Intubation

Endotracheal intubation in xenarthrans is undoubtedly one of the greatest challenges in the anesthesia of these animals. The main complications are the small opening of the oral cavity and the depth of the entrance of the glottis.

In armadillos and sloths, endotracheal intubation can be performed with the help of a straight-blade laryngoscope (Miller type), with the neck hyperextended to facilitate viewing of the glottis inlet.

In anteaters, this difficulty is much more pronounced, and it is impossible to observe the glottis without the help of an endoscope. In addition, even when it can be observed, the anatomy of its bone and cartilaginous structures greatly complicates this procedure (Borges et al. 2017). Although the tracheostomy approach has been proposed as a possible ventilatory access, the presence of the mandibular salivary glands and the depth of the glottis greatly complicate a tracheal approach even in cases of respiratory emergency in anthills (Brainard et al. 2008).

Sedation/Tranquilization Techniques in Xenarthrans

Pharmacological immobilization of xenarthrans is undoubtedly one of the most complicated areas of wildlife anesthesia for many reasons. The complexity of working with these species is due, among other things, to the lack of knowledge of the anatomy, physiology, and ethology of the different Xenarhthra species and the lack of knowledge of their pharmacological response to different anesthetics.

Sedation and Anesthesia Techniques for Captive Xenarthrans

Anteaters

Sedation and anesthesia procedures in anteaters in captivity are generally very simple to perform because they easily get used to being handled. This allows very direct access to them and in many cases means the use of prior physical restraint techniques that could be stressful is unnecessary.

Armadillos

Armadillos can be managed using many anesthetic combinations depending on the objective of the procedure. Both injectable anesthetic combinations as well as halogenated agents can be used in easily handleable animals.

Sloths

Sloths can be manually restrained and injected quite easily while they are resting. Once the anesthetic has been applied, the animals should be handled as little as possible and preferably left inside a containment box or transport box until the maximum induction effect of the anesthetics has been achieved. When the anesthetics has taken effect, the sloth should be held with gloves to avoid possible bites because although a sedated sloth is unable to grasp or hold onto a branch, it can still bite but with less force, especially sloths of the genus Choloepus. Sloths can also be held and sedated using masks and halogenated anesthetics. However, as sloths can hold their breath for prolonged periods of time, which makes mask inductions very difficult (West et al. 2014; Irving et al. 1942).

Chemical Immobilization of Free-ranging Xenarthrans

Anteaters

The first thing to consider is the remarkable differences in size and weight that exist between the three genera of anteaters, ranging from the giant anteater (35–55 kg), through lesser anteaters (6–10 kg) to pigmy anteaters (250–400 g) (Rojas Moreno 2014; Bermúdez 2014). Determining an accurate body weight will help when estimating the amount of anesthetic to be used in addition to determining the safest drug administration technique. The choice of anesthetic application technique for anteaters depends on factors such as the species (is it dangerous), age/size, typical behavior, and the situation of the animal at the time of capture (precaptured or free).

For the application of anesthetics, distance injection techniques for giant and lesser anteaters using darts propelled by blowpipes or dart guns eliminate the stress produced by prior physical restraint and the risk of the handlers' contact with the animal. In the case of juvenile specimens of the genera Myrmecophaga and Tamandua, or adults in Cyclopes, previous physical containment and manual application of drugs using simple syringes are recommended.

Armadillos

One field technique describes placing small armadillos in jars containing cotton balls impregnated with isoflurane; this process should be performed with extreme care since the isoflurane can be vaporized at high concentrations under normal atmospheric conditions, reaching concentrations of 33%. One complication with this technique is obviously overdose of inhalation, which in general does not happen when using a calibrated vaporizer where atmospheric pressure is controlled. Sedation and

short-term effective anesthesia have been achieved with isoflurane exclusively in *Cabassous unicinctus* specimens for blood sampling and claw-cutting procedures.

Recent publications describe the use of injectable combinations for the anesthesia of free-living armadillos with ketamine combinations.

Anesthetic Protocols in Xenarthrans

Anteaters

In anteaters different injectable combinations have been reported that can be used for immobilization in both wild and captive animals (Table 29.1).

Table 29.1 Anesthetics protocols used in anteaters.

Species	Drug Combination	Reversal	Comments	Reference
Silky anteater (*Cyclopes* spp.)	Ketamine 8–12 mg/kg Midazolam 0.4 mg/kg	None	Short noninvasive procedures	Rojas Moreno (2019)
Silky anteater (*Cyclopes* spp.)	Ketamine 4 mg/kg Dexmedetomidine 0.015–0.03 mg/kg Midazolam 0.1 mg/kg	Atipamezol 0.15–030 mg/kg	Rapid induction and recovery after the antagonist	Rojas Moreno (2012)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 11 mg/kg	None	Low anesthetic quality immobilization	Deem & Fiorello (2002)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 5–10 mg/kg Xylazine 0.5–1.5 mg/kg	Yohimbine 0.12–0.2 mg/kg	Without regurgitation	Deem & Fiorello (2002); West et al. (2014)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 2–4 mg/kg Medetomidine 0.02–0.04 mg/kg	Atipamezole at five times the medetomidine dose	Good muscle relaxation	Aguilar & Superina (2015)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 8–12 mg/kg Midazolam 0.4 mg/kg	Flumazenil 0.01–0.02 mg/kg	Short noninvasive procedures	
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 4 mg/kg Dexmedetomidine 0.015 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist in captive animals.	Rojas Moreno (2012)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 5 mg/kg Dexmedetomidine 0.0075–0.015 mg/kg Midazolam 0.15 mg/kg	Yohimbine 0.125–0.175 mg/kg or atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist For use in challenging environmental conditions and free-living wild animals Better option in bad condition animals	C. Rosas, Fundacion Rewilding, Argentina (pers. comm.)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 8.8 mg/kg Acepromazine 0.06 mg/kg Diazepam 0.3 mg/kg Buprenorphine 0.006 mg/kg	None	Associated with inhalatory anesthesia with isofluorane	Aguilar & Superina (2015)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 2 mg/kg Detomidine 0.15 mg/kg Midazolam 0.4 mg/kg	Yohimbine 0.2 mg/kg or atipamezol 0.1–0.15 mg/kg Flumazenil 0.01 mg/kg	Rapid induction and recovery after the antagonist	Soares-Neto, Pereira, and Santiago, Zoo Bauru, Brazil (pers. comm.)
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 4 mg/kg Medetomidine 0.02–0.03 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist	Author's experience

Table 29.1 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
Giant anteater (*Myrmecophaga tridactyla*)	Ketamine 5 mg/kg Medetomidine 0.01–0.02 mg/kg Midazolam 0.15 mg/kg	Yohimbine 0.125–0.175 mg/kg or atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist For use in challenging environmental conditions and free-living wild animals Used in more than 200 animals without complications linked with the anesthesia procedure	C. Rosas, Fundacion Rewilding, Argentina (pers. comm.)
Lesser anteater (*Tamandua* spp.)	Tiletamine/zolazepam 15 mg/kg	None	Rapid induction, but very prolonged recovery	Deem & Fiorello (2002)
Lesser anteater (*Tamandua* spp.)	Ketamine 8 mg/kg Midazolam 0.2 mg/kg	Flumazenil 0.01–0.02 mg/kg	Rapid induction and recovery	Author's experience
Lesser anteater (*Tamandua* spp.)	Ketamine 20 mg/kg Xylazine 1 mg/kg	Yohimbine 0.12–0.2 mg/kg	Good muscle relaxation	Fournier-Chambrillion et al. (1997)
Lesser anteater (*Tamandua* spp.)	Ketamine 4 mg/kg Dexmedetomidine 0.01–0.02 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist	Rojas (2012)
Lesser anteater (*Tamandua* spp.)	Butorphanol 0.1 mg/kg Detomidine 0.1 mg/kg Midazolam 0.1 mg/kg	Atipamezol 0.1–0.15 mg/kg Flumazenil 0.01 mg/kg	Rapid induction and recovery after the antagonist	Soares-Neto and Pereira, Zoo Bauru, Brazil (pers. comm.)

Armadillos

A variety of anesthetic agents have been used in different species of armadillos (Table 29.2) and many of these can be used for animals in free-living conditions. The thigh musculature is the best place for the application of intramuscular anesthetic drugs in armadillos (Fournier-Chambrillion et al. 2000; Orozco 2011; Rojas Moreno et al. 2013), although in species where the legs may be tucked completely under the carapace, e.g. *Tolipeutes*, the musculature at the base of the tail can be used with good results (Orozco 2011). Cyclohexamines are the pharmacological group most frequently used also in armadillos. Associations with alpha-2 agonists and/or benzodiazepines are the most frequently reported combinations for the different armadillo species (West et al. 2014; Fournier-Chambrillion et al. 2000; Hernandez et al. 2010; Orozco 2011; Rojas Moreno et al. 2013).

Free-living giant armadillos (*P. maximus*) are commonly caught using traps. Such individuals have been successfully immobilized with ketamine in combination with xylazine administered intramuscularly (West et al. 2014). Other reports describe the use of combinations of xylazine and midazolam for sedation and anesthetic support with isoflurane in giant armadillos in captivity (Falzone et al. 2013). Ketamine associated with xylazine has also been used with much success for anesthesia in *D. novemcinctus* (Fournier-Chambrillion et al. 2000; Hernandez et al. 2010; Miranda & Costa 2007) and *D. kappleri* (Fournier-Chambrillion et al. 2000).

Another combination that offers perhaps a better option for work with free-living animals, especially in field conditions, is the association of ketamine with medetomidine due to the ease of reversion of the effects of medetomidine (Fournier-Chambrillion et al. 2000; Vogel et al. 1998; Hanley et al. 2008). There is a report of the use of ketamine and medetomidine associated with butorphanol for intra-abdominal surgeries in *D. novemcinctus* (Hernandez et al. 2010). Although these animals metabolize the combination of ketamine with alpha-2 agonists very well, the use of antagonists such as yohimbine or atipamezole can

Table 29.2 Anesthetics protocols used in armadillos.

Species	Drug Combination	Reversal	Comments	Reference
Southern naked-tailed armadillo (*Cabassous unicinctus*)	Ketamine 5 mg/kg Dexmedetomidine 0.015 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist	Rojas Moreno (2019)
Southern naked-tailed armadillo (*Cabassous unicinctus*)	Isofluorane 4–5% induction 2–3% maintenance	None	Rapid induction and recovery Does not generate analgesia	Rojas Moreno (2019)
Andean hairy armadillo (*Chaetophractus vellerosus*)	Ketamine 15 mg/kg Xylazine 1 mg/kg Midazolam 0.4 mg/kg	Yohimbine 0.2 mg/kg	Without regurgitation, mild salivation Rapid recovery after the antagonist	Rojas Moreno et al. (2010)
Andean hairy armadillo (*Chaetophractus vellerosus*)	Ketamine 7 mg/kg Medetomidine 0.08 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.4 mg/kg	Rapid induction and recovery after the antagonist	Rojas Moreno (2019)
Andean hairy armadillo (*Chaetophractus vellerosus*)	Ketamine 7 mg/kg Dexmedetomidine 0.04 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.4 mg/kg	Rapid induction, good quality of anesthesia and recovery after the antagonist	Rojas Moreno (2019)
Greater long-nosed armadillo (*Dasypus Kappleri*) and nine-banded armadillo (*Dasypus novemcinctus*)	Ketamine 40 mg/kg Xylazine 1 mg/kg	Yohimbine 0.12–0.2 mg/kg	Without regurgitation, frequent salivation	Fournier-Chambrillion et al. (2000); Hernandez et al. (2010)
Greater long-nosed armadillo (*Dasypus Kappleri*) and nine-banded armadillo (*Dasypus novemcinctus*)	Ketamine 7.5 mg/kg Medetomidine 0.075 mg/kg	Atipamezole 0.15 mg/kg	Good muscle relaxation and rapid recovery after the antagonist	Fournier-Chambrillion et al. (2000)
Greater long-nosed armadillo (*Dasypus Kappleri*) and nine-banded armadillo (*Dasypus novemcinctus*)	Tiletamine/zolazepam 8 mg/kg	None	Rapid induction, but very prolonged recovery	Fournier-Chambrillion et al. (2000)
Nine-banded armadillo (*Dasypus novemcinctus*)	Ketamine 65–90 mg/kg	None	Low anesthetic quality immobilization	Deem & Fiorello (2002)
Nine-banded armadillo (*Dasypus novemcinctus*)	Ketamine 5–10 mg/kg Midazolam 0.2 mg/kg	Flumazenil 0.01–0.02 mg/kg	Rapid induction and recovery Short procedures	West et al. (2014)
Nine-banded armadillo (*Dasypus novemcinctus*)	Ketamine 15 mg/kg Medetomidine 0.07 mg/kg Butorphanol 0.1 mg/kg	Atipamezole 0.15 mg/kg	Good analgesia and muscle relaxation	Fournier-Chambrillion et al. (2000)
Nine-banded armadillo (*Dasypus novemcinctus*)	Ketamine 4 mg/kg Dexmedetomidine 0.015 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.15 mg/kg	Rapid induction and recovery after the antagonist	Rojas Moreno (2019)
Giant armadillo (*Priodontes maximus*)	Ketamine 5 mg/kg Xylazine 1 mg/kg	Atipamezole 0.1 mg/kg	Rapid recovery after the antagonist	West et al. (2014)
Giant armadillo (*Priodontes maximus*)	Xylazine 1.2 mg/kg Butorphanol 0.4 mg/kg Midazolam 0.2 mg/kg	Yohimbine 0.125 mg/kg Naltrexone 0.25 mg/kg	Maintenance with isoflurane Rapid induction and recovery after the antagonists	Falzone et al. (2013)

Table 29.2 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
Southern three-banded armadillo (*Tolypeutes matacus*)	Ketamine 30–32 mg/kg Xylazine 1 mg/kg	Yohimbine 0.12–0.14 mg/kg	Without regurgitation, frequent salivation Good muscle relaxation Taquipnea and apnea	Orozco (2011)
Southern three-banded armadillo (*Tolypeutes matacus*)	Tiletamine/zolazepam 4–12 mg/kg ♂ 4–9 mg/kg ♀	None	Rapid induction and anesthesia of medium duration. (~40 minutes) Regular muscle relaxation Taquipnea and apnea	Orozco (2011)
Southern three-banded armadillo (*Tolypeutes matacus*)	Tiletamine/zolazepam 3 mg/kg Medetomidine 0.06 mg/kg	Atipamezole 0.3 mg/kg	Used with isoflurane Rapid induction but very prolonged recovery	Orozco (2011)
Six-banded armadillo (*Euphractus sexcinctus*)	Ketamine 15 mg/kg Xylazine 0.5 mg/kg Midazolam 0.5 mg/kg Atropina 0.02 mg/kg	None	Used for intrabdominal surgery	Gasparotto et al. (2017)
Six-banded armadillo (*Euphractus sexcinctus*)	Ketamine 7 mg/kg Xylazine 1 mg/kg or ketamine 7 mg/kg Butorphanol 0.4 mg/kg plus propofol 5 mg/kg (IV)	None	Used for electroejaculation procedure	Sousa et al. (2016)

IV, intravenous.

accelerate recovery after handling (West et al. 2014; Orozco 2011; Rojas Moreno et al. 2013).

Combinations of cyclohexamines with benzodiazepines offer safe sedation of variable duration. Ketamine with diazepam or midazolam has been described as an option for armadillo chemical restraint (West et al. 2014; Divers 1986). These combinations have a short induction period, moderate muscle relaxation, and a relatively short period of sedation. The commercial association of tiletamine-zolazepam has also been described for the anesthesia of armadillos of the *Dasypus* spp. (Fournier-Chambrillion et al. 2000; Miranda & Costa 2007) and for Tolypeutes (Orozco 2011). The main characteristic of this combination is that it produces good muscular relaxation, but because of its prolonged recovery time, it is of limited use when working with free-living specimens (West et al. 2014; Orozco 2011).

Other injectable combinations that are relatively successful for armadillo restraint are the combinations of ketamine and acepromazine (Gillespie 2003), and droperidol and fentanyl (Tranquilli et al. 2007). Unfortunately, the first has a long recovery time and the latter is no longer on the market in its commercial form.

Most armadillo species can connected to a volatile anesthetic delivery system or placed in an induction chamber. Many volatile anesthetics, such as isoflurane and sevoflurane, have been successfully used in different species of armadillos (West et al. 2014; Miranda & Costa 2007; Deem & Fiorello 2002). However, it is important to note that armadillos have the capacity to hold their breath voluntarily and for prolonged periods, thus hindering the application of this method (West et al. 2014; Miranda & Costa 2007). The use of injectable premedication followed by immediate sedation of armadillos minimizes the occurrence of respiratory arrest (Gillespie 2003). Another technique that can reduce this problem is the administration of pure oxygen during the first minutes, then gradually increasing the concentrations of the anesthetic, ensuring that the animal continues breathing spontaneously and avoiding hyperventilation or apnea.

Sloths

A variety of injectable anesthetic combinations have been used in sloths (Table 29.3). Ketamine has been used alone or in combination with other anesthetics such as acepromazine, benzodiazepines (diazepam or midazolam), and alpha-2 agonists (xylazine, medetomidine, and dexmedetomidine).

In addition, commercial combinations such as tiletamine-zolazepam have been used with variable results (Vogel et al. 1998). More recently, the successful use of alpha-2 antagonists such as yohimbine and atipamezole

Table 29.3 Anesthetics protocols used in sloths.

Species	Drug Combination	Reversal	Comments	Reference
Brown-throated three-toed sloth (*Bradypus variegatus*)	Ketamine 5 mg/kg Medetomidine 0.02 mg/kg	Atipamezole 0.1 mg/kg	Rapid induction and recovery after the antagonist	Hanley et al. (2008)
Brown-throated three-toed sloth (*Bradypus variegatus*)	Ketamine 2 mg/kg Dexmedetomidine 0.011 mg/kg	Atipamezole 0.12 mg/kg	Short procedures in wildlife Requires supplementation of half dose	Kinney et al. (2013)
Brown-throated three-toed sloth (*Bradypus variegatus*)	Ketamine 2 mg/kg Dexmedetomidine 0.012 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.12 mg/kg	Rapid induction and recovery after the antagonist	Rojas Moreno (2019)
Maned sloth (*Bradypus torquatus*)	Ketamine 1.3 mg/kg Acepromazine 0.1 mg/kg	None	Mild sedation For clinic examinations and blood samples	Gilmore et al. (2000)
Hoffmann's two-toed sloth (*Choloepus hoffmanni*)	Ketamine 6 mg/kg	None	For taking blood samples	Deem & Fiorello (2002)
Hoffmann's two-toed sloth (*Choloepus hoffmanni*)	Ketamine 7 mg/kg Midazolam 0.1 mg/kg	Flumazenil 0.01–0.02 mg/kg	Short procedures	West et al. (2014)
Hoffmann's two-toed sloth (*Choloepus hoffmanni*)	Ketamine 2.5–2.9 mg/kg Medetomidine 0.02–0.04 mg/kg	Atipamezole 0.2 mg/kg	Short procedures Associated with isoflurane	Hanley et al. (2008)
Hoffmann's two-toed sloth (*Choloepus hoffmanni*)	Ketamine 2–6 mg/kg Dexmedetomidine 0.012 mg/kg Midazolam 0.1 mg/kg	Atipamezole 0.22 mg/kg	Rapid induction, good quality of anesthesia and recovery after the antagonist	Rojas Moreno (2011)
Southern two-toed sloth (*Choloepus didactylus*)	Ketamine 10 mg/kg Acepromazine 0.1 mg/kg	None	Rapid induction but poor sedation and muscle relaxation	Vogel et al. (1998)
Southern two-toed sloth (*Choloepus didactylus*)	Ketamine 10 mg/kg Xylazine 1 mg/kg	Yohimbine 0.12–0.2 mg/kg	Without regurgitation, frequent salivation	Vogel et al. (1998)
Southern two-toed sloth (*Choloepus didactylus*)	Ketamine 3 mg/kg Medetomidine 0.04 mg/kg	Atipamezole 0.2 mg/kg	Good muscle relaxation and rapid recovery after the antagonist	Vogel et al. (1998)
Southern two-toed sloth (*Choloepus didactylus*)	Tiletamine/zolazepam 6–10 mg/kg	None	Prolonged and irregular recovery	Vogel et al. (1998)
Southern two-toed sloth (*Choloepus didactylus*)	Ketamine 3 mg/kg Xylazine 1 mg/kg Midazolam 0.2 mg/kg	Yohimbine 0.12–0.2 mg/kg Flumazenil 0.01–0.02 mg/kg	Rapid induction and recovery after the antagonists Mild hypertension	Lescano et al. (2014)

has been reported as well as benzodiazepine antagonists such as flumazenil. The use of flumazenil may greatly reduce recovery times in sloths.

Combinations of ketamine and diazepam or midazolam are a good choice for short-term immobilizations in which the animal is not exposed to painful procedures. Combinations of ketamine with alpha-2 agonists (xylazine, medetomidine, and dexmedetomidine) have been presented as the best option for immobilization of sloths because they produce adequate muscle relaxation, some degree of analgesia, and the possibility of reversing their effects. However, it has been shown that the protocols with medetomidine and dexmedetomidine have less deleterious effects compared to combinations including xylazine (Vogel

et al. 1998; Hanley et al. 2008; Rojas Moreno et al. 2011; Lescano et al. 2014). Tiletamine-zolazepam is considered safe and effective for use in captive conditions, but it has a prolonged recovery time (West et al. 2014). This combination promotes deep anesthesia with good muscle relaxation, but in some cases can lead to respiratory depression (Aguilar & Superina 2015). All associations with ketamine, other than acepromazine-associated, promote dissociative anesthesia of about 40 minutes' duration (West et al. 2014; Miranda & Dejuste 2012; Hanley et al. 2008). Combinations of ketamine, alpha-2 agonists, and benzodiazepines provide more durable anesthesia times, reaching over 60 minutes, and very short recovery times, offering an anesthetic quality superior to that of other pharmacological combinations (Rojas Moreno et al. 2013; Lescano et al. 2014).

Anesthetics Monitoring in Xenarthrans

Anteaters

The monitoring of physiological parameters during the trans-anesthetic period is of the utmost importance in anteaters and can be performed in similar manner to that carried out for other mammalian species (Fig. 29.4). It is recommended that data are collected every 5–10 minutes, throughout the anesthetic procedure (Rojas Moreno 2014). The cardiac function (heart rate and cardiac rhythm) (see Table 29.4) can be monitored with the help of an adult-size stethoscope in giant and arboreal anteaters, and with a pediatric stethoscope in pygmy anteaters (Rojas Moreno & Miranda 2012). Electrocardiography is useful to detect arrhythmias that cannot be detected by cardiac auscultation alone (Rojas Moreno 2014). Respiratory function should be monitored continuously. Respiratory rate can be recorded by thoracic auscultation and visualization of respiratory movements (Rojas Moreno & Miranda 2012).

Oxygen saturation (SO_2) can be monitored using pulse oximetry by placing the clamp sensor on one finger in the case of arboreal anteaters (Fig. 29.5). In pygmy anteaters the pulse oximeter sensor can be placed on the plantar portion of the hind limb (Fig. 29.6) or on the tail. In giant anteaters the pulse oximeter sensor can be placed on the tongue (Fig. 29.7) or an esophageal sensor placed inside the mouth in direct contact with the oral mucosa can be used (Rojas Moreno 2014). When anesthetizing pigmy anteaters, the recording of body temperature should be evaluated in relation to the environmental temperature,



Figure 29.4 Anesthesia monitoring in anteaters.

Table 29.4 Values of heart rate, respiratory rate, and rectal temperature registered in xenarthrans with different anesthetic protocols.

Species	Drug Combination	Heart Rate (bpm)	Respiratory Rate (rpm)
Southern naked-tailed armadillo (*Cabassous unicinctus*)	Ketamine Dexmedetomidine Midazolam	79–98	38–43
Andean hairy armadillo (*Chaetophractus vellerosus*)	Ketamine/xylazine/midazolam	99–107	28–32
	Ketamine/medetomidine/midazolam	88–115	42–47
	Ketamine/dexmedetomidine/midazolam	81–109	42–47
Greater long-nosed and nine-banded armadillo (*Dasypus* spp.)	Ketamine/xylazine	52–168	30–70
	Ketamine/medetomidine	75–125	30–60
	Tiletamine/zolazepam	110–150	14–42
Giant armadillo (*Priodontes maximus*)	KetXylazine/medetomidine/ butorphanol + isofluorane	48–60	4–20
Southern three-banded armadillo (Tolypeutes matacus)	Ketamine/xylazine	90–112	60
	Tiletamine/zolazepam	110–140	variable
Giant anteater (Myrmecophaga tridactyla)	Ketamine/dexmedetomidine/midazolam	34–140	3–38
Lesser anteater (Tamandua spp.)	Ketamine/dexmedetomidine/midazolam	46–121	8–42
Silky anteater (Cyclopes spp.)	Ketamine/dexmedetomidine/midazolam	78–184	16–41
Hoffmann's two-toed sloth (*Choloepus hoffmanni*)	Ketamine/dexmedetomidine/midazolam	36–75	10–16
Southern two-toed sloth (*Choloepus didactylus*)	Ketamine/xylazine/midazolam	46–70	10–21
Brown-throated three-toed sloth (*Bradypus variegatus*)	Ketamine/dexmedetomidine/midazolam	30–60	8–14

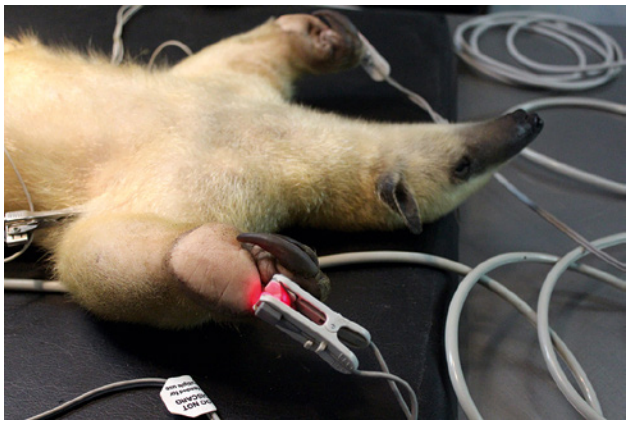


Figure 29.5 Oximetry pulse probe in the finger of a lesser anteater.

since the body temperatures of these animals may be partially dependent on their environmental temperature (McNab 1996).

Anesthesia Recovery in Anteaters

The use of antagonists is recommended to reduce recovery time and the animal should be accompanied in all cases until it shows adequate recovery. Giant anteaters should be monitored directly until head, thoracic, and



Figure 29.6 Anesthesia monitoring in a pigmy anteater.



Figure 29.7 Oximetry pulse probe on the tongue of a giant anteater.



Figure 29.8 Oximetry pulse and temperature monitoring in an Andean hairy armadillo.

pelvic limb movements are noted. After this the animal should be observed from a safe distance if it is free-ranging or kept in a suitable transport box until complete recovery. The box must allow an adequate extension of the animal's neck to avoid problems with obstruction of the respiratory tract by compression or the presence of secretions. Tamandua and Cyclopes anteaters can be monitored until almost total recovery because they are easily physically contained.

Armadillos

Special care during the induction process in armadillos because it is in this period that most anesthetic emergencies occur (Deem & Fiorello 2002). Among the parameters to be monitored, particular attention should be paid to significant changes in body temperature. In these species body temperature is usually low, varying from 30 to 35°C (Miranda & Costa 2007; West et al. 2007). In addition, armadillo body temperature is strongly influence by the environmental temperature so both temperatures should be monitored simultaneously. This is achieved using an environmental thermometer with a probe for external temperature measurement placed near the skin. A temperature probe can also be placed rectally to measure the animal's body temperature (Fig. 29.8). This may be achieved by using temperature sensors of multiparametric anesthetic monitors (Fig. 29.9).

Heart rate can be monitored by cardiac auscultation using a pediatric stethoscope or by an electrocardiogram, or indirectly by pulse oximetry (Fig. 29.8). The respiratory rate can be assessed by visually counting respiratory movements (Fournier-Chambrillon et al. 2000; Rojas Moreno 2013). The use of hemogasometry in armadillos is very complicated, mainly due to the difficulty of locating and channeling the arteries in these animals. However, blood gases should be monitored when possible (West et al. 2007) and mixed blood can be collected with great care from the heart. Pulse oximetry is used in armadillos by placing the sensor on the tongue, or on the penis in the case of males (Fournier-Chambrillon et al. 2000). There are reports of sensor placement in the thigh of animals (Deem & Fiorello 2002). Technical problems, mainly related to the sensitivity of the sensor, can make it difficult to register this parameter. Other locations for placing the oximeter sensor are the jaw, the fingers or even the palmar and plantar surface in small species (Figs 29.8 and 29.9). Heart and respiratory rate in anesthetized armadillos may vary in relation to the species and the drugs used for anesthesia (Table 29.3).



Figure 29.9 Multiparametric monitoring anesthesia in an Andean hairy armadillo.

Anesthesia Recovery in Armadillos

Excessive salivation caused by various drugs can be reversed using atropine (Divers 1986; Gillespie 1993). Armadillos have been reported to recover spontaneously from ventricular fibrillation without any treatment; likewise, armadillos can tolerate long periods of apnea and hypoxia compared to other mammals (Thurmon et al. 1996). Many cardiovascular abnormalities can occur when using alpha-2 agonists for immobilization procedures (Sinclair 2003). Alpha-2 agonists may be antagonized with atipamezole or yohimbine, both to negate cardiovascular adverse effects as well as to initiate anesthetic recovery of the animal (West et al. 2007). Reversing the effect of benzodiazepines using flumazenil may reduce recovery time, but the short duration of the antagonism action time of flumazenil (60 minutes) makes its use impractical in free-living conditions since benzodiazepine effects may last for more than 4 hours (West et al. 2007). In general, it is important to keep armadillos in confinement or under observation until their full recovery before being released.

Anesthesia Monitoring in Sloths

Heart rate can be monitored by auscultation with the help of a pediatric stethoscope or with the support of an electrocardiograph. Respiratory rate is verified by visual counting of respiratory movements (Hanley et al. 2008). Blood pressure can be monitored in sloths by indirect methods due to the difficulty in catheterizing arteries in these species (West et al. 2007). In sloths, blood pressure can be measured by placing a Doppler vascular flow sensor over the radial artery, with a 5-cm pediatric blood pressure cuff on the arm of the animal connected to a sphygmomanometer (Hanley et al. 2008) or a multiparameter monitor (Fig. 29.10). Sloths present extreme variation in blood pressure values and stress factors may influence these values (Gilmore et al. 2000).



Figure 29.10 Multiparametric monitoring anesthesia in two-toed sloth.

Pulse oximetry is used in sloths to monitor cardiorespiratory function. Values may be influenced by hypothermia, hypotension, and tissue pigmentation (West et al. 2007). Pulse oximeter sensor placements include the tongue, jaw (Fig. 29.10), preputial, and rectal mucosa (Hanley et al. 2008).

Anesthesia Recovery in Sloths

Many cardiovascular abnormalities can occur when alpha-2 agonists are used for immobilization of animals (Sinclair 2003) and these effects can be antagonized by

using atipamezole. Using atipamezole to antagonize the effects of alpha-2 agonists can improve cardiovascular function and negatively affect the anesthetic recovery of the animal (West et al. 2014). Flumazenil rapidly antagonizes the effects of benzodiazepines by reducing the postanesthetic recovery time, especially in captive animals (Lescano et al. 2014), but the short duration of the effect of flumazenil (60 minutes) makes its use impractical in free-living conditions because the duration of benzodiazepine effects may be more than 4 hours (West et al. 2014).

In general, sloths may require confinement during recovery until they can grab the branches on their own again. Good confinement prevents self-inflicted injuries associated with excitation events during recovery (West et al. 2014).

Complications and Other Considerations

Support and Trans-anesthetic Management

Some procedures make working with some species of anteaters safer. In the specific case of giant anteaters, it is recommended that a protective bandage is placed around the front claws to avoid possible injuries to personnel if the animal suddenly comes out of anesthesia. In general, if the animal is properly anesthetized, this procedure is not required.

In sedated animals in the wild, special care must be taken to protect the eyes. The use of eye drops or artificial tears is recommended to avoid dryness of the cornea and the eyes should be covered with a bandage or hood to protect them from the sun and further reduce dryness problems as well as light stimuli during anesthesia (Rojas Moreno 2014).

Due to the small opening of the oral cavity of anteaters, endotracheal intubation is impossible to perform. If oxygen support is necessary or maintenance with inhalational anesthetics is required, this can be achieved using masks for small cats.

Trans-anesthetic support fluid therapy can be performed subcutaneously using combinations of 0.9% sodium chloride and 5% dextrose. Fluid volumes can vary from 10 to 20 mL/kg depending on the condition of the animal. The fluid should be administered warm and injected into the larger skin folds near the hip and femur joints.

If anesthesia with benzodiazepines is delayed or very high doses were used, the use of flumazenil can help speed up the recovery process. However, it must be remembered that this drug has a half-life of 60 minutes in the individual and that some benzodiazepines can have a half-life of more than 4 hours (West et al. 2014). Because of this, observation of the animal is recommended for a reasonable time. Even after the antagonism with flumazenil, resedation can occur and careful post-anesthetic monitoring should occur.

Cardiovascular Emergencies

There are many drugs that can cause severe cardiovascular abnormalities. Alpha-2 agonists are undoubtedly the main promoters of negative cardiovascular effects, including bradycardia and hypo or hypertension. The main agents to counteract these effects in emergencies are alpha-2 antagonists such as yohimbine and atipamezole, which applied intramuscularly can prevent deleterious effects, promoting a relatively rapid recovery (Table 29.5). In anteaters with vascular decompensation or severe dehydration where immediate venous access is required, jugular vein phlebotomy is recommended. This can be used in both giant and lesser anteaters. The main complications to perform this technique in both species are related to the thickness of the skin and the long extension of their salivary glands (Gillespie & Adams 1985; Gillespie 2003). In emergency cases in which the use of this technique is feasible, intraosseous or intraperitoneal fluid administration can be performed (West et al. 2014). In sloths, the brachial vein can be accessed and in armadillos a venous access can be placed in the saphenous vein for the administration of fluids and emergency drugs.

Respiratory Emergencies

Respiratory arrest has been associated with the use of ketamine and xylazine for pharmacological immobilization of xenarthrans. Periods of momentary apnea are generally associated with the use of high doses of medetomidine and dexmedetomidine (Rojas Moreno 2012), but in most cases oxygen supplementation via a mask solves the problem.

In more complicated situations in sloths and armadillos, where respiratory arrest does not cease and SO_2 levels are very low, endotracheal intubation can be performed with the help of a Miller-type laryngoscope or a rigid endoscope. In anteaters a tracheotomy is recommended, facilitating the placement of an endotracheal tube, and thus offering effective assisted ventilation. Stimulating drugs that act on the respiratory centers of the central nervous system, such as doxapram (Table 29.5), can be used in patients exhibiting bradypnea and hypoventilation (West et al. 2014).

Table 29.5 Emergency drugs used in xenarthrans.

Drug	Dose (mg/kg)	Route	Comments
Doxapram	1–4	IM/IV	For the treatment of hypoventilation, recent respiratory arrest or as support for recovery after inhalation anesthesia
Yohimbine	0.12–0.2	IM/IV	For the treatment of cardiac depression and hypersecretion of the upper airways and in cases of hypersalivation or to prevent regurgitation
Atipamezole	1 mg/10 mg xylazine Five times the dose of medetomidine Ten times the dose of dexmedetomidine	IM/IV	For the treatment of cardiac depression and postanesthesia recovery with alpha-2 agonists
Flumazenil	0.02–0.05	IM	For the treatment of depression or prolonged sleepiness caused by benzodiazepine
Atropine	0.02–0.04	IM/IV	For the treatment of hypersecretion of the upper airways and in cases of hypersalivation or to prevent regurgitation

IM, intramuscular; IV, intravenous.

Hyperthermia

Considering the low corporal temperature of the different species of xenarthrans, if the temperature of these animals exceeds 37°C, the possibility of hyperthermia must be considered. The management of hyperthermia is complicated when the cause is pharmacological because in the case of ketamine, there are no antagonists and many of the antipyretic drugs used in human or veterinary medicine have not been shown to be 100% effective in xenarthrans. Undoubtedly, prevention is the most important factor to avoid events related to hyperthermia. Working during daylight hours, with little sunlight and pleasant ambient temperatures can reduce the chances of hyperthermia, and administration of cold fluids and wetting the animal's limbs with alcohol help to dissipate body heat.

Hypothermia

Hypothermia occurs mainly in field conditions (West et al. 2014) and therefore it is difficult to manage and treat. In general, the lack of adequate heat sources when working with free-living animals forces researchers to work as much as possible during the day when temperatures are not extreme (too cold or hot), avoiding days that are too cold or rainy to avoid exposing the animals to low temperatures. In field conditions, the administration of pre-warmed fluids rich in energy (dextrose or aminoacids) can help to control hypothermia. Keeping the animal's coat dry, reducing heat dissipation, and covering the animal with a blanket can also help. In captivity, hypothermia can be managed simply by working in a controlled environment or using a heat source that maintains the animal's temperature at ideal conditions. Infrared lamps, heaters, hot water bottles or electric blankets are useful for all species of Xenarthra.

Regurgitation and Excessive Salivation

Regurgitation is normally avoided in captive conditions by following the fasting time guidelines for each species. However, in free-living conditions this is more difficult. In this situation, even though physiologically these species do not usually regurgitate or vomit, it is recommended to keep the head slightly higher than the rest of the body to avoid any possible reflux during anesthesia. Excessive salivation is commonly seen with the use of protocols that include xylazine as one of their components; this can be controlled with the administration of anticholinergics such as atropine. Blood pressure should be monitored when xylazine is used or when other alpha-2 agonists are used. If atropine is administered for the treatment of bradycardia while using alpha-2 agonists, then blood pressure and heart rate should be closely monitored (Sinclair 2003).

Analgesia and Analgesic Techniques

There are no pharmacological studies on the use of analgesics in xenarthrans, but some opioid drugs and nonsteroidal anti-inflammatory drugs have been used with relative success to treat pain in various species of xenarthrans kept in captivity in zoos and other rescue centers (Table 29.6). It is important to note that the efficacy and safety of these drugs have not been critically evaluated in this species.

Local anesthetic techniques such as infiltrative and neural blocks should always be considered for intraoperative and postoperative pain control. Lidocaine and bupivacaine in doses similar to those used in domestic canine/feline patients have been shown to be very effective in Xenarthra species.

Table 29.6 Analgesic drugs used in xenarthrans.

Drug	Dose (mg/kg)	Route	Comments
Butorphanol	0.4–0.5 (all species)	IM/IV	Mild to moderate sedation and analgesia lasting 1–2 hours
Tramadol	0.5–4 (all species)	SC	Mild to moderate analgesia lasting 6–8 hours Can generate ileus in high and repeated doses
Ketoprofen	1–2 (armadillos/anteaters)	IM	Short to medium duration analgesia (12–24 hours) Do not use on sloths (hypothermia) Do not use for more than 3 days
Flunixin meglumine	1 (all species)	SC	Visceral analgesia (colic) Single application Do not apply to dehydrated animals (causes acute kidney failure)
Meloxicam	0.1 (all species)	IM	Moderate analgesia Once every 24 hours

IM, intramuscular; IV, intravenous; SC, subcutaneous.

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30

Aardvarks

Felicia Knightly

Introduction

Data on captive husbandry, medicine, and anesthesia of aardvarks under human care in zoological institutions remains limited. When this species is part of a zoological collection it is preferable to house the animals in an environment that is designed with their primarily nocturnal lifestyle in mind. An enclosure or building with a reversed light cycle is ideal for appropriate observations by care takers and visitors alike as the animals are inherently more active. In zoological institutions, aardvarks can live upwards of 20 years, which is quite favorable in comparison to many other insectivorous mammals.

Tubulidentata

The aardvark (*Orycteropus afer*) is the only living representative of the order Tubulidentata. Their natural habitat is confined to Africa south of the Sahara Desert. They are primarily nocturnal and sleep most of the day in underground burrows (Nowak 1991). They have solid bodies, typically ranging from 50 to 70 kg in weight. Their thick skin is sparsely covered with bristly hair and they have powerful legs with long spade-like toenails used for digging underground burrows, unearthing food, and self-defense. Aardvarks have a long snout and large ears, with excellent senses of smell and hearing. Interestingly, aardvarks have a 30-cm long, extensible tongue required for collecting insects such as termites and ants. In addition, aardvarks have a total of 20 cheek teeth. Each tooth is composed of numerous hexagonal prisms of dentin surrounding a tubular pulp cavity. This composition gives the order its name, Tubulidentata (tubule-toothed). The dental formula is I 0/0, C 0/0, P 2/2, M 3/3 (Fig. 30.1). All of the cheek teeth are continuously growing and lack enamel, which predisposes them to malocclusion and dental disease. Dental disease is one of the most common medical conditions requiring veterinary intervention in this species (Nowak 1991) (Fig. 30.2).

Aardvarks are extremely strong and react quickly to any undesirable stimulation. They have a powerful kick and are capable of displacing perceived threats with surprising accuracy. Manual restraint of adult aardvarks is not recommended. An adult aardvark can often be desensitized and conditioned for noninvasive examination, with some animals allowing minor clinical procedures, including wound care and diagnostic sampling (swabbing, skin scraping). Neonates and juveniles can be manually restrained for similar procedures until they approach 10 kg in body weight. In general, sedation or general anesthesia is highly recommended for thorough physical examinations of individuals over 10 kg. Venipuncture, ophthalmic examinations, and more invasive procedures can be completed safely when the animal is immobile.

Historically, a variety of anesthetic agents and protocols have been used successfully in aardvarks (Table 30.1) (Langan 2003; Stetter 2003). These include tiletamine and zolazepam, ketamine and detomidine (Vodicka 2004), ketamine and xylazine (Nel et al. 2000), ketamine and midazolam (Nel et al. 2000), ketamine and droperidol in combination with fentanyl (Dieterich 1986), and etorphine with acepromazine (Stetter 2003). Currently, a combination of ketamine and medetomidine administered intramuscularly continues to be the most widely used anesthetic protocol (Langan 2003; Stetter, 2003). When administered appropriately this combination typically results in smooth timely induction, reliable anesthesia for at least 30 minutes, and the ability to partially reverse anesthesia for an uneventful recovery.

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Figure 30.1 Normal dentition of the aardvark. Dental formula I 0/0, C 0/0, P 2/2, M 3/3.

Intramuscular injection by hand syringe or via pole syringe in this species can be remarkably unreliable and inconsistent. This is due to many factors, including the aardvark's thick skin, explosive reactions to needle insertion, and leakage of liquid from the injection site. Successful intramuscular administration of the anesthetic drug combination is most reliably achieved via remote CO_2-propelled dart. Pliers may be necessary to remove a dart from the thick skin and pressure should be applied to the area as the dart is removed to prevent the accumulation of air subcutaneously through the dart site. On completion of the procedure, partial anesthetic reversal is recommended by administering atipamezole intramuscularly. Attention should be given to the length of the procedure to gauge the presence of residual ketamine and/or gas anesthetic. Smoother recovery is typically achieved if appropriate time has passed for ketamine metabolism and gas exhalation prior to reversal administration.

Supplementation with gas anesthesia is highly recommended if prolonged, invasive, or surgical procedures are necessary. Inhalant anesthetics reportedly used in aardvarks include halothane and isoflurane (Nel et al. 2000; Langan 2003; Stetter 2003). Gas anesthesia is typically administered via an appropriately fitting face mask or an endotracheal tube. Precautions must be taken to prevent prolonged circumferential nasal pressure and subsequent nasal edema caused by either tight-fitting face masks or ties used for securing an endotracheal tube in place.

Intubation is preferable for most anesthetic procedures as the airway is then protected from potential aspiration and can be maintained during repositioning. Also, intubation allows for positive pressure ventilation if episodes of apnea occur or imaging (radiographs, CT) requires deep and/or prolonged inhalation. Thorough examination of the oral cavity, including the tongue and dentition, should be accomplished using a long, narrow laryngoscope blade prior to intubation because there is often inadequate room to do this afterward.

The long and narrow oral cavity of the aardvark makes intubation challenging (Fig. 30.3). In addition, dental disease and other medical issues affecting the tongue may increase the difficulty. Blind intubation with a 10-mm endotracheal tube in adult aardvark or a 3-mm endotracheal tube in juvenile (1 month) aardvark is reliable when the animal is anesthetized to an adequate depth and is breathing spontaneously.

The animal can be positioned in either lateral or sternal recumbency. The head and neck are maximally extended while gentle traction is used to extend the tongue straight out of the oral cavity (Fig. 30.6). If the animal is not at an adequate anesthetic depth this will not be possible and



Figure 30.2 Lateral radiograph of intubated aardvark with dental abnormalities.

Table 30.1 Chemical restraint agents used for aardvarks.

Immobilization Drug	Dose	Antagonist	Dose	Reference
Tiletamine/zolazepam	4–5 mg/kg	Flumazenil	0.01 mg/kg	Langan (2003)
Ketamine/medetomidine	3 and 0.03–0.07 mg/kg	Atipamezole	0.15–0.4 mg/kg	Langan (2003)
Ketamine/detomidine	4–8 and 0.09–0.18 mg/kg	Atipamezole	0.05–0.09 mg/kg	Vodicka (2004)
Ketamine/midazolam	15–20 and 0.28–0.68 mg/kg			Nel et al. (2000)
Ketamine/xylazine	14 and 0.94 mg/kg	Atipamezole	0.3 mg/kg	Nel et al. (2000)
Ketamine/diazepam	11 and 0.26 mg/kg			



Figure 30.3 Lateral view of the extent to which the oral cavity can be opened in the aardvark.

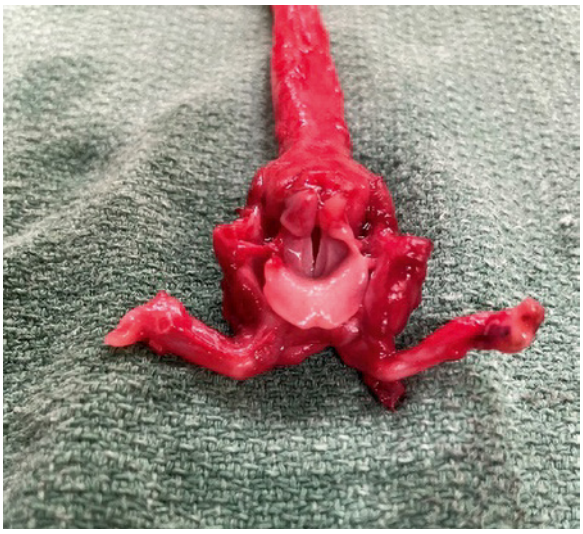


Figure 30.4 Larynx of 1-month-old aardvark.

swallowing is typically appreciated while attempts to retract the tongue occur. Often in this situation the endotracheal tube will be inadvertently advanced into the esophagus and any subsequent air, oxygen, or gas will be delivered into the stomach.

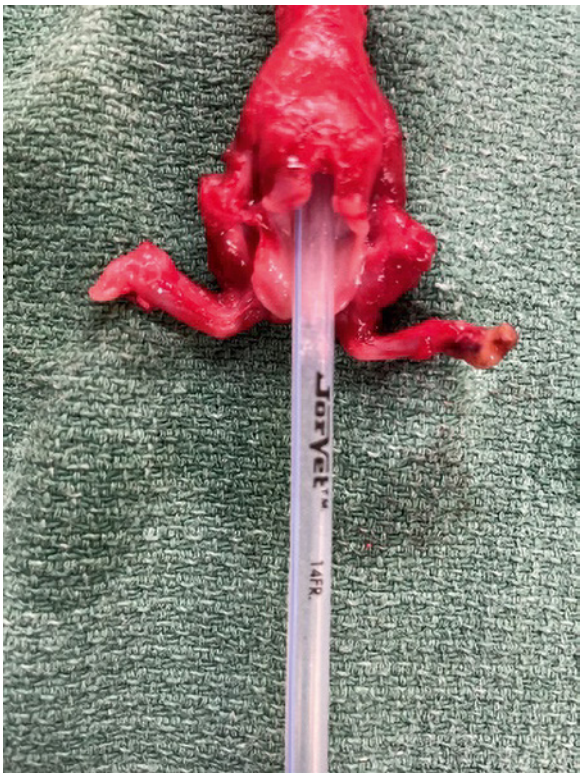


Figure 30.5 Larynx of 1-month-old aardvark with 3-mm endotracheal tube in place.

Once the aardvark is at an appropriate plane of anesthesia the endotracheal tube is advanced along the midline over the base of the tongue toward the larynx. While listening closely with an ear at the proximal end of the tube for maximum respiratory sounds, the tube is advanced into the trachea during inspiration. Slight rotation of the tube during this process may facilitate placement as well. In situations when an aardvark is not breathing spontaneously some form of endoscopic intubation will most likely be required. The tongue should be kept moist and manually returned to the oral cavity after the animal is intubated to prevent lingual edema and care should be taken to avoid any trauma during subsequent procedures (e.g., dentistry)

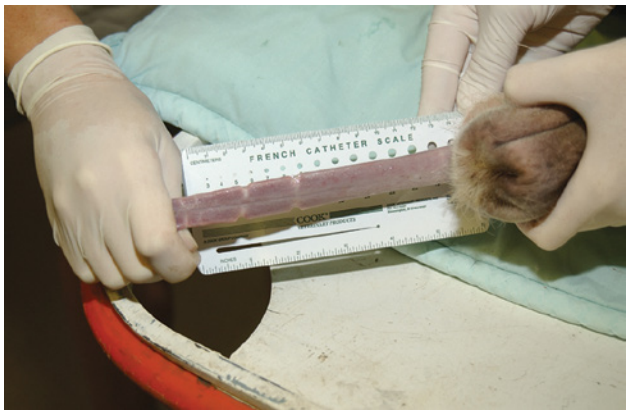


Figure 30.6 Withdrawing the aardvark's long tongue out of the mouth provides the needed space within the oral cavity and larynx to intubate the animal with an endotracheal tube.



Figure 30.7 Venipuncture from the medial saphenous vein in an aardvark.

as well as transport/recovery (e.g., extubation). Another issue that has been reported in aardvarks within the first 24–72 hours following immobilization is excessive pacing resulting in open wounds developing on feet and toenails. A short course of an anxiolytic (e.g., 10 mg of diazepam) in an adult aardvark administered prior to the animal's nocturnal activity has been recommended (Langan 2007). Another occasion when the use of low doses (0.25–0.45 mg/kg once daily or twice daily) of oral diazepam may be useful in this species is for females immediately after parturition. Some dams are very restless, which prevents sufficient nursing by newborn offspring and may also result in inadvertent injuries to them. Denning or nesting boxes constructed with or without creep areas for the new cub may also be useful because in the wild this species gives birth in a subterranean burrow, limiting excessive movements. Typically, females can be weaned off of diazepam after 3–4 weeks once the cub is sufficiently mobile and successful nursing is reliable.

A compilation of anesthetic data from Brookfield and Memphis Zoo between 1999 and the present revealed heart rate ranges between 60 and 95 beats per minute, respiratory rate ranges between 12 and 18 breaths per minute, and temperature ranges between 35 and 37.8°C (95 and 100°F). Anesthetic monitoring using auscultation, pulse oximetry, capnography, electrocardiogram and non-invasive blood pressure (NIBP), and temperature is conducted as it is in other mammals, with a few precautions due to aardvark anatomy. Out of an abundance of caution, this author avoids using pulse oximetry transmittance probes on the aardvark's tongue. Although most probes do not apply excessive pressure, applying them to the distal aspect of the tongue for a prolonged period of time could cause vascular and/or neurologic damage. NIBP cuffs are typically placed around the base of the tail or around the front leg (radius/ulna). Systolic, diastolic, and mean values vary depending on drug protocol, length of procedure, and obviously the health of the patient. Arterial blood samples for blood gas analysis can be obtained from the femoral or auricular arteries. Arterial catheter placement in the auricular artery may be used for direct blood pressure monitoring.



Figure 30.8 Intravenous catheter placement in the medial saphenous vein.

Blood collection and intravenous catheterization are best accomplished from the medial saphenous vein but are also possible using the cephalic, ventral tail, or facial veins. Peripheral veins are visible and somewhat prominent, but when venipuncture is attempted the appearance of the vascular diameter is misleading. The aardvark's skin is thick and tough, and has some elasticity. Stabilizing the skin by stretching it directly over the vessel prior to attempting blood collection decreases skin folding and vessel rolling. A modified cut-down technique over the vessel prior to intravenous catheter placement significantly improves success. After clipping and aseptic preparation of the site, the skin is pulled lateral to the vein before making a small stab incision using a scalpel blade or large-gauge needle. The skin is allowed to return to its normal position over the vessel, allowing for the placement of the intravenous catheter. Catheters can subsequently be secured in place with a combination of surgical glue, surgical tape, Vet-wrap, or Elasticon (Fig. 30.8).

Field techniques used to capture free-ranging aardvarks include the use of nets and funnel traps set at burrow entrances. All captured animals required anesthetic immobilization for safe handling and examination (Nel et al. 2000).

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31

Lemurs

Catherine Williams and Randall E. Junge

Introduction

The group of primates referred to as prosimians or strepsirhine primates includes lemurs, lorises, pottos, and bush babies. All lemurs are endemic to the island of Madagascar. Under current classification, there are five families and over 90 separate species of lemurs recognized (Mittermeier et al. 2010), although taxonomic groupings continue to change as more information on their genetics becomes available. Lorises, pottos, and bush babies are small-bodied, nocturnal primates. Lorises are native to Southeast Asia and India, while pottos and galagos are endemic to Africa (Nowak 1999; Rowe 1996).

When using anesthetic agents in prosimians, it is important to remember that there is very little controlled data on the pharmacokinetics of any drug class in these species. The information contained in this chapter is predominately derived from the authors' personal experiences and the few published reports that mention the use of a particular drug without apparent side effects. Thus, the doses provided here may not be the most pharmacologically appropriate, and there is no guarantee the drugs are entirely safe even though problems have not been documented. It is important to use all drugs conservatively in this group and to monitor animals' physiologic and behavioral responses carefully to minimize complications.

Prosimians are a very diverse group of primates and physiological responses to a particular drug may vary by species. It is unknown if prosimians respond to anesthetic agents similar to other primates but, in most instances, studies performed in anthropoid primates are the best resource from which to derive information when extrapolating drug doses. The reader is referred to chapters in this book discussing anesthesia in monkeys, gibbons, and great apes, and to other selected references for more extensive information on the pharmacologic action of anesthetic agents particular to higher primates (Horne 2001; Popilskis & Kohn 1997).

Special Physiology

Prosimian primates exhibit considerable anatomical and physiological variation (Mittermeier et al. 2010; Rowe 1996; Sussman 1999). Size ranges from 30 g for the smallest mouse lemur (*Microcebus myoxinus*) to more than 8 kg for some members of the Indridae family: diademed sifakas (*Propithecus diadema*) and indri (*Indri indri*). Table 31.1 gives approximate adult weight ranges for a variety of prosimian species. Prosimians have a low basal metabolic rate compared to other primates (Ross 1992). Several behaviors exhibited by lemurs, such as basking and huddling, are related to energy conservation and thermal regulation. Dwarf lemurs (*Cheirogaleus* sp.) and the mouse lemur (*Microcebus* sp.) are unique among primates in that they hibernate or undergo periods of torpor, an adaptation which allows them to conserve energy during periods of reduced food and water availability (Hladik et al. 1980; Schmid et al. 2000; Schülke & Ostner 2007).

The body temperature of lemurs and bush babies generally ranges between 36 and 37°C, however dwarf and mouse lemurs undergoing torpor may have temperatures significantly below 32°C (Dausmann et al. 2005; Schmid et al. 2000). Core body temperatures of fat-tailed dwarf lemurs track ambient temperatures for hours or days a time during deep torpor (Dausmann et al. 2005). The rectal temperature of lorises is slightly lower than that of lemurs and bush babies, and ranges between 35 and 36°C at normal room temperatures (Müller et al. 1985; Whittow et al. 1977).

Prosimians have no active mechanism for cooling, such as sweating or panting, and temperature regulation is accomplished primarily by limiting activity, seeking cool locations during hot weather, and licking hands to

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Table 31.1 Body weight ranges for various prosimian species.

Scientific Name	Common Name	Adult Weight (kg)
Avahi	Woolly lemur	1.0–1.5
Cheirogaleus medius	Fat-tailed dwarf lemur	0.16–0.25
Daubentonia	Aye-aye	2.5–3.0
Eulemur coronatus	Crowned lemur	1.5–2.0
Eulemur fulvus	Brown lemur	2.0–2.7
Eulemur macaco	Black lemur	2.0–2.5
Eulemur mongoz	Mongoose lemur	1.4–1.6
Galago moholi	Southern lesser bush baby	0.15–0.25
Hapalemur griseus	Eastern lesser bamboo lemur	0.75–2.50
Indri indri	Indri	6.00–7.25
Lemur catta	Ring-tailed lemur	2.0–3.0
Lepilemur	Sportive lemur	0.5–1.0
Loris tardigradis	Slender loris	0.15–0.25
Microcebus murinus	Mouse lemur	0.06–0.09
Mirza spp.	Giant mouse lemur	0.028–0.320
Nycticebus pygmaeus	Pygmy loris	0.35–0.45
Nycticebus coucang	Slow loris	0.80–1.30
Otolemur crassicaudatus	Thick-tailed greater bush baby	0.70–0.85
Perodicticus potto	Potto	0.85–1.60
Propithecus coquereli.	Coquerel's sifaka	3.3–4.5
Varecia sp.	Ruffed lemur	3.0–3.8

generate evaporative cooling. Therefore, capture and handling during warm weather should be done either early in the morning while outdoor ambient temperatures are cool or indoors in temperature-controlled environments.

The amount of time necessary to withhold food prior to anesthesia varies by species due to differing rates of gastric emptying. While all prosimians have simple stomachs, the size and conformation of the cecum and large bowel varies depending on the dietary profile of the species. Campbell et al. (2004) measured gastric emptying times in four species of lemurs. Gastric emptying times ranged from 3 to 4 hours in the ruffed lemur (*Varecia variegata*), a frugivorous species, and up to 24 hours in eastern lesser bamboo lemurs (*Hapalemur griseus*) and Coquerel's sifaka (*Propithecus coquereli*), both species that are highly folivorous. The brown lemur (*Eulemur* sp.), a generalist feeder, had gastric emptying times of 8 hours. Thus, while withholding food for 8 hours is sufficient for the majority of lemur species, longer periods of fasting are likely necessary for highly folivorous species.

Restraint

Physical restraint of small prosimians weighing <1 kg is relatively simple. Animals are restrained by grasping initially over the back of the neck and around the mandible with a gloved hand to control the head while using a second hand to control the lower abdomen and back legs.

For animals weighing between 1 and 4 kg, the animal is first netted in its enclosure or out of a transport kennel. The head is initially controlled by placing one hand around the back of the neck with fingers extending under the jaw to secure the animal. The second hand is then placed under the neck and mandible to prevent serious bites. The animal is allowed to grasp the handler's arm with front and back limbs. Limited examinations and minor treatments, such as the administration of subcutaneous fluids or subcutaneous or intramuscular (IM) injections, can be performed with animals in this position (Fig. 31.1). When manually restraining lemurs, it is recommended that the handler wear arm guards to protect against scratches when animals grasp the handler's forearm. If more control is needed, a second handler is employed to restrain the hind limbs and extend the hind legs while the animal is positioned on its back (Fig. 31.2). It is important that the person restraining the hind legs grasps the thighs above the stifles to prevent injury to the knee joint. Although it is possible for experienced handlers to physically restrain lemurs weighing more than 5 kg, the larger species are usually anesthetized for procedures.

Squeeze cages can also be used to restrain medium- to large-size lemurs for the administration of IM injections. Animals should be squeezed slowly to avoid undue stress.



Figure 31.1 Single-handler technique for manual restraint of lemurs weighing 1–4 kg.



Figure 31.2 Two-handler technique for manual restraint of lemurs for physical examination or collection of blood and urine.

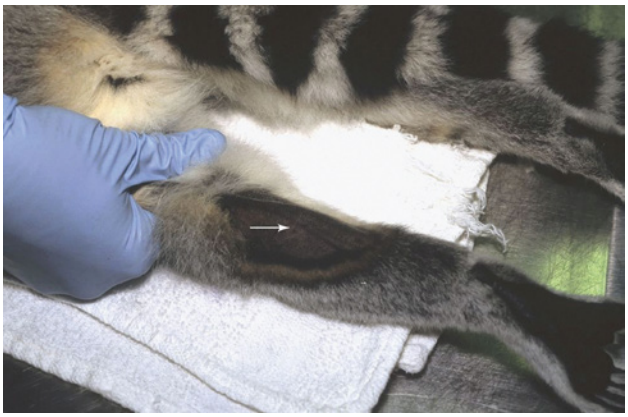


Figure 31.3 Route of the external saphenous vein on the caudal aspect of the tibia and positioning for occlusion of the proximal venous return in a ring-tailed lemur.

Vascular Access Sites

Several standard sites are accessible in prosimians; however, the preferred site depends on the species, the size of the animal, and whether it is under manual or chemical restraint. Blood can be collected from the cephalic, external saphenous, and jugular veins, and from the femoral artery or vein. Peripheral veins, such as the cephalic and external saphenous, tend to collapse easily, making withdrawal of more than minimal amounts of blood difficult from these sites. The authors prefer the region of the femoral triangle site in the inguinal region for blood collection requiring more than 1 mL of blood. With the animal in dorsal recumbency, the pulse of the femoral artery is palpable in the femoral triangle. The femoral vein lies immediately adjacent and medial to the femoral artery. In most cases, the close approximation of the vessels means that the artery is sampled nearly as often as the vein. The main disadvantage with using this site for blood collection is the increased risk of hematoma formation if the artery is sampled and inadequate attention paid to ensuring proper hemostasis after needle withdrawal. This is particularly true in animals that are manually restrained as blood pressure can be substantially higher than in animals under chemical restraint. In extreme cases, lemurs have died from exsanguination secondary to inadequate hemostasis following blood collection from the femoral artery.

For indwelling catheter placement in lemurs, the external saphenous vein is most accessible; however, the cephalic and jugular veins can be used in larger species. When placing a catheter in the external saphenous vein, position the animal in ventral recumbency with the hind legs extended behind the animal. After shaving and preparing the skin of the caudal aspect of the tibia, an assistant grasps the caudal thigh of the hind leg and places his/her thumb horizontally across the mid- to lower thigh, thus closing off the proximal return of the external saphenous vein. The route of the external saphenous vein is visible along the posterior aspect of the tibia (Fig. 31.3).

Endotracheal Intubation

Endotracheal intubation is relatively straightforward in most prosimians but can be challenging in select species. In lemurs, the epiglottis is long and points dorsally, completely obscuring visualization of the glottis. With the animal in sternal recumbency, the tongue is grasped and pulled forward to visualize the epiglottis. A small blade laryngoscope is useful to aid visualization and move the epiglottis ventrally to expose the glottis. When inserting the endotracheal tube, direct the tube toward the ventral aspect of the glottis.

Some lemurs, in particular aye-ayes (*Daubentonia madagascariensis*) and ring-tailed lemurs (*Lemur catta*), are more challenging to intubate. The heavy musculature of the jaws in aye-ayes prevents the mouth from opening widely and the long upper and lower incisors obscure visualization of the caudal oral and pharyngeal cavities. In ring-tailed lemurs, the opening of the vocal folds is narrow compared with other species. Intubation is most easily performed in both aye-ayes and ring-tailed lemurs by first inserting an 8-Fr plastic urinary catheter into the trachea as a guide, then passing the endotracheal tube over the catheter into the trachea. Once the endotracheal tube is in place, the guide catheter is removed.

Prosimians, like other primates, have a short trachea. Care must be taken to avoid inserting the endotracheal tube too far and thus intubating a mainstem bronchus.

Measuring the length of the endotracheal tube relative to the animal prior to intubation is advised. Once the tube is in place, auscult both sides of the chest for air sounds and monitor end-tidal CO2 by capnography whenever possible. Cuffed endotracheal tubes ranging in size from 3.0 to 4.5 mm are suitable for animals weighing between 1.5 and 5 kg, while 2.5-mm uncuffed Murphy tubes can be used for individuals ranging in size between 750 g and 1.5 kg. For animals weighing less than 1 kg, infant feeding catheters or urinary catheters can be used as endotracheal tubes (Morris et al. 1997).

Preanesthetic Considerations

As with any animal, disease or abnormalities that alter metabolic pathways or gas exchange affect the safety of anesthesia in prosimian primates. It is important to do a thorough preanesthetic evaluation when possible prior to using anesthetic agents. The ease of manual restraint in prosimians makes it possible to perform limited examinations and even draw blood without chemical immobilization in many cases. However, if preanesthetic evaluations are not possible, careful selection of agents, using the minimum dosage necessary to accomplish the procedure, improves safety.

When developing a preoperative regime, it is important to consider the analgesic potential of the drugs under consideration. Analgesia is most effective when provided preemptively and the administration of analgesics preoperatively decreases the amount of drugs needed to manage pain postoperatively and may lessen the amount of anesthetic needed by blunting pain perception during the procedure.

It is not always possible to give preanesthetic medications, but when possible, their administration provides a smoother induction, a more stable plane of anesthesia, and decreases the amount of other drugs needed to produce general anesthesia. Nonsteroidal anti-inflammatory drugs (NSAIDs), benzodiazepines, alpha-2 agonists, and opioids have all been used in prosimians successfully. Each can be combined with other drugs to take advantage of the synergistic effects of using drugs that have differing mechanisms of action. Dosages of anesthetic agents commonly used in prosimians are given in Table 31.2 and doses of analgesic drugs are given in Table 31.3.

Nonsteroidal Anti-inflammatory Drugs

NSAIDs have no inherent sedative qualities; however, their analgesic effects make their use beneficial perioperatively as well as for the management of acute and chronic pain not associated with surgery. NSAIDs used in prosimians without obvious side effects include acetaminophen, aspirin, ibuprofen, ketoprofen, meloxicam, and flunixin meglumine (Table 31.3). As a class cyclooxygenase, inhibitory NSAIDs may be associated with adverse gastrointestinal side effects and renal toxicity. All animals receiving NSAIDs should be closely monitored for signs of gastric ulceration or bleeding and remain well hydrated during treatment. Because of potential side effects on renal and platelet function, the use of NSAIDs preoperatively is controversial (Crandell et al. 2004; Lemke et al. 2002; Lobetti & Joubert 2000). Careful patient and drug selection is important if this class of drugs is used preemptively.

Benzodiazipines

Benzodiazepines are beneficial premedication agents due to their antianxiety, sedative, and muscle relaxant effects, and for antiseizure activity. Diazepam and midazolam have

Table 31.2 Drugs commonly used for sedation and anesthesia in prosimian primates.

Agent	Dosage (mg/kg)	Route	Duration	Reversal[a]
Diazepam	0.5–2.5	IV	30 minutes	Flumazenil
Midazolam	0.1–0.3	IM, IV	30 minutes	Flumazenil
Butorphanol	0.1–0.4	IM, IV, SC	3–4 hours	Naloxone
Dexmedetomidine	0.02	IM	30–60 minutes	Atipamazole
Ketamine	5–15	IM, IV	30 minutes	None
Tiletamine/zolazepam	3–5	IM		None/flumazenil
Propofol	3–6	IV	10–15 minutes	None
Fentanyl	0.001–0.03/h	IV CRI		Naloxone

CRI, constant rate infusion; IM, intravenous; IV, intravenous; SC, subcutaneous.
[a] Doses for reversal agents: atipamizole (0.2 mg/kg IM), naloxone (0.02 mg/kg IM), flumazenil (0.02 mg/kg IV).

Table 31.3 Doses of analgesic drugs used in prosimian primates.

Agent	Dosage (mg/kg)	Frequency	Route
NSAIDS Acetaminophen	10–15	q 8–12 h	PO
Aspirin (acetylsalicylic acid)	10–20	q 8–12 h	PO
Ibuprofen	10	q 8–12 h	PO
Ketoprofen	2 first dose then 1	Once q 24 h	PO, SC, IM, IV
Flunixin meglumine	0.25–0.50	q 24 h	SC, IM, IV
Meloxicam	≤0.2 first dose then ≤0.1	Once q 24 h	PO, SC, IV
Opioids Butorphanol	0.1–0.4	q 3–4 h	SC, IM, IV
Buprenorphine	0.01–0.02	q 8–12 h	SC, IM, IV
Tramadol	1–4	q 12 h	PO

IM, intravenous; IV, intravenous; PO, per os; q3–4h, every 3–4 hours; q8–12h, every 8–12 hours; q12h, every 12 hours; q24h, every 24 hours; SC, subcutaneous.

similar pharmacological actions; however, midazolam has advantages over diazepam in that it can be given IM whereas diazepam is incompletely absorbed when given IM. When used alone in lemurs, midazolam provides minimal or no detectable sedation, but when used in conjunction with other medications it has a synergistic effect. When midazolam is combined with ketamine for induction, muscle relaxation is improved and the likelihood of seizures is reduced. The authors frequently use midazolam in combination with dexmedetomine prior to induction with gas anesthesia. The combination produces a moderate level of sedation, increasing the ease of handling during mask induction.

Opioids

Information on the physiologic response of prosimians to opioids is limited. Butorphanol has been shown to cause profound respiratory depression in primates. This is largely due to the fact that in primates, butorphanol's effect on the μ receptor is one of a strong agonist rather than the weak agonist or antagonistic effect seen in domestic species (Butelman et al. 1995). Whether butorphanol has the same respiratory depressant effects in lemurs or other prosimians is unclear. Studies in ring-tailed lemurs (*Lemur catta*) using butorphanol at 0.3 mg/kg IM in combination with medetomidine and ketamine, or medetomidine and midazolam to provide complete anesthesia resulted in only mild decreases in respiratory rates relative to animals receiving no butorphanol. Oxygen-hemoglobin saturation, end-tidal CO_2, and $PaCO_2$ (arterial partial pressure of carbon dioxide) values were not affected, suggesting oxygenation was not compromised. Butorphanol is used by the authors both for short-term analgesia and as a pre-medication prior to inhalation anesthesia in lemurs; however, until more data are available on receptor activity in this group of primates, it is recommended that respiratory parameters be monitored.

The authors routinely use buprenorphine and tramadol for relief of moderate pain postoperatively with good results. Buprenorphine is often combined with an NSAID to provide stronger analgesia for moderate to severe pain. Although there are no references for the use of morphine in prosimians, it is reasonable to expect that it can be employed safely if used judiciously and animals are appropriately monitored.

Alpha-2 Agonists

Alpha-2 agonists are very useful in prosimians both for their sedative and analgesic qualities and as a means of decreasing the amount of other anesthetic agents needed. The alpha-2 agonist medetomidine is one of the few agents studied in lemurs. Medetomidine administered IM to ring-tailed lemurs under isoflurane had no effect on heart rate, blood pressure, or oxygen-hemoglobin saturation (Williams et al. 2003). In contrast, bradycardia occurs in many domestic animals as a compensatory response to rapid and intense vasoconstriction, resulting in significant hypertension (Cullen 1996; Paddleford & Harvey 1999). Dexmedetomidine combined with midazolam is used at the Duke Lemur Center for premedication prior to inhalation anesthesia. The use of dexmedetomidine preoperatively decreases the amount of inhalant anesthesia needed and reduces the degree of hypotension seen when isoflurane or sevoflurane are used alone.

Induction Agents

Ketamine is a widely used anesthetic agent in primates for chemical restraint. The effect of ketamine on prosimians, however, is variable. There are both species and individual differences in the degree and duration of immobilization, the character of recovery, and the frequency of side effects. When used alone, ketamine provides unpredictable levels of immobilization, poor muscle relaxation, and frequently vomiting on recovery. In the authors' experience, seizures may occur in ruffed and black lemurs at doses of 5–10 mg/kg IM. Side effects of ketamine are diminished and the quality of anesthesia improved when it is combined with either midazolam and/or dexmedetomidine; however, the duration of effective immobilization remains short at only 10–15 minutes.

Telazol®, a combination of tiletamine and zolazepam, is frequently used in lemurs, particularly for field immobilizations. Benefits of using Telazol include a wide margin of safety, good muscle relaxation, and smooth recoveries. The main disadvantages include prolonged recovery times in the range of 2–6 hours and a short shelf life of the reconstituted drug. In a clinical setting, reversible injectable combinations allow better control over recovery time and depth of anesthesia.

In a study in ring-tailed lemurs, combining medetomidine with either ketamine and butorphanol, or midazolam and butorphanol produced heavy sedation to complete immobilization lasting from 20 to 60 minutes (Williams et al. 2003). Both combinations can be used for induction prior to gas anesthesia or as complete injectable regimes. The combinations produce minimal cardiorespiratory effects, and the level of analgesia is sufficient to perform minor surgical procedures. Members of the *Eulemur* genus (brown and black lemurs) tend to require higher doses of the drug combinations than ring-tailed lemurs, ruffed lemurs, and Coquerel's sifaka (*Propithecus coquereli*) to produce equal effects. When mild to moderate sedation is desired for premedication or to increase the ease of handling during manual restraint, administering dexmedetomidine in combination with midazolam is effective. Table 31.4 lists several useful combinations.

Propofol is an injectable alkylphenol that acts similarly to the ultra-short-acting barbiturate thiopental. Propofol can be used for induction to provide short duration immobilization for diagnostic procedures or as a constant rate infusion to achieve a light plane of anesthesia for longer periods (Short & Bufalari 1999). Because the compound must be administered intravenously for use in prosimians, it is most feasible in animals receiving premedication in advance of induction. Propofol decreases cardiac contractility and is a potent vasodilator, which can result in hypotension. It is also a respiratory depressant. Administering propofol slowly and to effect minimizes the occurrence of cardiopulmonary effects. The quality of induction and the rapid rate of metabolism, and hence recovery, make the use of propofol advantageous in some circumstances.

Inhalation Anesthesia

Both isoflurane and sevoflurane work well in prosimians and are safe in most species; however, respiratory arrest has been reported in giant mouse lemurs (*Mirza* spp.) induced with isoflurane and inhalation agents should be used with extreme caution in this species until more information is available. Both isoflurane and sevoflurane are potent vasodilators, and hypotension is frequently observed in prosimians anesthetized with these agents. It is important to monitor blood pressure in animals under inhalant anesthesia and be prepared to administer intravenous fluids or other supportive measures as necessary to maintain adequate blood pressure. Information is not available regarding the mean alveolar concentration (MAC) of either agent in prosimians; however, it is the authors' impression that MAC may vary by species. Aye-ayes, in particular,

Table 31.4 Useful combination regimes for prosimian primates[a].

Drug Combination	Dosage[a] (mg/kg)	Duration of Effect (minutes)	Level of Sedation
Dexmedetomidine/midazolam	0.02/0.2	30–40	Light to moderate sedation
Dexmedetomidine/ketamine	0.02/3–5	10–20	Heavy sedation to complete immobilization
Butorphanol/dexmedetomidine/ketamine	0.3–0.4/0.02/3–5	15–30	Complete immobilization
Butorphanol/dexmedetomidine/midazolam	0.3–0.4/0.02/0.2–0.3	20–50	Complete immobilization

[a] All drugs are given intramuscularly.

seem acutely sensitive to inhalant anesthetics and require lower concentrations relative to other lemur species to achieve a surgical plane of anesthesia. Hypotension unresponsive to fluid administration alone is a frequent complication of inhalant anesthetic use in lemurs. Until more information is available, it is advisable to intensively monitor cardiopulmonary function and be prepared to support blood pressure if needed.

Prosimians can be induced with gas anesthetics via facemask or in an induction chamber. Administering premedication markedly improves the quality of mask induction. Sevoflurane offers advantages over isoflurane for mask or chamber induction as it is nonirritating to airways. Animals induced by mask with sevoflurane are more compliant than those induced with isoflurane and appear less stressed during the initial phases of induction. Induction rates are faster with sevoflurane compared with isoflurane due to the very low blood and tissue solubility of sevoflurane. The cardiopulmonary effects of sevoflurane are similar to those of isoflurane (Clark 1999).

Monitoring

All anesthetic agents have the potential to adversely affect the major organ systems of the body. Body temperature, heart rate and rhythm, respiratory rate, and capillary refill time can be monitored in even the smallest lemur or loris. With experience and the proper equipment, monitoring cardiac electrical activity (ECG) and obtaining reliable readings for oxygen-hemoglobin saturation (pulse oximetry), end-tidal CO2 (capnography), and blood pressure (oscillotometry) can be accomplished in patients weighing more than 1.0 kg. Monitoring should start in the preoperative phase and continue until the animal is in sternal recumbency or until safety precludes further measurements.

Lemurs are highly prone to developing hypothermia under anesthesia due to their lean body confirmation and high surface area to body mass ratio. Heat loss is further compounded by shaving and using skin cleansing solutions during aseptic preparation of the surgical site. Opening a body cavity during surgery further enhances the loss of body heat. Hypothermia decreases liver and renal blood flow and slows the elimination of anesthetic agents, prolonging recovery (Sessler 2000). It is important to monitor temperature regularly during anesthetic procedures. Heat loss can be minimized by insulating animals from cold surfaces using warm water-circulating blankets, warm air blankets, placing hot-water bottles under the drapes, and minimizing exposure by covering body areas outside of the surgical field. Additional precautions include pre-warming surgical skin preparation solutions and fluids used for intravenous support or lavage (Haskins 2007).

Blood pressure can be measured directly by arterial catheterization or indirectly using either Doppler sphygmomanometry or automated oscillotonometry. In the majority of instances, the authors find that automated oscillotonometry units made for small companion animals are easy to use and provide reliable readings in animals over 1.5 kg. The cuff is placed on the hind leg just above the tarsal joint. Additional sites for cuff placement in lemurs include the base of the tail and the upper forearm close to the axilla. It is important to maintain the mean arterial pressure above 60 mmHg to ensure adequate tissue blood flow.

Pulse oximetry can be challenging in prosimian primates. Their tongues are short and thin, and probes tend to slip off easily. Several lemur species have heavy pigmentation of the tongue, mucous membranes of the oral cavity, and skin of the hands and feet, making readings inconsistent and difficult to obtain. In lightly pigmented animals, reliable readings can generally be obtained by placing a fingertip probe on the cheek wall, tongue, or first digit of the fore or hind limbs. In heavily pigmented lemurs, rectal readings using a rectal probe provide reliable readings. To ensure proper placement of the rectal probe, place the animal in dorsal recumbency and direct the probe signal toward the dorsal wall of the rectum. Manual evacuation of feces in the rectum avoids trapping feces between the probe and rectal mucosa, which interferes with signal transduction.

The use of capnography in prosimians is similar to that in other small animals. Capnography provides important information on cardiac function and pulmonary perfusion. For more information on the use of capnography and interpretation of end-tidal CO_2 measurements, the reader is referred to articles describing their use in veterinary patients (Grosenbaugh 1998; Marshall 2004).

Arterial blood gas analysis is the most reliable method of assessing pulmonary function. The development of relatively inexpensive hand-held analyzers makes measuring blood gases possible and practical, even in field settings. In prosimians, arterial blood samples are easiest to obtain from the femoral artery.

Recovery

The quality and speed of recovery depends on the agent used, the general health of the animal, and the success of maintaining physiological processes within optimal ranges through the use of monitoring and appropriate supportive care. Reversible agents allow smooth and controlled recovery from anesthesia. Providing supplemental heat during recovery is beneficial for animals in which body

temperatures drop during anesthetic procedures. Animals should be recovered in a quiet, confined space and prevented from attempting to climb or jump until well coordinated.

Remote Immobilization and Field Techniques

Remote immobilization of lemurs is routinely performed in the field; however, the safety of the procedure is related to the skill of the darter, the type of darting equipment used, and the extent to which animals are monitored during immobilization. Lemurs present a difficult target, particularly when high up in a tree. Lemurs are small animals with lean body conformation and safe sites for dart placement are limited. The caudal thigh muscles provide the safest location to dart lemurs. Because of lemurs' small size and minimal muscle mass, low-impact delivery devices such as blow guns are the least traumatic and provide the greatest margin of safety when darting. The lower impact pressure of darts delivered by blow gun may result in incomplete delivery of anesthetic in some instances, however, resulting in the need to use more than one dart for successful immobilization. While complete drug delivery is more likely to occur when using CO_2-powered remote injection devices, it is important that the discharge power be adjusted downward as much as possible to minimize tissue injury associated with high-pressure dart impact. Dissociative anesthetics are the most frequently used class of drugs for field immobilizations in lemurs. Telazol is widely used and provides rapid induction and a wide margin of safety, although muscle relaxation may not be adequate for some procedures, such as taking dental impressions. A main disadvantage of Telazol is a long recovery time, in the range of 4–6 hours. Published doses for Telazol used in lemurs in the field vary from 10 to 20 mg/kg (Dutton et al. 2003; Glander et al. 1992; Junge & Louis 2005; Larsen et al. 2011). Larsen et al. (2011) reported that young ring-tailed lemurs (2–4.9 years of age) required both higher initial doses and higher total doses of Telazol for successful immobilization than mature lemurs (≥5 years of age) in the field. The authors commented that young animals in the study were smaller and leaner than mature animals, making dart placement more challenging and resulting in incomplete injections.

Initial doses of Telazol provide 30–40 minutes of immobilization. If longer periods of immobilization are needed, supplemental doses of either Telazol or alpha-2 agonists, with or without the addition of butorphanol, can be given via hand syringe. In one study, depth of anesthesia and muscle relaxation improved following the administration of medetomidine (0.04 mg/kg) IM or medetomidine (0.04 mg/kg) + butorphanol (0.2 mg/ kg) IM 20 minutes after initial induction with Telazol (Larsen et al. 2011). The authors noted that the time to recovery in mature lemurs was correlated with total Telazol dose. The ability to reverse both medetomidine and butorphanol may result in quicker recoveries for animals needing supplementation than if additional doses of Telazol are given.

Ketamine at doses of 17–50 mg/kg (Garell & Meyers 1995; Glander et al. 1992; Richard et al. 1991) has been used for field immobilizations in lemurs, but the results are generally inferior to those produced with Telazol. Ketamine immobilizations are typically plagued by poor muscle relaxation, unpredictable levels of restraint, and rocky recoveries. Vomiting on recovery is common.

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32

Monkeys and Gibbons

Rolf-Arne Ølberg and Melissa Sinclair

Taxonomy and Biology

Monkeys belong to the suborder Haplorrhini (higher primates) which, excluding great apes and humans, contains five families and over 200 species (Table 32.1). The Tarsiidae, Cercopithecidae, and Hylobatidae families are Old World primates from Africa or Asia, while the Callitrichidae and Cebidae are New World primates from the neotropics.

Tarsiers are small nocturnal insectivourus species; they can turn their head 360° and some can leap as far as 5–6 m between trees. Callitrichids (marmosets and tamarins) are small, diurnal, and live in family groups. They have good eyesight and hearing, and are usually active and agile. Their thumbs are not apposable and they have clawlike nails on all digits except the thumbs. Cebids (Cebidae) vary in weight from 1 to 15 kg and many have prehensile tails. Most are good jumpers and runners. The *Cercopithecidae* all have longer hindlimbs than forelimbs, none have prehensile tails and they range in weight from 1 to 55 kg. The upper canines are elongate while the lower are curved slightly inward and backward. Hylobatidae include gibbons and siamangs. They all lack a tail and have a slender body, relatively long arms, and prominent canine teeth. For an extensive description of the various species, the reader is referred to *Walker's Mammals of the World* (Nowak 1999).

Physiology

Primates have a large surface-area-to-body-mass ratio; consequently, rapid body heat loss commonly occurs during anesthesia. This is compounded by drug suppression of hypothalamic thermoregulation and impairment of shivering. Heat loss is most pronounced in small species. Normal rectal temperature for rhesus macaques is listed as 36.7 to 38.9°C (Bourne 1975).

There are few reports of normal reference ranges for cardiovascular and respiratory values in primates. Values obtained while the primate is physically restrained are likely not representative of "normal" resting values. Unsedated rhesus macaques restrained in chairs had the following mean values: mean arterial pressure 113 mmHg, heart rate 174, cardiac output 1.31 L/min, stroke volume 7.5 mL, blood volume 73–77 mL/kg, respiratory tidal volume 12.5 mL/kg, respiratory minute volume 479 mL/kg, and respiratory rate 39/min (Bourne 1975). For cynomolgus macaques, also restrained in chairs, the mean arterial pressure is reported to be 87 mmHg and the heart rate 227 beats per minute (bpm) (Morita 1995). Heart rates are approximately 100–200 bpm for animals ≥1 kg and 200–300 bpm for primates ≤1 kg (Bourne 1975; Johnson-Delaney 1994; Haruo 1995). For most species the respiratory rate is 20–50 breaths per minute. Physiological parameters and blood biochemistry may be altered by anesthetic agents (Hernandez-Godines et al. 2019; Bush et al. 1977; Liu & DeLauter 1977; Lugo-Roman et al. 2010).

Human Safety

Most primates when restrained or confined deliver a nasty bite that may transmit several zoonotic pathogens. Herpes B virus is endemic and nonpathogenic in macaques, but can be fatal in humans (Hummeler et al. 1959; Ott-Joslin 1993), therefore a primary aim when handling primates is prevention of traumatic injury and transmission of zoonoses to humans.

Vascular Access

Common vascular access sites are the femoral and the saphenous (popliteal) veins (Figs 32.1 and 32.2). The femoral vein is entered just distal to the inguinal canal. With

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Table 32.1 Taxonomy of monkeys including approximate adult body weights.

Scientific Name	Common Name	ABW (kg)
Family: *Tarsiidae*		
Tarsius/5 species	Tarsiers	0.08–0.17
Family: *Callitrichidae*		
Callimico/1 species	Goeldi's monkey	0.4–0.9
Saguinus/12 species	Tamarins	0.2–0.9
Callithrix/17 species	Marmosets	0.2–0.5
Cebuella/1 species	Pygmy marmoset	0.08–0.15
Family: *Cebidae*		
Lagothrix/2 species	Woolly monkey	5–11
Ateles/6 species	Spider monkeys	6–8
Brachyteles/1 species	Woolly spider monkey	7–10
Alouatta/9 species	Howler monkeys	4–12
Pithecia/5 species	Sakis	0.7–1.7
Cacajao/2 species	Uakaris	2.7–3.5
Callicebus/13 species	Titi monkeys	0.5–2.0
Aotus/10 species	Night monkeys	0.6–1.0
Cebus/6 species	Capuchins	1.1–4.3
Saimiri/5 species	Squirrel monkeys	0.7–1.1
Family: *Cercopethicidae*		
Erythrocebus/1 species	Patas monkey	7–13
Chlorocebus/4 species	Savannah guenons	2–9
Cercopithecus/20 species	Guenons	2–12
Miopithecus/1 species	Talapoin	0.7–1.2
Cercocebus/3 species	Mangabeys	3–20
Lophocebus/1 species	Black mangabeys	4–11
Macaca/20 species	Macaques	2–18
Papio/5 species	Baboons	14–41
Mandrillus/2 species	Mandrills	12–25
Theropithecus/1 species	Gelada baboon	13–20
Nasalis/1 species	Proboscis monkey	7–22
Simias/1 species	Pig-tailed langur	7
Pygathrix/1 species	Douc langur	
Rhinopithecus/4 species	Snub-nosed langurs	
Presbytis/8 species	Langurs	5–8
Semnopithecus/1 species	Hanuman langur	5–24
Trachypithecus/9 species	Brown-ridges langurs	4–14
Colobus/5 species	Black-white colobus	5–15
Piliocolobus/5 species	Red colobus	5–12
Procolobus/1 species	Olive colobus	3–5

the animal on its back and its legs abducted, the pulsing femoral artery is palpated. The femoral vein lies caudal to the artery and just under the skin in the triangle formed



Figure 32.1 Blood collection from the femoral vein of a cotton top tamarin. The vein is located in the femoral triangle, medial to the artery. It is important to provide good hemostasis; a small primate can become hypovolemic and die from blood loss into a large hemotoma.



Figure 32.2 Blood collection from the saphenous vein of an anesthetized spider monkey. This vessel can also be used for intravenous catherization.

by the abdominal, sartorius, and pectineus muscles (Fig. 32.1). The saphenous (popliteal) vein is located superficially on the caudal aspect of the lower leg (Fig. 32.2). It is suitable for catheter placement in most primates, including callitrichids. Less common vascular access sites include the jugular and the cephalic veins. In monkeys with tails, the lateral coccygeal veins can also be used. They are palpable on the dorsolateral surface of the base of the tail.

Physical Restraint

There are a variety of physical restraint techniques in primates that are safe for both the handler and the primate. These include nets, squeeze cages, and head-lock devices. However, any restraint is stressful to the animal

and its duration must be minimized (Bush et al. 1977). Physical restraint also increases the possibility of human bites and contact with secretions infected with zoonotic pathogens.

Hoop nets are useful for catching smaller species (≤4 kg). The animal is physically secured within the net by pinning it to the ground or closing off the entrance by twirling the net. The animal is then moved directly to a transport cage or induction box and injected with an anesthetic drug or administered inhalant anesthetic through the net using a mask placed over the nose and mouth.

Manual restraint is excellent for small species like tamarins and marmosets. These species are caught in a hoop net and then secured by locking the head with thumb and index finger, the upper body with the other three fingers, and the hindlegs with the other hand. This restraint technique is suitable for minor procedures such as inspection of wounds, to facilitate injection of drugs, and blood sampling. Leather gloves or a towel will reduce the risk of bite wounds.

Squeeze cages are indicated for animals too dangerous to handle by hand. Once in a squeeze cage, the animal is compressed for intramuscular (IM) injection of a parenteral anesthetic. A properly compressed primate will not be able to move, allowing accurate injection.

Psychological Restraint (Taming)

Taming and training methods are used for "psychologically restraining" animals. This is a common method used for domestic animals like horses and dogs, but it can also be used on nondomestic animals to facilitate, for example, hand injection of drugs. Through positive reinforcement, many primates will accept an IM injection or even extend an arm out of the cage for blood collection (Phillippi-Falkenstein & Clarke 1992) or intravenous (IV) injection.

Endothracheal Intubation

Endothracheal intubation is readily achieved in most species with the aid of a laryngoscope and a suitable endothracheal tube. Intubation can be achieved with the primate positioned in dorsal recumbency on a table with the head flexed slightly backwards (Fig 32.3). Alternatively, the animal is placed in a sitting position and an assistant flexes the head backwards. The tongue is gently pulled outwards to visualize the glottis with a laryngoscope. The use of a topical local anesthetic on the glottis is recommended and will reduce the potential for laryngospasm and coughing during and after intubation. Lidocaine 2% can be diluted to 10 mg/mL or lower to ensure dosing of local anesthetic does not exceed 4 mg/kg.

Primates have a relatively short trachea, with the bifurcation located close to the neck. It is easy to introduce an endotracheal tube too far, intubating a main bronchus and ventilating only one lung (Horne 2001). To prevent this, the endotracheal tube length is premeasured to the base of the neck before placement. Once the tube is in position, the animal is ventilated and both the left and right thorax auscultated. If the tube is located in one bronchus, there will be no respiratory sound on the opposite side. In addition, if a pulse oximeter is used desaturation may be noted with one lung intubation. For species smaller than a squirrel monkey, an endotracheal tube can be made from a urinary catheter or infant feeding tube. For species the size of a squirrel monkey, an uncuffed 2.0–2.5-mm tube can be used. For most other species between 1 and 20 kg a cuffed tube ranging in size from 3 to 5 mm is usually appropriate (Horne 2001).

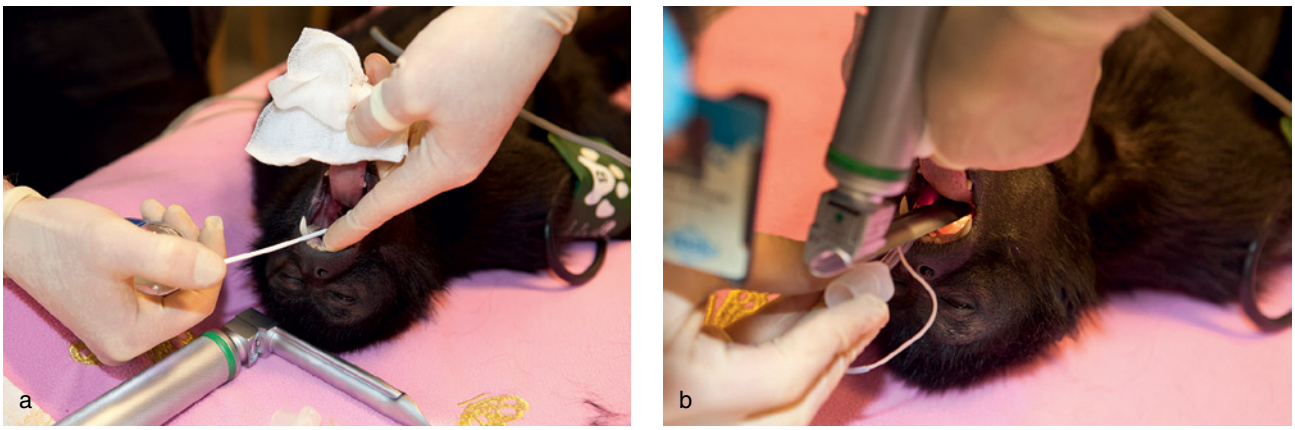


Figure 32.3 Endotracheal intubation in primates, as in this spider monkey, is facilitated by placing the animal in dorsal recumbency, extending the head and neck, using a laryngoscope and applying topical anesthetic to the glottis to reduce laryngospasm.

Preanesthetic Considerations

Observing the animal prior to the anesthetic procedure will provide useful information about its health status. Social interaction, lethargy, diarrhea, vomiting, anorexia, body condition, and the presence of wounds can often be evaluated this way. If possible, it is recommended to withhold food from primates for 6–8 hours and water for 1–2 hours prior to the procedure.

Sedation and General Anesthesia

There are several options for administering drugs to primates. Drugs can be administered orally, parenterally, or by inhalation of anesthetic gases.

Oral Administration of Drugs

Drugs can be administered orally by squirting the sedative or anesthetic dose into the mouth or mixing it into liquid or solid treats (Martin et al. 1972; Knottenbelt & Knottenbelt 1990; Miller et al. 2000; Pulley et al. 2004; Ølberg 2004; Winterborn et al. 2008). Ingestion of the full drug dose by the animal is a voluntary action and depends primarily on the palatability of the drug mixture. It can also be influenced by the animal's response and knowledge of the person presenting the food and any alteration in the food from normal. Another challenge with this route of administration is unpredictable absorption. There is a difference in bioavailability and absorption time of drug dose depending on how much is absorbed through the oral mucosa compared to the intestinal mucosa. If the drug is swallowed, first-pass metabolism may have a significant effect on lowering the effective drug concentration (Paine et al. 1996). Despite the positive aspect of voluntary oral drug administration to sedate or anesthetize primates, there are no reports of using this as a consistent, safe, and reliable method.

Parenteral Anesthesia

Hand injection requires physical or psychological restraint. For larger species, the use of a projectile dart to deliver drugs is common practice, and darts are typically used for immobilizing primates in the wild (Burroughs 1993; Sapolsky & Share 1998). Darting is fast and effective, but has significant disadvantages, including stress, pain, and even trauma on injection. Primates have relatively small target areas for darting and these can be difficult to hit, especially on a moving animal. Targets usually used for injection are the muscles in the hip and thigh area or, in rare instances, the triceps or shoulder area of larger primates.

Several review articles describe parenteral anesthesia of primates (Beck 1972; Martin et al. 1972; Cohen & Bree 1978; Horne 2001). Most recommendations include a dissociative anesthetic alone or in combination with an alpha-2 adrenoceptor agonist or benzodiazepine. It is common to combine two or more drugs to achieve immobilization of primates (Jalanka 1989; Horne 2001). This is done to minimize volume, increase potency, achieve a stable safe plane of anesthesia with adequate muscle relaxation and analgesia, improve recovery quality and time, and minimize side effects.

Ketamine

Ketamine has been used alone in a wide variety of primates, and most reports describe it as safe and reliable (Martin et al. 1972; Vercruysse & Mortelmans 1978). The duration of effect is relatively short (depending on dosage), mainly due to rapid redistribution from the central compartment and efficient metabolism in the liver. Ketamine causes reliable immobilization and maintains stable cardiopulmonary function while maintaining the laryngeal reflex.

Effective intramuscular dosages vary from 5 to 12 mg/kg for chemical restraint and up to 10–30 mg/kg for surgical anesthesia (Beck & Dresner 1972; Ochsner 1977). Some authors give a general recommendation of dosages from 5 to 40 mg/kg IM (Cohen & Bree 1978). A significant advantage of ketamine is its high therapeutic index. It has been given experimentally to five squirrel monkeys at dosages of 250 mg/kg without any deaths (Greenstein 1975). It can be administered safely several days in a row for repeated anesthesia (Bree et al. 1967).

However, there are several disadvantages to using ketamine alone, such as poor muscle relaxation, spontaneous movement, and hypersalivation. When high dosages of ketamine are used alone, the recovery period is prolonged and rough (Banknieder et al. 1978; Sun et al. 2003). A severe and common side effect of ketamine alone in humans is emergence delirium (Reich & Silvay 1989), which occurs in approximately 5–30% of cases (White et al. 1982). This state is associated with visual, auditory, proprioceptive, and confusional illusions (Stoelting 1999). The same effects are likely the cause of poor recoveries with ketamine alone in monkey and gibbon species. There are no antagonists to ketamine.

The dosage of ketamine can be markedly reduced by adding sedative agents such as alpha-2 agonists or benzodiazepines (Lilburn et al. 1978; Levanen et al. 1995), which in turn will minimize side effects. In addition, both the

alpha-2 agonists and the benzodiazepines are reversible. Using these anesthetic drugs in combination with ketamine at lowered doses will likely reduce side effects and thereby enhance the safety of the procedure.

Ketamine/Benzodiazepine

The combination of ketamine (10 mg/kg IM) and 1 mg/kg midazolam (1 mg/kg IM) in common marmosets and black-tufted marmosets resulted in rapid immobilization and good muscle relaxation with a duration of 30–45 minutes (Furtado et al. 2010).

Ketamine/Alpha-2 Adrenoceptor Agonist

The addition of an alpha-2 agonist to ketamine has several beneficial effects. It increases muscle relaxation and analgesia and decreases the hypersalivation while lowering the required dose of ketamine for immobilization. It also adds the possibility of reversing the effects of the alpha-2 agonist with an alpha-2 adrenoceptor antagonist. A disadvantage of the alpha-2 agonists is their dose-dependent cardiovascular depressant effects. Many dosage variations have been used in different species of primates to investigate the effects and give recommendations, as outlined below.

The combination of ketamine (5.25 mg/kg IM) with xylazine (0.45 mg/kg IM) enhanced analgesia, anesthesia, and muscle relaxation in rhesus macaques compared to ketamine alone (Banknieder et al. 1978). Animals remained anesthetized for 44 minutes (range 23–63 minutes). However, an important observation with this combination is that anesthetic emergence was fast. Animals were alert and standing only a few minutes after the anesthetic period. The presence of the pedal reflex preceded the end of the anesthetic immobilization by only 2–3 minutes. This duration likely coincides with ketamine redistribution and the quick recovery is probably due to the arousability noted with alpha-2 agonists. Hence, the veterinarian needs to monitor depth closely and be aware of the procedure time with these combinations.

In rhesus macaques the minimum effective IM dosages were 2.5 mg/kg ketamine with 0.25 mg/kg xylazine (Naccarato & Hunter 1979). These investigators found a wide safety margin with this combination, although xylazine markedly reduced the thermoregulatory abilities of the animals. The IM dosages of 5 mg/kg ketamine and 0.5 mg/kg xylazine produced safe immobilization for 30 minutes, while increasing the dosage of xylazine to 1 and 2 mg/kg prolonged immobilization time to 60 and 80 minutes, respectively. Similar results were obtained with ketamine (5 mg/kg IM) and xylazine (1 mg/kg IM) in Japanese macaques (Hayama et al. 1989). Yellow baboons receiving ketamine (11 mg/kg IM) and xylazine (0.5 mg/kg IM) were easily intubated, and anesthesia lasted from 90 to 125 minutes (White & Cummings 1979). Another recommendation, for wild savanna baboons, is ketamine (10–15 mg/kg IM) combined with xylazine (1 mg/kg IM) (Sapolsky & Share 1998).

Medetomidine is a more selective, potent, and specific alpha-2 agonist than xylazine (Chapter 2). Medetomidine alone is not sufficient to immobilize rhesus macaques even at intravenous dosages as high as 0.2 mg/kg (Capuano et al. 1999). Intravenous dosages of 0.05, 0.10, 0.15, and 0.2 mg/kg medetomidine produced similar and significant bradycardia, hypotension, loss of thermoregulation, decrease in respiratory rate, and inconsistent sedation. However, the advantages of medetomidine with ketamine are similar to those of xylazine, for example enhanced analgesia, anesthesia, and muscle relaxation.

Ketamine with medetomidine has been used in several primate species (Jalanka 1989; Lewis 1993; Horne et al. 1998; Vie et al. 1998). Rhesus macaques anesthetized with ketamine (2 mg/kg IM) and medetomidine (0.075 mg/kg IM) had a heart rate of 135 bpm 5 minutes after injection, declining to 115 bpm 25 minutes after injection. Mean arterial pressures were 70 and 65 mmHg, respectively. The animals started to recover 35–45 minutes post injection (Settle et al. 2010).

In cynomolgus macaques there was little difference in the level of sedation, anesthesia time, and recovery time between ketamine alone (10 mg/kg IM) andr a combination of ketamine (2 mg/kg IM) and medetomidine (0.05 mg/kg IM). However, due to some unexpected quick recoveries, the investigators felt that this combination was unreliable and recommended caution in using it at these dosages (Young et al. 1999). In the same species a dosage of ketamine (3 mg/kg IM) and medetomidine (0.15 mg/kg IM) provided good muscle relaxation when compared to ketamine (10 mg/kg IM) alone (Lee et al. 2010). Another study in capuchin monkeys demonstrated that ketamine (4 mg/kg IM) combined with medetomidine (0.15 mg/kg IM) provided rapid induction of anesthesia sufficient for handling, while ketamine (2 mg/kg IM) and medetomidine (0.2 mg/kg IM) was not sufficient for handling (Theriault et al. 2008). In this study, the evaluation of the lower dose of ketamine was based on only one capuchin monkey and the monkeys were reversed shortly after induction.

Japanese macaques given ketamine (5 mg/kg IM) and medetomidine (0.05 mg/kg IM) had a mean induction time of 4 minutes and anesthetic duration of 65 minutes, with excellent muscle relaxation (Ølberg et al. 2018). After induction they had an initial heart rate of 100 bpm that slowly decreased to 60 bpm during anesthesia. The mean arterial pressure also decreased slowly from approximately 110 mmHg after induction to 70 mmHg at the end. The respiratory rates were 40 breaths per minute throughout anesthesia. Hypoxemia ($PaO_2 < 60$ mmHg) was evident in

Japanese macques after induction on room air. A normal SpO_2 and PaO_2 were measured when the monkeys were given supplemental oxygen through a face mask (4 L/min).

At lower dosages the negative cardiopulmonary effects of alpha-2 agonists are reported to be minor and not clinically noticeable (Dyck et al. 1993; Horne et al. 1997; Capuano et al. 1999), suggesting that low-dose medetomidine might be favourable, but further investigations are warranted to confirm this.

Dexmedetomidine, containing only the active ananiomer of the sedative medetomidine, has also been investigated in monkeys. In golden-headed lion tamarins a combination of dexmedetomidine (0.01 mg/kg IM) with ketamine (5 mg/kg IM) produced anesthesia with good muscle relaxation for 45 minutes with minor cardiovascular effects and arterial oxygen saturation over 94% in room air (Selmi et al. 2004a). The same dosage of dexmedetomidine and higher ketamine (10 mg/kg IM) had a similar effect but longer duration and a slight decrease in mean arteral pressure. In the same species, medetomidine (0.02 mg/kg IM) with ketamine (10 mg/kg IM) had a similar effect and was evaluated as safe and reliable in this species (Selmi et al. 2004a). A lower dosage of dexmedetomidine (0.005 mg/kg IM) with ketamine (10 mg/kg IM) had poor muscle relaxation and anesthetic quality compared to the higher dexmedetomidine dose.

Based on these reports and clinical experience, ketamine ≤2 mg/kg may not be sufficient even in combination with medetomidine or dexmedetomidine. In the protocols using a relatively low dosage of ketamine (2 mg/kg), the corresponding dose of medetomidine is relatively high (0.05–0.15 mg/kg). In the authors' opinion, a higher dose of ketamine (>2 mg/kg IM) and a lower dose of medetomidine is preferable for cardiorespiratory stability, as well as anesthesia quality and time.

It is difficult to give minimum dose recommendations for the combination of ketamine and medetomidine. For most species, the author would recommend a ketamine dose of 5–8 mg/kg combined with a low dose of medetomidine of 0.02–0.04 mg/kg for induction or short-duration anesthesia.

Tiletamine/Zolazepam

Tiletamine/zolazepam has been widely used in primates (Bree et al. 1972; Bree 1972; Horne 2001; Gray et al. 1974; Schobert 1987). Wild black spider monkeys were anesthetized with dosages ranging from 11.6 to 18 mg/kg (Karesh et al. 1998), with the higher dosage resulting in more reliable and stable planes of anesthesia. Induction times were 2–4 minutes with immobilization lasting from 80 to 150 minutes. Adult, free-living red howler monkeys were anesthetized with 22.5 mg/kg IM and juveniles received 30.5 mg/kg IM. With these dosages, the induction period was 1–6 minutes and immobilization lasted from 40 to 300 minutes, with no apparent adverse effects (Agoramoorthy & Rudran 1994).

Other researchers also describe the use of tiletamine/zolazepam for field anesthesia in various species with a good overall effect (Glander et al. 1991; Sleeman et al. 2000). In cynomolgus macaques and vervet monkeys tiletamine/zolazepam (5–10 mg/kg IM) was adequate for ophthalmologic surgery. These dosages produced a rapid onset and 30–50 minutes of surgical anesthesia, excellent muscle relaxation, absence of ocular movement, and a gradual emergence with no adverse effects (Kaufman & Hahnenberger 1975). In rhesus macaques, this combination induced little or no impairment of thermoregulation (Holmes & Hunter 1980).

Tiletamine/zolazepam has a high therapeutic index, as reflected by the variety of published dosage recommendations. There are likely species differences, but the dosages probably reflect the different subjective opinions of investigators and no dose titration studies are available. Recommended dosages for capture of free-living animals are high compared to those used in captive animals. A major advantage of this combination is high potency, which allows a small drug volume.

There are no reversal agents for tiletamine and prolonged recovery periods are common. Hence, the investigator may have to spend time monitoring the recovery of immobilized wild animals that cannot be abandoned in a sedated state.

Tiletamine/Zolazepam/Medetomidine

Tiletamine/zolazepam (0.8–2.3 mg/kg IM) with medetomidine (0.02–0.06 mg/kg IM) have been used in Bornean orangutans, Bornean gibbons, and long-tailed and pig-tailed macaques (Fahlman et al. 2006). This combination results in rapid smooth induction within 1–7 minutes, good muscle relaxation, and anesthesia, although the data suggest hypotension and hypoxemia in some animals. For the gibbons and macaques, respiratory rates were 20–56 breaths per minute, heart rate ranged from 68 to 160 bpm and SpO_2 ranged from 88% to 99%. A major advantage observed by the investigators was that induction in wild orangutans with this comination resulted in a gradual descent from the trees compared to rapid loss of consciousness and falling from the trees with tiletamine/zolazepam alone.

Medetomidine/Midazolam

The combination of medetomidine and midazolam has been tried in Japanese macaques as an alternative to using dissociative anesthetics. An IM dose of 0.03 mg/kg medetomidine with 0.3 mg/kg midazolam gave heavy sedation and leteral requmbency in five out of six animals that

lasted for an average of 74 minutes (Miyabe et al. 2001). A higher dose of medetomidine (0.06 mg/kg) with 0.3 mg/kg midazolam IM gave reliable immobilization within 13–19 minutes, with profound sedation and moderate muscle relaxation (Kimura et al. 2007). The animals were given atipamezole 30 minutes after medetomidine/midazolam injection and completely recovered within 12 minutes. This drug combination might be useful for minor short procedures, although cardiovascular and pulmonary effects were not evaluated.

Opioids

Opioid agonists are powerful analgesic agents, but one should exercise care when using them in primates due to their strong ventilatory depressant effects. In rhesus monkeys fentanyl IV produced respiratory depression and analgesia at dosages as low as 2 μg/kg and apnea was seen consistently at 60 μg/kg (Nussmeier et al. 1991). There may be large differences in dosage requirements among different species due to variations in the concentration and distribution of opioid binding sites (Robson et al. 1985). This difference may be marked when compared to unrelated species, such as dogs which do not develop apnea even at 3000 μg/kg IV (Arndt et al. 1984; Bailey et al. 1987). Butorphanol is an example of an agonist-antagonist opioid. However, it has significant respiratory depressent effects in primates (Liguori et al. 1996) compared to the minimal respiratory depressent effects seen in other animals such as dogs and cats. Minute ventilation in rhesus monkeys is reduced by 60–75% by butorphanol (0.1–0.3 mg/kg IM). Interestingly, the same dosage of butorphanol in ring-tailed lemurs does not result in hypoxemia in room air (Williams et al. 2003). There might be a difference in the opioid effects between lemurs and other primate species.

Naloxone, naltrexone, and nalbuphine are μ opioid receptor antagonists and effectively displace the agonists from the receptor binding sites, reversing the effects (Stoelting 1999).

Fentanyl/Medetomidine/Midazolam

This drug combination has the advantage of being fully reversible. A dosage of 0.02 mg/kg medetomidine, 0.5 mg/kg midazolam, and 0.01 mg/kg fentanyl given IM to rhesus macaques provided immobilization. Following an induction time of approximately 8 minutes the sedation was described as deep and reliable. These animals had a heart rate of 97 bpm and a systolic bloodpressure of 101 mmHg, decreasing to 85 bpm and 90 mmHg after 20 minutes. The monkeys were given supplemental oxygen through a face mask and maintained normal SpO_2 levels.

The duration of effect has not been described as the animals were reversed after 20 minutes. Recovery took approximately 10 minutes after reversal with naloxone and atipamezole and had good quality (Bertrand et al. 2016).

Similar effects in the same species were achevied with a dosage of 0.05 mg/kg medetomidine, 0.25 mg/kg midazolam, and 0.05 mg/kg fentanyl (Votava et al. 2011). Breathing room air, SpO_2 values were within 94 ± 4% throughout the 20 minutes of measurement. Heart rates were 116 bpm 5 minutes after drug administration and decreased to 108 bpm at 20 minutes. Animals given atipamezole after 20 minutes recoved in aproximately 3 minutes, whereas animals receiving no reversal recovered after 55 minutes. Recovery was described as smooth with no side effects such as vomiting or agitation.

Fentanyl (0.015 mg/kg IM) combined with midazolam (0.3 mg/kg IM) and ketamine (5 mg/kg IM) gave an immobilization similar to ketamine (5 mg/kg IM) and medetomidine (0.05 mg/kg IM) (Ølberg et al. 2018). The main difference was a more gradual and predictable recovery with the fentanyl combination, but more pronounced respiratory depression with the opioid combination requiring close monitoring.

Butorphanol/Medetomidine/Midazolam

A combination of 0.4 mg/kg butorphanol with 0.04 mg/kg medetomidine and 0.3 mg/kg midazolam given IM to patas monkeys gave a light plane of anesthesia for 50 minutes (Kalema-Zikusoka et al. 2003). The animals were fully awake within 7 minutes after reversal with atipamezole, naloxone, and flumazenil. This combination gave hypoxemia after induction that was rapidly corrected with supplemental oxygen.

Butorphanol/Acepromazine/Medetomidine

A combination of butorphanol, acepromazine, and medetomidine in dosages widely used for other wildlife species gave pronounced hypoxemia in rhesus macaques breathing room air (Malinowski et al. 2019). This hypoxemia was treated with supplementation of oxygen. Effective dosages were 0.43–0.66 mg/kg butorphanol, 0.15–0.22 mg/kg acepromazine, and 0.17–0.26 mg/kg medetomidine given IM. The animals had a smooth, rapid induction and immobilization for at least 25 minutes, and a smooth recovery after atipamezole reversal. The disadvantages of this combination were bradycardia, hypotension, and mild to moderate spontaneous movements during immobilization. Coupled with the severe initial hypoxemia, caution was recommended when using this combination for immobilization of rhesus macaques.

Alfaxalone

Alfaxalone is a neuroactive steroid and classified as an intravenous injectable general anesthetic. It can also be administered intramuscularly for sedation and anesthesia

in cats or rabbits. Recent research has also used this route in monkeys. Alfaxalone atdosages of 12–15 mg/kg IM produced a short induction time of 2–3 minutes followed by anesthesia of approximately 50 minutes, with good muscle relaxation and minimal side effects (Bakker et al. 2013; Ansel et al. 2016). Pulse oximetry readings indicated hypoxemia on room air, therefore supplemental oxygen is recommended (Konoike et al. 2017; Bakker et al. 2013). With alfaxalone, the recovery period was approximately 15 minutes and described as good, with some muscle twitching just before awakening. The time before the animals were fully awake was approximately 50 minutes.

A combination of 2 mg/kg alfaxolone, 0.02 mg/kg medetomidine, and 0.3 mg/kg midazolam given subcutaneously induced anesthesia with good muscle relaxation in rhesus macaques (Bertrand et al. 2017). Cardiovascular mesurements were stable and SpO_2 levels were high when breathing 100% oxygen though a face mask. Reversal with atipamezole did not appear to alter the depth of anesthesia, which lasted 50–60 minutes.

Inhalation Anesthesia

Inhalation anesthesia may be used alone or to maintain anesthesia after induction with injectable agents. The most commonly used inhalants, isoflurane and sevoflurane, have minimum alveolar concentrations in primates of 1.2% and 2%, respectively (Soma et al. 1988). Small primates (i.e., tamarins and marmosets) can be manually restrained in a net and induced with an inhalant anesthetic through a face mask or in an induction chamber (Fig. 32.4). Two clear advantages of inhalant anesthetics are reversibility and the use of oxygen as the carrier gas. This normally ensures adequate partial pressure of oxygen in the arterial blood during anesthesia. As in other species, inhalants are expected to cause dose-related cardiovascular and respiratory depression in primate species (Thurmon et al. 1996).

A combination of 0.015 mg/kg butorphanol, 0.3 mg/kg midazolam, and 10 mg/kg ketamine IM followed by 5% sevoflurane by mask has been recommended in commom marmosets to reduce stress during induction and improve



Figures 32.4 Small primates such as this cotton top marmoset can be manually restrained and masked induced with an inhalant anesthetic.

induction quality (Ishibashi 2015). These animals were maintained on 3% sevoflurane for short procedures.

Monitoring

A preanesthetic physical examination with full laboratory evaluation (Complete blood count (CBC) and biochemistry panel) is typically not possible without major sedation or general anesthesia. Once the animal can be restrained adequately or is induced, heart rate, respiratory rate, capillary refill time, mucous membrane colour, peripheral pulse, and airway should be assessed. If available, pulse oximetry and indirect blood pressure will provide additional information on circulation and oxygenation. Endtidal CO_2 measurements will give valuable information about hypoventilation if available. An accurate body weight, rectal temperature, hematocrit, serum total protein, urea, and creatinine should also be obtained. Careful monitoring of cardiovascular and respiratory function as well as reflexes will give information on anesthetic depth. Keeping track of time and record keeping is an important part of the monitoring procedure as with any other anesthetized species.

Analgesia

Buprenophine, an opioid agonist-antagonist, has much less respiratory depressant effect in primates than fentanyl or butorphanol (Liguori et al. 1996). It is approximately 30 times more potent analgesic than morphine and the duration of action is at least 8 hours in humans (Stoelting 1999). A study in rhesus monkeys suggests that buprenophine has a wide margin of safety in clinical use (Kishioka et al. 2000). It has been used for postoperative analgesia in a siamang monkey at a dose of 5 μg/kg IM (Weiland et al. 2007).

Ketamine, medetomidine, or dexmedetomidine have good analgesic properties and are often used in the anesthetic protocol to supplement analgesia in addition to their anesthetic and sedative effects.

Complications

Catching the animal and administering anesthetic agents for sedation or induction are two critical parts of primate anesthesia. There is a possibility of causing a traumatic injury when using projectile darts. Furthermore, there is a possibility that the primate will fall down if sitting in a tree or on a shelf once it becomes sedated. Nets can be used to catch the sedated primate before it hits the ground. Once induction of anesthesia is achieved, complications are often related to the health state of the animal, the drugs used, and the delivered dose of each drug. Hypothermia is common and body temperature should be monitored throughout the procedure.

Hypoxemia may occur due to hypoventilation, pulmonary shunting, or ventilation-perfusion mismatch. The use of a pulse oximeter will help evaluate oxygen saturation throughout the procedure and indirectly monitor for hypoxemia. Most anesthetic agents or drug combinations will cause mild to severe hypoxemia if the animals are breathing room air. Supplemental oxygen should be administered through a face mask or an endotracheal tube to all anesthetised primates. The use of reversible anesthetic agents adds safety to the procedure. A laryngoscope and a suitable endotracheal tube should always be available during anesthesia, as well as equipment necessary to give intravenous fluids.

Recovery

Recovery is performed in a quiet, confined space that prevents climbing and allows constant monitoring. A towel or other insulating material minimizes heat loss to the floor. The primate should not be reunited with its group until it is fully recovered.

Field Immobilization (Wild Capture)

Anesthesia of free-living primates comprises numerous challenges compared to controlled captive environments. One should carefully consider factors including environment, temperature, humidity, use of darts or traps, species, social groups, and potential for zoonotic diseases (Sapolsky & Share 1998).

It is possible to use traps (Aguiar et al. 2007) as well as remote darting equipment depending on the species and situation. With darting one must consider the risk that the animal will fall from high trees during induction or get lost after darting. Other considerations are hyperthermia/hypothermia and aspiration of regurgitated food material. A small dart volume and fast induction times are favourable when darting free-ranging primates. Recommended drug combinations are tiletamine/zolazepam (Karesh et al. 1998), tiletamine/zolazepam/medetomidine(Fahlman et al. 2006), or ketamine/medetomidine (Vie et al. 1998). Remote areas may restrict the amount of equipment available, and one may not have oxygen supplementation during anesthesia. One should also keep the primate in a cage until fully recovered before release back into the wild.

Table 32.2 Anesthesia of monkeys and gibbons.

Drug	Dosage (mg/kg)	Reversal	Comments	References
Ketamine Medetomidine	5–8 0.02–0.05	None Atipamezole	Commonly used in many primate species for induction or short-term anesthesia. Fast induction and anesthesia for 30-45 minutes with good muscle relaxation. Be aware that recovery can be very fast.	Ølberg et al. (2018) Selmi et al. (2004)
Ketamine Xylazine	5 0.5–1	None Yohimbine or atipamezole	Approximately 30 minutes of immobilization with good muscle relaxation. Be aware that recovery can be very fast.	Naccarato & Hunter (1979) Hayama et al. (1989)
Ketamine Midazolam	10 1	None Flumazenil	Rapid immobilization, good muscle relaxation for 30-45 minutes in marmosets.	Furtado et al. (2010)
Tiletamine/zolazepam Medetomidine	1–3 0.02–0.06	None Flumazenil Atipamezole	Rapid induction in macaques and gibbons, with a smooth induction. Good muscle relaxation.	Fahlman et al. (2006)
Medetomidine Midazolam	0.06 0.3	Atipamezole Flumazenil	Sedation/immobilization in Japanese macaques. Induction within 13–19 minutes. Cardiovascular and pulmonary effects not evaluated. Minor, short procedures.	Kimura et al. (2007)
Medetomidine Midazolam Fentanyl	0.050. 250. 005	Atipamezole Flumazenil Naloxon	Fast induction in rhesus macaques. Immobilization for 55 minutes. Smooth recovery.	Votava et al. (2011)
Alfaxalone	12–15	None	Immobilization for 50 minutes in marmosets. Hypoxemia on room air. Fast induction in rhesus macaques after subcutaneous injection. Surgical anesthesia for at least 20 minutes. Total duration immobilization approximately 50 minutes.	Bakker et al. (2013)
Alfaxalone Medetomidine Midazolam	2 0.02 0.3	None Atipamezole Flumazenil		Bertrand et al. (2017)

See general text for other drug combinations and dosages.

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33

Apes

Jennifer D'Agostino

Introduction

Anesthesia of great apes is often necessary to conduct diagnostic analysis, provide therapeutics, facilitate surgical procedures, and enable transport and translocation for conservation purposes. Anesthesia of great apes can be challenging due to their relatively large size, physical strength, agility, and intelligence. In particular, great apes can be very sensitive to changes in their normal environment. Even very subtle perturbations can cause apes to become excited or aggressive, such that anesthetic induction can be very distressing to both animal and anesthesiologist. However, there are sizeable populations of great apes in zoological collections and research institutions due to their endangered status and use as animal models for human diseases, respectively. Consequently, anesthesia is frequently performed on these species, which has resulted in the development of a body of knowledge. However, captive apes often suffer from medical conditions such as cardiomyopathy that can complicate anesthetic events. In order to improve the overall success of anesthesia, focus has been on orally administered, transmucosally absorbed, anesthetic agents and behavioral training for hand injections as alternative, less stressful methods of premedication and anesthetic induction. Finally, there is increasing conservation management of in situ great ape populations, which has resulted in the development of field anesthesia techniques for free-living great apes for the purposes of translocation, reintroduction into the wild, and clinical interventions.

Taxonomy, Biology, and Anatomical Considerations

Great apes include the bonobo (*Pan paniscus*), four subspecies of chimpanzees (*Pan troglodytes*), two species of gorillas (*Gorilla gorilla* and *Gorilla beringei*), each with two subspecies, and three species of orangutans, the Sumatran orangutan (*Pongo abelii*), the Bornean orangutan (Pongo *pygmaeus*), and the newly described Tapanuli orangutan (*Pongo tapanuliensis*). They are all tropical Old World species, and the chimpanzee and bonobo are considered endangered while all species of gorilla and orangutan are considered critically endangered (IUCN 2020).

Bonobos are the smallest of the great apes, with an adult weight range of 25–45 kg. Chimpanzees have an adult weight range of 40–90 kg and orangutans have an adult weight range of 30–50 kg for females and 50–100 kg for males. Gorillas are the largest, with an adult weight range of 70–120 kg for females and 140–270 kg for males (Murphy 2015). Males are larger than females for all species. All are social animals with complex social structures and behaviors, except for orangutans, which are solitary. Great apes have a close taxonomic relationship with humans. Consequently, there are many anatomical similarities, and human anesthetic equipment, such as facemasks, is often used in preference to veterinary equipment. In addition, there is a high potential for pathogen exchange between humans and great apes, necessitating appropriate disease-preventive measures.

Their large size, agility, and physical strength, as well as large teeth and strong jaws, create the potential for human injury during anesthetic procedures. For this reason, physical restraint and sedation of apes is generally not practical, and most procedures require the animal to be at least stage III of anesthesia. Human safety is of paramount importance during any anesthetic event involving great apes, and it is important to have an experienced, well-trained team of individuals. Due to the zoonotic disease concerns mentioned earlier, all persons in close proximity to apes must wear personal protective equipment, such as facemasks and latex gloves. It would also be prudent to establish escape and bite-wound protocols, as well as have access to a bite-wound kit for first-aid treatment of persons who may be bitten.

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Figure 33.1 Intravenous catheter placed in the cephalic vein of a western lowland gorilla.

Unique respiratory anatomical features of great apes include laryngeal air sacs, which are present in all species, but are most extensive in gorillas and orangutans (Lawson et al. 2006; Nishimura et al. 2007; Raven 1950). In addition, great apes have relatively short tracheas, and care must be taken to ensure that a primary bronchus is not inadvertently intubated (Loomis 2003). Excessive caudal pharyngeal tissue, thick tongues, and long flaccid soft palates may create challenges for airway maintenance during anesthesia (Kenny et al. 2003). Captive apes are also prone to obesity, which may further complicate access to the airway.

Some Old World nonhuman primates in estrus will develop large genital tumescence. This swelling of the sexual skin can be quite prominent in chimpanzees, and is very vascular and friable. Care must be taken to avoid darting this area as severe hemorrhage may result (Fowler 2008).

Venous access can be accomplished at several sites. The femoral vein at the femoral triangle is readily available. In addition, the saphenous vein on the posterior surface of the lower leg and the cephalic vein are usually visible, especially in larger animals. Intravenous (IV) catheters are typically placed in the cephalic or saphenous vein. IV access is important for administration of fluids and to provide a rapid route of anesthetic drug supplementation or emergency drug administration should the need arise (Fig. 33.1).

Preanesthetic Considerations

As with any species, a preanesthetic assessment is vital. However, this can be challenging in great apes and significant diseases may go unrecognized. Furthermore, estimated body weights are often inaccurate, with one study reporting that even experienced personnel overestimated the weights of chimpanzees by as much as 28% (Adams et al. 2003).

Historically, it has been recommended that great apes be fasted and water withheld for 12–24 hours prior to anesthesia (Loomis 2003). However, this is often a clue that a procedure is imminent and can result in increased stress, leading to increased drug tolerance and stereotypic behaviors (such as pica and coprophagy). Across species, studies have shown that prolonged fasting can adversely affect gut health and may in fact exacerbate the potential for regurgitation and aspiration (Moyao-Garcia et al. 2001). Current recommendations for preanesthetic fasting in human patients is 2 hours for a liquid diet and 6 hours after a light meal (American Society of Anesthesiologists 2017). Ardente et al. (2011) showed that gastric emptying time in chimpanzees is approximately 3 hours, indicating that a shorter fasting time may be more appropriate than a typical overnight fast (often 15–16 hours) in this species. Given the differences in gastrointestinal anatomy and physiology across species, a single recommendation for preanesthetic fasting is not likely to be applicable for all great apes or even for each individual. Clinicians should evaluate each patient individually and use their discretion to determine the appropriate minimum preanesthetic fasting time.

Cardiovascular disease is the leading cause of morbidity and mortality in great apes under human care. Prevalence of cardiovascular disease increases with age, but disease and death can occur in nongeriatric individuals (Lowenstine et al. 2016). Anesthetic drugs can have significant cardiovascular effects, therefore careful consideration of anesthesia protocol is warranted in these species. Pharmacologic changes in cardiovascular function can adversely affect cardiovascular examination results and lead to anesthetic complications in individuals with underlying cardiovascular disease. Techniques to obtain echocardiograms and blood pressure reading in conscious great apes through behavioral training have been described (Boyd et al. 2019; Clyde et al. 2002, 2015). Preanesthetic evaluation of cardiovascular health, when available, should be considered when planning an anesthetic procedure.

Preanesthetics/Sedatives

Due to the stress of remote delivery injection of anesthetic agents, oral delivery and/or transmucosal absorption of preanesthetic and anesthetic agents has been evaluated. The techniques described can have variable and unpredictable results, but are a useful alternative method of delivery to consider. Use of metoclopramide (0.4 mg/kg) and ondansetron (0.15 mg/kg) orally to prevent emesis prior to anesthetic induction in gorillas and an orangutan, respectively, has been described (Miller et al. 2000; Gyimesi et al. 2015). Use of anticholinergics either as a premedication or in

conjunction with induction agents may help to control hypersalivation and/or bradycardia when needed. Atropine sulfate administered at 2–5 mg intramuscular (IM) in juvenile chimpanzees (April et al. 1982), 0.04 mg/kg IM in gorillas (Raphael et al. 2001), and 0.01 mg/kg IM in an orangutan (Hendrix 2006) has been reported. Glycopyrrolate administered at 0.01 mg/kg IM in orangutans (Greenberg et al. 1999; Gyimesi et al. 2015) has also been reported.

Benzodiazepines

Benzodiazepines have minimal effects on cardiopulmonary function and are considered safe to use in primates (Horne 2001). Diazepam can be given orally as a preanesthetic agent and may provide some degree of sedation prior to anesthetic induction. Raphael et al. (2001) reported administering 5 mg of diazepam orally to juvenile gorillas 2 hours prior to anesthetic induction with ketamine by hand injection. In addition, Miller et al. (2000) described the use of diazepam for its sedative effect at 0.2 mg/kg given orally 90–120 minutes prior to anesthetic induction. Premedication with midazolam (0.7–1.2 mg/kg per os [PO]) delivered in orange juice has been described in chimpanzees and orangutans (Hess et al. 2010). Effects ranged from slight to marked sedation.

Opioids

Transmucosal fentanyl formulations approved for human use have also been used in great apes. Hunter et al. (2004) trained animals to accept, after an overnight fast, a placebo candy lollipop and to suck on it slowly. After 4–6 weeks of training, the apes were then offered the fentanyl lollipop at an intended dose of 10–15 μg/kg. Orangutans and gorillas accepted the treated lollipops and displayed signs of adequate sedation in 30–45 minutes, and responded minimally to darting. However, the chimpanzees' acceptance of the fentanyl lollipops was suboptimal and visible sedation was not appreciated. The authors suggested a greater fentanyl concentration in the treated lollipop may be necessary to achieve sedation in chimpanzees. The resulting plasma concentrations of fentanyl in animals accepting treated lollipops supported transmucosal absorption. The success of this technique was dependent on an effective training program, cooperation of the keeper staff, and adequate housing facilities.

Neuroleptic Agents

For anxiolytic effects, the neuroleptic drug zuclopenthixol at dosages of 0.1–0.36 mg/kg by mouth twice daily was used in gorillas undergoing a prolonged journey (Vogelnest 1998). These animals were calm, traveled well, and maintained good appetites during their transportation. Zuclopenthixol 0.2 mg/kg by mouth twice daily for 3 days prior to anesthesia and 0.27 mg/kg by mouth on the day of anesthesia has been described in gorillas prior to immobilization with ketamine, medetomidine, and midazolam combination administered by dart. Mild sedation was noted in each animal prior to induction, but agitation in response to the darting was still observed in all individuals (Wenger et al. 2013).

Opioid/Neuroleptic Combinations

The administration of oral droperidol at a dose of 1.25 mg for a juvenile chimpanzee and 2.5 mg for adult chimpanzees 45 minutes prior to transmucosal carfentanil administration at 2.0 μg/kg provided an effective premedication regimen that produced profound sedation prior to the IM delivery of tiletamine-zolazepam for anesthetic induction (Kearns et al. 2000). Carfentanil was administered by enticing the animal to the front of the cage and expelling the drug from a 0.5-mL syringe directly onto the oral mucosa. This combination produced smooth induction and heavy sedation or light anesthesia approximately 25 minutes after carfentanil administration (Kearns et al. 2000). At that time, naltrexone and tiletamine-zolazepam were combined into one IM injection for anesthetic induction. Naltrexone was administered at 100 times the carfentanil dose in milligrams. The primary side effect noted was respiratory depression, but this was adequately managed by administration of the narcotic antagonist at the time of anesthetic induction with tiletamine-zolazepam. However, the authors also recommended providing supplemental oxygen as well as preparing a naltrexone dart in advance as a precaution. In addition, a side effect of facial pruritis was noted in some individuals. Kearns et al. (2000) noted that during initial carfentanil dosing trials, direct application of carfentanil onto the oral mucosa produced the deepest level of sedation, followed by offering the drug in foods that contact the mucosa, such as marshmallow crème. When the drug was administered in fruit, only stage 2 or 3 of sedation was reached, which was attributed to the poor gastric absorption of narcotics compared with mucosal absorption.

Alpha-2 Agonists

Medetomidine transmucosally administered at 50–100 μg/kg in marshmallow crème prior to immobilization with ketamine by injection resulted in variable effects (Kearns et al. 1998). Some animals that had not had previous immobilization experience were noticeably sedated, whereas other more experienced chimpanzees showed little or no sedation. Naples et al. (2010) compared chimpanzees

receiving oral medetomidine at 0.1 mg/kg in marshmallow crème or applesauce prior to immobilization with tiletamine-zolazepam at 3 mg/kg IM by remote injection, with animals that were immobilized with medetomidine at 0.05 mg/kg and tiletamine-zolazepam at 3 mg/kg both given IM by remote injection. Although there was not a significant difference between the two groups in the time between tiletamine-zolazepam administration and a degree of sedation considered safe for human contact, animals receiving oral medetomidine exhibited less excitatory behavior and agitation associated with darting than animals that did not receive medetomidine as a premedication.

Induction Agents

Intramuscular induction agents can be given by hand injection or remote delivery into a large muscle mass, such as the shoulder or thigh. Immobilization with ketamine and tiletamine-zolazepam/ketamine combination by darting has been shown to elicit both short-term and long-term stress response in chimpanzees (Anestis et al. 2006; Whitten et al. 1998). Urinary cortisol was also demonstrated to be significantly higher in chimpanzees following remote injection with tiletamine-zolazepam than other stressful events, including restriction to an indoor enclosure due to a hurricane and changes in group composition (Anestis 2009). Positive reinforcement training techniques are used frequently with great apes to train both medical and husbandry behaviors. In a study by Lambeth et al. (2006), chimpanzees that voluntarily presented for a hand injection of anesthetic had significantly lower total white blood cell counts, percentage of segmented neutrophils, and blood glucose than those that were immobilized by dart gun. This indicates that animals that voluntarily presented for a hand injection experienced less of a stress response than those that were darted involuntarily.

Operant conditioning for hand injection should be utilized for induction of anesthesia when available, otherwise the least traumatic remote delivery system should be used to prevent injury. All attempts should be made to dart the animal without warning as once alerted the individual, or group, will become agitated and mobile, making darting very difficult. Protective clothing, including face shields, may be necessary as chimpanzees have a propensity to spit water, throw fecal matter and other material with surprising accuracy, as well as returning darts with some force. In addition, apes have surprisingly long limbs and will grab at loose clothing, glasses, and even the dart gun. Ideally, potent drugs that require a small volume for injection should be used as apes can remove a dart very quickly prior to full injection of the drug (Fowler 2008).

Darting individuals housed in a social group can be particularly challenging and isolation of the targeted individual from the group prior to anesthesia may not be possible, or could be very stressful. Once alerted to the event the whole group may act aggressively toward humans in close proximity, which can be very intimidating. However, it is important to have a mechanism to isolate and retrieve the anesthetized individual, especially in the event of an anesthetic emergency. Appropriate facilities that allow shifting of animals and securing areas or rooms is very helpful. Removal of enclosure furniture and bedding prior to darting may be beneficial as apes can be very adept at hiding or adopting body positions to avoid the dart.

A variety of anesthetic protocols have been used successfully in great apes. The Zoological Information Management System (ZIMS) has summarized anesthetic drug usage by member organizations for all ape species. A selection of injectable induction agents and dosages commonly used alone or in combination is listed in Table 33.1. The protocols described in this section pertain to great apes under human care unless otherwise noted.

Ketamine Hydrochloride

Ketamine is a dissociative anesthetic and has been shown to have a wide margin of safety in many species. In apes, induction is generally smooth and rapid, and provides a level of anesthesia sufficient for minor procedures (April et al. 1982; Lewis 1993; Raphael et al. 2001). Cardiopulmonary effects are minimal, which makes it an attractive option for anesthesia in compromised individuals or those with unknown cardiovascular health status. Dissociative agents can increase heart rate and sympathetic tone, but echocardiographic indices are generally unaffected, making ketamine a beneficial agent to use in individuals undergoing cardiac assessment (Boyd et al. 2019). Ketamine is irreversible, but duration of action is short and sudden, unexpected recoveries can occur (Lewis 1993). Incremental doses of ketamine given IV will prolong anesthesia for more invasive procedures but can result in an extended recovery time of several hours, and repeated use has been associated with development of anesthetic tolerance (April et al. 1982; Lewis 1993). Prolonged anesthesia with ketamine has been described in a gorilla to assist vaginal delivery of an infant after prolonged labor (Cole 2000) and in an orangutan for repeated surgical treatment of a retroperitoneal abscess (Chai et al. 2009). Ketamine does maintain laryngeal reflexes to some extent, but this does not obviate the need for careful airway management. The presence of laryngeal reflexes can make airway management challenging and additional anesthetic (IV or inhalant) may be required for successful intubation. Ketamine can

Table 33.1 Range of dosages of injectable anesthetic induction agents used in great apes (ZIMS 2020a–c).

Drug	Bonobo	Chimpanzee	Gorilla	Orangutan
Induction agents				
Ketamine	8.4 (3.23–15)	8.55 (3.67–15.67)	7.44 (2.17–14.66)	B: 6.88 (2.88–15) S: 7.42 (2.2–13.27)
Ketamine/ medetomidine	5.1 (2.7–9.9) K, 0.045 (0.014–0.09) M	4.39 (1.74–9.46) K, 0.042 (0.015–0.09) M	3.88 (1.64–8.05) K, 0.046 (0.016–0.27) M	B: 4.32 (1.71–7.8) K, 0.43 (0.016–0.08) Me S: 3.92 (1.26–7.37) K, 0.041 (0.016–0.1) M
Ketamine/ medetomidine/ butorphanol		3.46 (0.02–8.86) K, 0.024 (0.013–0.048) M, 0.21 (0.024–0.4) B	2.81 (1.33–3.94) K, 0.027 (0.018–0.05) M, 0.22 (0.09–0.31) B	S: 3.02 (1.64–4.78) K, 0.031 (0.021–0.04) Me, 0.11 (0.07–0.22) Bu
Ketamine/ medetomidine/ midazolam			3.64 (1.58–6.08) K, 0.041 (0.019–0.08) Me, 0.25 (0.013–1.19) Mi	B: 4.08 (1.68–8.32) K, 0.38 (0.008–0.08) Me, 0.19 (0.03–0.97) Mi
Ketamine/midazolam	8.33 (2.88–11.43) K, 0.21 (0.06–0.75) M			S: 8 (3.07–11.22) K, 0.12 (0.015–0.51) Mi
Ketamine/midazolam/ butorphanol				B: 6.67 (3.83–15.21) K, 0.11 (0.1–0.13) Mi, 0.11 (0.08–0.13) Bu
Ketamine/xylazine		9.96 (4.57–14.33) K, 0.4 (0.15–0.91) X	6.35 (4.22–9.51) K, 0.27 (0.21–0.4) X	B: 6.39 (3.0–9.45) K, 0.51 (0.34–0.86) X S: 5.49 (2.51–9.05) K, 3.07 (0.75–4.52) X
Tiletamine-zolazepam	4.14 (1.85–7.19)	4.65 (2.2–7.87)	3.19 (1.65–5)	B: 3.99 (1.74–8.11) S: 3.71 (1.72–5.98)
Tiletamine-zolazepam/ ketamine	2.05 (0.67–4.41) T, 3.68 (1.32–7.13) K	3.82 (1.23–6.64) T, 2.64 (0.86–8.7) K	2.72 (1.12–4.64) T, 2.23 (0.53–5.15) K	B: 3.09 (0.53–5.67) T, 2.89 (0.83–6.8) K S: 2.92 (1.52–5.47) T, 2.25 (0.66–7.44) K
Tiletamine-zolazepam/ ketamine/xylazine		2.58 (1.38–5.09) T, 2.0 (1.03–4.72) K, 0.64 (0.18–1.39) X	1.55 (0.9–2.35) T, 1.45 (0.86–2.6) K, 0.39 (0.18–0.86) X	
Tiletamine-zolazepam/ medetomidine		2.21 (1.05–5.63) T, 0.026–0.005–0.06) Me		

B, Bornean orangutan; Bu, butorphanol; K, ketamine; Me, medetomidine; Mi, midazolam; S, Sumatran orangutan; T, tiletamine-zolazepam; X, xylazine.
Dosages listed as mean (range) in mg/kg for IM administration.

also induce hypersalivation, which can be prevented or controlled using an anticholinergic agent (Martinez 2001). Another disadvantage of ketamine when used alone is the large volume required. A concentrated 200 mg/mL solution may aid delivery in larger animals.

Ketamine and Alpha-2 Agonists

The disadvantages of ketamine resulted in the development of protocols combining ketamine with alpha-2 agonists, which is now one of the most commonly used anesthetic drug combinations used in great apes (ZIMS 2020a–c). April et al. (1982) reported the use of a combination of ketamine (15–20 mg/kg) and xylazine (1 mg/kg) in chimpanzees delivered IM that resulted in similar induction time compared with ketamine alone, but with a greater depth of anesthesia characterized by greater muscle relaxation and analgesia, as well as cardiopulmonary stability, and longer but uneventful recoveries.

When medetomidine is delivered in combination with ketamine, the total ketamine dose can be reduced to at least one-fifth of the ketamine dose if it is used as the solo agent (Horne 2001). Delivery of ketamine in combination with medetomidine IM has been shown to provide a rapid and safe method of anesthetic induction in great apes, with sufficient short-term anesthesia for

minor procedures (Horne et al. 1997; Lewis 1993; Adams et al. 2003; Napier et al. 2013). Spontaneous arousal/recovery can occur in animals anesthetized with alpha-2 agonist drug combinations. It is important to leave the animal undisturbed for 10–15 minutes prior to manipulation to help prevent rapid arousal (Horne et al 1997; Melis et al. 2012).

Medetomidine produces a biphasic cardiovascular response. First- and second-degree atrioventricular heart block and profound vasoconstriction are commonly seen in the initial phase. Hypertension caused by the vasoconstriction results in reflex bradycardia. In the second phase, vascular resistance decreases, leading to hypotension. These effects are significantly more pronounced when the drug is administered IV versus IM (Posner & Burns 2009). Anesthetic protocols including medetomidine may exacerbate or artificially induce signs of heart disease in great apes. Napier et al. (2013) investigated the effect of three phases of an anesthetic protocol, ketamine and medetomidine, ketamine and medetomidine with isoflurane, and ketamine and medetomidine, after reversal with atipamezole on echocardiogram and indirect blood pressure measurements. Heart rate was not significantly different between the protocols and bradycardia was not seen. Indirect blood pressure was significantly higher with ketamine and medetomidine as compared to those that had been reversed with atipamezole. Ejection fraction improved in all animals after reversal of medetomidine with atipamezole.

Atencia et al. (2017) evaluated the effect of four anesthetic protocols on heart rate and indirect blood pressure in wild-born chimpanzees. Heart rate was lower and indirect blood pressure higher with combinations including ketamine and medetomidine as compared to those that included tiletamine-zolazepam. Parameters were noted to be least stable for animals induced with ketamine and medetomidine and maintained on isoflurane by endotracheal tube. The effects of anesthetic protocol must be considered when evaluating the cardiovascular health of great apes under anesthesia.

Detomidine is a less specific alpha-2 agonist compared to medetomidine. Orally administered detomidine (0.32 mg/kg) and ketamine (9.6 mg/kg) have been investigated as anesthetic induction agents in gorillas (Miller et al. 2000). Some animals received diazepam (0.2 mg/kg PO) and metoclopramide (0.4 mg/kg PO) 90–120 minutes prior to delivery of other agents. Lateral recumbency was achieved at 17 minutes in one animal that received a full dose of oral detomidine and ketamine, but supplemental tiletamine-zolazepam was administered (0.94 mg/kg) by remote injection. For the other animals that received partial doses, the first signs of sedation were seen around 15 minutes, and tiletamine-zolazepam was required to achieve lateral recumbency. In all cases, the gorillas had only mild responses to darting and were subjectively judged to be less stressed than with darting alone based on decreased screaming, charging, and other stress behaviors. Ketamine (4–5 mg/kg) and detomidine (50–60 μg/kg) administered IM by dart has been utilized for immobilization of chimpanzees (Melis et al. 2012). The concentration of detomidine allowed for a smaller volume injection than with other ketamine drug combinations. Animals frequently required supplemental ketamine due to spontaneous arousal or arousal during stimulation when performing minor procedures. Most of the animals exhibited hypoxemia and hypothermia, and bradycardia was occasionally seen. Reversal with atipamezole resulted in recovery within 10 minutes, but recovery was highly variable if no antagonist was administered.

Napthylmedetomidine use has been investigated in chimpanzees and orangutans (Hess et al. 2010). Animals were premedicated with midazolam (0.7–1.2 mg/kg PO) and immobilized with ketamine (3 mg/kg IM) and hyaluronidase (150 units) and either medetomidine (0.02–0.03 mg/kg) or napthylmedetomidine (0.05–0.07 mg/kg IM). Immobilization with napthylmedetomidine was less complete and shorter in duration than that with medetomidine, and was incompletely antagonized by atipamezole. However, although cardiorespiratory parameters were not statistically evaluated, animals receiving medetomidine had lower heart rates after treatment than animals receiving napthylmedetomidine. In addition, napthylmedetomidine provided anti-aggressive effects in the postoperative period.

Tiletamine-Zolazepam and Tiletamine-Zolazepam Combinations

Tiletamine, a cyclohexamine, and zolazepam, a benzodiazepine in a 1:1 combination (Telazol™) used alone or in combination with other injectable anesthetic drugs is the most common anesthetic agent utilized in all great ape species (ZIMS 2020a–c). Several reports show that tiletamine-zolazepam alone, or in combination with medetomidine, produces smooth rapid induction with stable cardiopulmonary parameters (Horne et al. 1998; Cerveny et al. 2012; Strong et al. 2018; Atencia et al. 2017). Strong et al. (2018) investigated the effects of tiletamine-zolazepam (3–4 mg/kg) and tiletamine-zolazepam (2 mg/kg) and medetomidine (0.02 mg/kg) combination on heart rate, blood pressure, and echocardiographic parameters in chimpanzees. Tiletamine-zolazepam and medetomidine combination resulted in a significantly lower heart rate, mean arterial blood pressure, systolic arterial blood pressure, and oxygen saturation than tiletamine-zolazepam alone, but there was no change in echocardiographic parameters. Quality of anesthesia with the tiletamine-zolazepam and medetomidine combination was higher

and no supplemental anesthesia administration was required. Atencia et al. (2017) showed in wild-born chimpanzees that mean heart rate was higher and mean indirect blood pressure was lower in animals immobilized with tiletamine-zolazepam or tiletamine-zolazepam and medetomidine when compared to those immobilized with ketamine and medetomidine. Individuals receiving tiletamine-zolazepam and medetomidine exhibited predictable hemodynamics with an initial increase, then steady decrease in heart rate and indirect blood pressure with plateau reached in 30–40 minutes.

Tiletamine-zolazepam combined with ketamine is also a common anesthetic induction protocol documented in all great ape species (ZIMS 2020a–c). Hanley et al. (2006) reported the use of a combination of ketamine (5.66 mg/kg) and tiletamine-zolazepam (3.4 mg/kg) delivered IM to induce anesthesia in an orangutan. Gyimesi et al. (2015) also report immobilization of an orangutan with ketamine (1.9 mg/kg) and tiletamine-zolazepam (1.9 mg/kg) IM after oral premedication with midazolam (1.0 mg/kg).

Tiletamine-zolazepam delivered orally at a dosage of 16 mg/kg, administered in about 30 mL of a cola beverage, was used to successfully immobilize a chimpanzee (Knottenbelt & Knottenbelt 1990). Lateral recumbency was achieved within 7 minutes, with no response to external stimuli. Cardiopulmonary function was considered stable, and both pharyngeal and laryngeal reflexes were present. The chimpanzee began to respond to external stimuli after 40 minutes and recovery was uneventful.

Fowler (2008) noted that the recovery time for tiletamine-zolazepam alone is dose dependent and recommended the use of low doses for quick procedures. Excessive prolonged recovery times in silverback western lowland gorillas immobilized with tiletamine-zolazepam and maintained with inhalation agents has been noted (Cerveny et al. 2012; J. Sleeman, unpubl. data). In one case, an initial dose of 4.36 mg/kg given intramuscularly was only partially received and two supplemental doses of 2.02 mg/kg (estimate 30% was received) and 2.45 mg/kg were given. Time from cessation of administration of inhalation agents until voluntary movement of the animal was 13.5 hours. Other gorillas supplemented with ketamine following tiletamine-zolazepam delivery did not experience profoundly prolonged recoveries, and the authors recommend ketamine supplementation if necessary. Furthermore, recoveries from tiletamine-zolazepam and medetomidine anesthesia in chimpanzees were prolonged (1–5 hours) and were characterized by signs of extreme drowsiness, dizziness, ataxia, and adverse gastrointestinal effects, such as vomiting. Flumazenil (0.025 mg/kg IV) transiently increased alertness but did not significantly enhance the speed or quality of recovery (Horne et al. 1998). A similar effect after administration of flumazenil to gorillas has been noted (Sleeman et al. 2000).

Carfentanil

Preliminary trials with orally delivered, transmucosally absorbed carfentanil citrate alone at dosages of 2–4 μg/kg in chimpanzees provided nearly complete or complete immobilization after 22 minutes, but were accompanied by severe respiratory depression, including one case of respiratory arrest and death (Kearns et al. 1999). Consequently, administration of transmucosal carfentanil alone for immobilization of chimpanzees is not recommended.

Other Combinations

ZIMS data show several additional drug combinations that have been used in great apes (Table 33.1). Ketamine and midazolam induction has been reported in a chimpanzee (2.5/0.25 mg/kg IM; D'Agostino et al. 2007) and a gorilla (9/0.05 mg/kg IM; Liang et al. 2005). Vitale et al. (2017) report induction of an orangutan with ketamine (2.8 mg/kg), medetomidine (0.028 mg/kg), and midazolam (0.09 mg/kg) for colonoscopy. Bailey et al. (2019) report coinduction of adult gorillas with ketamine (4–5 mg/kg), midazolam (0.2–0.3 mg/kg), and either fentanyl (0.01–0.015 mg/kg) or sufantanil (0.025–0.03 mg/kg) administered IM. Both combinations resulted in smooth calm induction with rapid recovery. Fentanyl and sufentanil are short-acting μ opioid agonists with minimal cardiovascular depression and may be an effective choice for individuals with existing cardiovascular disease and prevention of drug-induced alteration of cardiovascular measurements.

Anesthetic Maintenance

Endotracheal Intubation

Maintenance of the airway and provision of oxygen is an important aspect of anesthesia in great ape species. At a minimum, flow-by oxygen should be provided. For prolonged procedures, intubation and maintenance of anesthesia using inhalation agents delivered in oxygen is recommended. For most of the induction agents mentioned earlier, the plane of anesthesia may not be adequate to allow intubation, and it may be necessary to deliver inhalation agents using a tightly fitting human facemask prior to intubation. Great apes are best intubated in dorsal recumbency with the head extended off the edge of the table, which will help to extend the neck (Fig. 33.2). Pulling the tongue forward may help to visualize the larynx. The base of the tongue should then be depressed using a Macintosh laryngoscope blade. Great apes are prone to hypersalivation and laryngospasm, especially when ketamine is given at high doses as the sole anesthetic agent (Horne 2001). Applying small amounts of lidocaine or



Figure 33.2 Intubation of an infant western lowland gorilla. Extending the head off the table can help straighten out the airway and provide better visualization of the larynx in apes.

cetacaine to the glottis several minutes before intubation will help to prevent this (Adams et al. 2003; Horne 2001). Great apes require cuffed Murphy tubes ranging in size from 6 to 12 mm. As mentioned, the short tracheas predispose to intubation of a primary bronchus, thus, once the tube is in place, both sides of the chest should be auscultated and monitored for air sounds.

Laryngeal Mask Airway

The laryngeal mask airway (LMA) is an alternative to endotracheal intubation that creates a seal around the larynx with an inflatable cuff (Brain 1983). LMA use has been reported in pediatric chimpanzees (Johnson et al. 2010) and one adult (Vilani et al. 2000). Cerveny et al. (2012) found the LMA to be an effective device for airway control in western lowland gorillas (Fig. 33.3). Gorillas were immobilized with tiletamine-zolazepam IM, and anesthesia was maintained with sevoflurane delivery via either LMA or endotracheal tube. Arterial oxygen was significantly greater in the animals in which LMAs were placed 15 and 45 minutes after placement of the device. The authors speculate that this was due to intubation of a bronchus in the animals in which an endotracheal tube was placed. The LMA is easy to insert and can be used during spontaneous and intermittent positive pressure ventilation. In human patients, LMA use has proved to have several additional advantages compared to endotracheal tubes such as increased hemodynamic stability at induction and recovery, decreased anesthetic requirement for placement, minimal rise in intraocular pressure, decreased coughing and sore throat post-procedure, and increased oxygen saturation at recovery (Brimacombe 1995). However, the LMA does not protect against aspiration and should not be used in animals that have not been fasted.



Figure 33.3 Removal of a laryngeal mask airway during anesthesia recovery of a western lowland gorilla.

Inhalatory Agents

Isoflurane is commonly used to prolong and maintain anesthesia in great apes (Adams et al. 2003; Cook & Clarke 1985; Hendrix 2006; Horne et al. 1997, 1998; Liang et al. 2005); however, it has potent vasodilatory properties that can cause severe hypotension (Horne 2001). In addition, as most animals will have received an anesthetic induction agent, the minimum alveolar concentration (MAC) of isoflurane must be reduced accordingly. For example, chimpanzees and gorillas induced with medetomidine and ketamine required masking with 2–3% isoflurane in 100% oxygen to permit intubation followed by 0.5–1.5% isoflurane for anesthetic maintenance using a nonrebreathing circuit (Horne et al. 1997). Blood pressures were elevated immediately following induction but steadily decreased and remained within normal limits after the first 15 minutes, as did heart rate, respiratory rate, hemoglobin saturation (SpO_2), and end-tidal CO_2. Animals induced with medetomidine and tiletamine-zolazepam required a lower MAC and could be maintained at a mean level of 0.8% isoflurane in 100% oxygen (Horne et al. 1998). In addition, the latter anesthetic induction combination appeared to potentiate the vasodilatory effects of isoflurane, placing the animals at risk for hypotension, requiring close monitoring of blood pressure.

Sevoflurane is less noxious than isoflurane and can be useful for facemask delivery of an inhalant agent but is more expensive. Like isoflurane, sevoflurane had minimal effects on cardiac output at typical anesthetic concentrations (1.2 times MAC) in domestic dogs (Bernard et al. 1990). In humans, sevoflurane does not appear to sensitize the myocardium to catecholamines, a situation that may induce arrhythmias (Navarro et al. 1994). Cerveny et al. (2012) reported use of sevoflurane for anesthetic

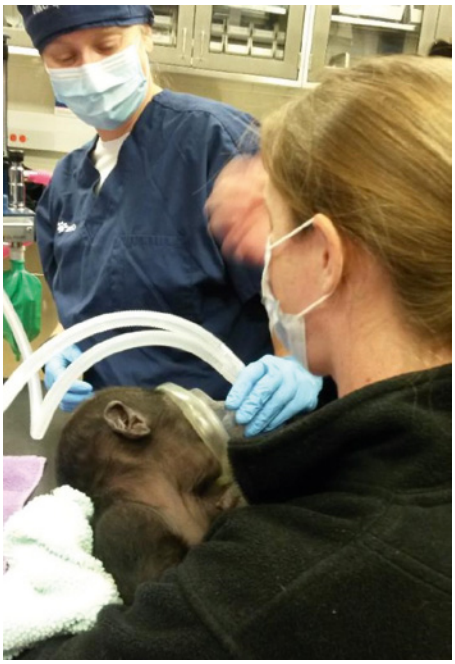


Figure 33.4 Facemask induction with sevoflurane of an infant western lowland gorilla after IM midazolam premedication.

maintenance of western lowland gorillas. Induction of an infant gorilla with sevoflurane after premedication with midazolam (0.15 mg/kg) IM has been described (Romanoski 2019) (Fig. 33.4).

Intravenous Anesthesia

Total intravenous anesthesia (TIVA) and partial intravenous anesthesia (PIVA) have the potential to improve hemodynamics and recovery times over conventional inhalant anesthesia. TIVA and PIVA protocols have been evaluated in gorillas, a bonobo, and an orangutan (Ferrell et al. 2017). Once induced, anesthesia was maintained with constant rate infusions of a single agent or combination of agents, including fentanyl 0.5–2.0 μg/kg/h, remifentanil 0.1–0.5 μg/kg/h, and propofol 20–150 μg/kg/h. PIVA protocols also included intubation with administration of isoflurane or sevoflurane in oxygen. TIVA protocols with ketamine or ketamine combination induction with maintenance of anesthesia by supplemental IV doses of ketamine have been reported but can result in prolonged recovery (Lewis 1993; Cole 2000; Chai et al. 2009). Ketamine infusion (50 μg/kg/min) and low-dose isoflurane between 0.2% and 1%, in a 1:1 air:oxygen mixture, was used to maintain anesthesia in a juvenile orangutan undergoing heart surgery (Greenberg et al. 1999). Postoperatively the patient was maintained on vecuronium (1–3 mg/kg/h), fentanyl (1–5 μg/kg/h), and midazolam (0.05–0.1 mg/kg/h) via constant rate infusion. Hendrix (2006) reported the use of thiopental (2.1 mg/kg IV) to allow intubation after anesthetic induction with IM ketamine (1 mg/kg) and midazolam (0.03 mg/kg) in an orangutan undergoing laparoscopic tubal ligation. After intubation, the animal was maintained on 1.5–2.25% isoflurane delivered in 100% oxygen at 1.5 L per minute via a rebreathing system. Use of propofol to maintain anesthesia has been reported in an orangutan at 50 mg/kg (total dose) IV in a drip, although this did not provide sufficient sedation (Kenny et al. 2003). Propofol has also been administered to an orangutan at 0.19 mg/kg/min IV in combination with intermittent supplemental boluses of ketamine (Hanley et al. 2006), as well as a gorilla (dose not reported; Raphael et al. 2001).

Neuromuscular Blocking Agents

Neuromuscular blocking agents (NMBAs) are frequently used in human anesthetic regimens, primarily to facilitate intubation and abdominal insufflation during laparoscopic surgical procedures. NMBAs are most commonly used in veterinary medicine to facilitate tracheal intubation, allow control of artificial respiration, and to facilitate surgical procedures (ophthalmic and orthopedic) in companion animals (Adams 2009). The nondepolarizing NMBA rocuronium bromide was used in two western lowland gorillas (one adult female and one infant male) to facilitate laparoscopic umbilical hernia and bilateral inguinal hernia repair, respectively (Romanoski 2019). In the adult female, a single dose of 0.6 mg/kg IV resulted in complete muscle paralysis, allowing sufficient abdominal insufflation to facilitate robot-assisted laparoscopic umbilical hernia repair. A train of four (TOF) monitor was utilized to confirm paralysis and monitor the patient throughout the surgery. In the infant, a dose of 0.3 mg/kg IV appeared to result in adequate paralysis, but spontaneous respirations returned within 15 minutes and two supplemental doses of 0.3 mg/kg were given at 15-minute intervals until the completion of the surgical procedure. A TOF monitor was not available for this procedure therefore complete paralysis in this case could not be confirmed. In both cases, rocuronium was reversed with Suggamadex sodium IV (2.4 mg/kg in the adult female and 2.0 mg/kg in the infant male). The NBMA vecuronium (0.1 mg/kg) IV has also been used to achieve neuromuscular blockade in a juvenile orangutan undergoing open-heart surgery (Greenberg et al. 1999). Reversal was achieved using neostigmine 1.0 mg IV at the conclusion of the procedure. It is important to remember that NMBA use will result in paralysis of the diaphragm and a means of providing artificial respiration for the patient must be available (Adams 2009).

Analgesia

Although there is little pharmacologic data available for great ape species, provision of analgesia is important for managing pain associated with a procedure, postoperative pain, or pain associated with a medical condition. Both human and veterinary drugs are used and dosages and frequency of administration are often empirical and based on human data. Acute pain can often be managed effectively using a combination of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and locoregional anesthesia, when possible (Boesch 2012). It is recommended to treat acute pain due to injury or surgery for at least 72 hours. Chronic pain is more difficult to manage and generally requires multimodal therapy, which may include opioids, NSAIDs, anticonvulsants (such as gabapentin), nutraceuticals, laser therapy, acupuncture, and local anesthesia (Boesch 2012). Respiratory depression with opioid use has been reported in humans (Taylor et al. 2005), as well as other nonhuman primates (Carpenter 1998; Liguori et al. 1996), so caution is warranted when administering these drugs to great apes. Administration of opioid antagonists may ameliorate these effects. Synthetic opioids are frequently administered in painful conditions in human medicine and may prove useful for great apes. Tramadol at 1 mg/kg PO twice daily given to a silverback western lowland gorilla appeared to have a mild sedative effect (S. Cerveny et al., unpubl. data). Meloxicam and ibuprofen are the most commonly prescribed NSAIDs in great apes (ZIMS 2020a–c). NSAIDs should be administered with caution if dehydration or renal disease is suspected. Some commonly prescribed analgesic drugs and dosages are listed in Table 33.2.

Monitoring

Careful and close anesthetic monitoring is warranted for great apes. A pulse oximeter probe can be placed on the tongue to monitor SpO_2 (Fig. 33.5). End-tidal CO_2 (capnography) can be obtained through an endotracheal tube or LMA. A cuff can be placed on a limb for indirect oscillometric blood pressure measurement. Eichberg and Shade (1987) documented significant increases in blood pressure with increasing age in chimpanzees. Hypertension in humans also increases with age, thought to be due to increasing stiffness of arteries. Cardiac disease increases with age in apes and gross heart lesions and pathologic changes in arterial vessels are suggestive of hypertension (Lowenstine et al. 2016). Although anesthetic drugs can affect blood pressure, as previously noted, it is important to monitor blood pressure during anesthesia, especially in patients with known cardiovascular disease.

Cardiac electrical activity (ECG) can be monitored with leads in standard placement. ECGs were evaluated in three chimpanzees receiving a premedication of 30 mg of diazepam and anesthetized with ketamine and xylazine (Erickson & Olsen 1985). Values were similar to previous studies of

Table 33.2 Dosage ranges of selected analgesic drugs used in captive great apes.

Drug	Bonobo	Chimpanzee	Gorilla	Orangutan
Acetylsalicylic acid PO		1.19–14.52 SID-BID	0.42–9.99 SID-BID	0.8–4.8 SID
Buprenorphine IM		0.002–0.03 once		0.002–0.02 once
Carprofen PO		0.02–4.00 SID-BID	0.91–4.0 SID-BID	
Celecoxib PO		2.31–5.41 SID	0.68–3.34 SID-BID	0.75–3.38 SID-BID
Fentanyl IV			0.01–0.02 once	
Flunixin IM		0.24–1.85 SID	0.52–1.36 once	
Gabapentin PO		0.02–23.87 SID-TID	1.32–5.4 SID-BID	2.22–11.7 BID
Ibuprofen PO	2.94–23.04 SID-TID	0.03–17.7 SID-TID	2.09–19.63 SID-TID	2.41–19.03 SID-TID
Ketoprofen PO, IM		0.46–3.13 SID	0.78–2.26 SID	0.52–4.9 SID
Meloxicam PO, IM, SC	0.08–0.22 SID	0.06–0.3 SID-BID	0.06–0.26 SID	0.07–0.33 SID
Morphine PO		0.13–0.15 TID		
Naproxen PO		3.11–6.0 SID	1.21–4.22 BID	1.52–6.56 BID
Paracetamol PO	6.27–21.31 BID	4.28–19.12 BID-TID	0.77–18.18 SID-QID	3.37–17.86 SID-TID
Tramadol PO	0.64–2.0 BID	0.35–2.69 SID-BID	0.21–2.17 SID-TID	0.09–3.17 SID-BID

BID, twice daily; IM, intramuscular; IV, intravenous; PO, per os; QID, four times daily; SC, subcutaneous; SID, once daily; TID, three times daily. Dosages listed as compiled ranges for each species in mg/kg.



Figure 33.5 Western lowland gorilla under anesthesia with monitoring equipment in place. Note pulse oximeter probe placement on the tongue, side-stream capnography, and blood pressure cuff placement on the lower left hindlimb.

unanesthetized chimpanzees, although QT and PR intervals were slightly longer due to a lower heart rate in anesthetized chimpanzees. A retrospective study of ECGs from chimpanzees anesthetized with tiletamine-zolazepam found ventricular premature contractions to be the most commonly detected arrhythmia (Doane et al. 2006). Other arrhythmias included atrial premature contractions, second-degree AV block, right bundle branch block, trigeminy, and accelerated idioventricular rhythm. A significantly higher incidence of arrhythmias was found in males, animals with structural heart disease, and animals between 20 and 39 years as compared with those younger than 20 or older than 39.

Frequent analysis of arterial blood gases can also be very useful. Hendrix (2006) reports the use of the dorsal pedal artery as a site for direct blood pressure measurement and blood-gas sampling in an orangutan. Arterial blood gas can also be sampled from the tibial or femoral arteries. Reference intervals for blood gas analysis are summarized in Table 33.3.

Anesthetic Recovery

As noted previously, once reversed, recovery can be quite sudden. Consequently, except for emergency situations, these agents should only be administered once the animal is safely secured. The immobilized animal should be allowed to recover in isolation to prevent attack from other members of the group. If the procedure has lasted for only a few hours, then return to the group should be uneventful. If an animal must be separated for longer periods, then behavioral problems may ensue with reintroduction (Fowler 2008).

Maintenance of airways is critically important in animals in the recovery phase. Excessive ventroflexion of the head can lead to airway occlusion and hypoventilation, especially in large male gorillas and orangutans, and individuals that are overweight. Animals should be recovered in lateral recumbency with the down arm extended cranially supporting the head in an extended position (Fig. 33.6). Extubation should occur as far into recovery as possible while maintaining staff safety (Murphy 2015).

Complications

A retrospective study of anesthetized great apes in the United Kingdom and Ireland found a 30-fold risk of perianesthetic mortality in animals over 30 years of age when compared with animals between 10 and 30 years (Masters

Table 33.3 Selected blood gas reference intervals for great apes (ZIMS 2020a–c).

Blood Gas Value	Chimpanzee	Gorilla	Bornean Orangutan	Sumatran Orangutan
Oxygen partial pressure – arterial (mmHg)	301 (56–547)[a]	228 (32–570)[a]		
Oxygen partial pressure – venous (mmHg)	193 (22–413)[a]	150 (39–309)[b]		
Oxygen saturation (%)	100 (100–100)[b]	99 (92–100)[b]	93 (60–100)[a]	98 (87–100)[a]
Partial pressure carbon dioxide (mmHg)	50 (29–67)[b]	45 (28–72)[b]	47 (31–75)[a]	47 (32–63)[b]
Bicarbonate (mEq/L)	31.9 (24.0–41.1)[b]	30.2 (22.2–40.3)[b]	30.2 (19.5–37.0)[b]	28.2 (21.5–34.0)[b]
pH – arterial	7.4 (7.3–7.6)[b]	7.4 (7.2–7.5)[b]		7.4 (7.1–7.6)[a]
pH – venous	7.4 (7.3–7.6)[a]	7.4 (7.2–7.6)[b]	7.4 (7.2–7.6)[b]	
Base excess – arterial (mEq/L)	8.6 (−5.3–17.8)[b]	3.6 (−5.1–13.1)[b]	6.0 (06.0–13.0)[a]	3.6 (−2.0–9.0)[a]
Base excess – venous (mEq/L)	6.8 (−0.9–12.0)[a]	5.0 (−1.0–17.0)[a]		

[a] Mean (lowest–highest value).
[b] Mean (reference interval).



Figure 33.6 A Sumatran orangutan recovering from anesthesia. Note the right forelimb is extended forward under the head to help keep the neck extended preventing airway occlusion. The endotracheal tube should be left in place as long as possible for airway support.

et al. 2007). Animals that were preanesthetically assessed as sick were associated with a 26 times greater risk. Overall, perianesthetic mortality risk was 1.35% when cases of euthanasia were excluded from the data, with 80% of deaths occurring in the postanesthetic period.

Cardiovascular diseases are a significant cause of morbidity in captive great apes. Fibrosing cardiomyopathy and aortic dissection are particularly common in older male gorillas (Lowenstine et al. 2016). Unexpected death due to cardiovascular causes was reported in 13 chimpanzees at a captive facility, with systemic hypertension reported in two of the animals (Lammey et al. 2008). Cardiac dysrhythmia was speculated as the cause of death, as all of the animals had exhibited antemortem cardiac arrhythmias. Other cardiac conditions include, for example, idiopathic cardiomyopathy (Seiler et al. 2009), congestive heart failure, and coronary atherosclerosis (Loomis 2003). All of these conditions could complicate anesthesia or result in anesthetic death. Older apes, as well as animals with a history of cardiovascular disease, should be carefully evaluated prior to anesthesia and carefully monitored during the procedure. Consultation with human anesthesiologists experienced with these medical conditions in human patients may be beneficial.

In a retrospective study of 226 great ape chemical restraint procedures at the San Diego Zoo, difficulty with airway maintenance was the primary reported complication (Robinson & Lambert 1986). Excessive salivation and upper airway obstruction caused by pharyngeal tissue were reported. Laryngeal air-sac infections due to bacteria or yeast have been described frequently in great ape species (Hastings 1991; Hill et al. 2001; Lawson et al. 2006). Laryngeal air sacculitis could complicate general anesthesia due to the risk for fatal pneumonia from the aspiration of purulent material. Apes with air sacculitis should be intubated with cuffed endotracheal tubes, and the condition should be treated prior to any elective anesthesia.

Fatal acute respiratory distress syndrome due to negative pressure pulmonary edema was reported in an orangutan under tiletamine-zolazepam-induced anesthesia (Kenny et al. 2003). The authors speculated that an acute upper airway obstruction was the precipitating factor. During early anesthetic induction, this orangutan was noted to be slumped forward, with the head flexed toward the chest. The propensity of orangutans for laryngospasm during anesthesia as well as the pharyngeal anatomy of this species may predispose these animals to this syndrome during anesthesia. Obesity and respiratory disease could also create further complications for respiratory function during anesthesia. Kenny et al. (2003) recommended that orangutans should be properly positioned with a patent airway during anesthetic induction, as well as the use of thick-walled, armored, or reinforced endotracheal tubes with a stylet to facilitate rapid intubation.

Field Anesthesia

There is increasing conservation management of in situ great ape populations, which has resulted in the development of field anesthesia techniques for free-living great apes for the purposes of translocation, reintroduction into the wild, and clinical interventions. Anesthesia of great apes under field conditions is inherently riskier for the animals and humans conducting the procedure due to more variables and less control over the animal. Field anesthesia techniques generally rely on injectable anesthetic agents alone due to the challenges of taking equipment into the field. Incremental injections given to prolong anesthesia may significantly increase recovery times, resulting in danger to the animal. Inhalation agents can be used to deepen or prolong anesthesia without significantly prolonging recovery time. Lewis (2004) described a compact, lightweight, modified vaporizer that can deliver inhalant anesthetic in air during field immobilizations. The unit has been utilized in field immobilizations of a chimpanzee, western lowland gorilla, and orangutan with good results. Since the unit uses air to deliver the anesthetic gas instead of oxygen, hypoxia is a potential concern, therefore it is recommended to monitor oxygen saturation via pulse oximetry, especially at high altitudes.

Sleeman et al. (2000) summarized the field anesthesia of 24 free-living human-habituated mountain gorillas

(*Gorilla beringei beringei*) using either ketamine (dosage 7 mg/kg) or tiletamine-zolazepam (dose range 90–325 mg) delivered by remote injection. Anesthesia was mostly performed to facilitate medical treatment. The induction time for both agents was approximately 5 minutes, and recovery was significantly shorter for ketamine (mean 42 minutes) compared with tiletamine-zolazepam (mean 75 minutes). The authors concluded that anesthesia could be safely performed, even among a large group of gorillas, although the procedures frequently required the entire day. The success of the procedures was dependent on the assistance of local field staff, who had extensive knowledge of gorilla behavior as well as the landscape. Other key factors included darting the animals without warning, keeping the other gorillas away from the anesthetized animal by creating a visual barrier, remaining with the gorilla until it was fully recovered and able to rejoin its group, and reassuring the patient during recovery by grooming the animal and mimicking gorilla vocalizations. Neither drug appeared to produce novel physiologic effects, although some gorillas had low SpO_2 values (range 86–88%). The authors reported that the relatively high altitude at which the procedures were performed may have contributed to the apparent hypoxemia, and consequently recommended providing supplemental oxygen (Fig. 33.7).

Habitat destruction and fragmentation result in scattered and isolated populations of orangutans, and translocation of isolated individuals to protected habitat is an important, albeit somewhat controversial, conservation strategy (Andau et al. 1994; Kilbourn et al. 1997, 2003). The use of various anesthetic protocols to assist with orangutan translocations have been described, including tiletamine-zolazepam (3–6.9 mg/kg; Andau et al. 1994; Kilbourn et al. 1997, 2003) combined with ketamine (5–7 mg/kg) and xylazine (1–1.4 mg/kg) (Andau et al. 1994; Kilbourn et al. 1997, 2003), as well as medetomidine (0.018–0.025 mg/kg) combined with tiletamine-zolazepam (0.8–2.3 mg/kg) (Fahlman et al. 1999, 2006). Kilbourn et al. (1997) recommended tiletamine-zolazepam due to shorter induction times and smaller dart volume. However, Andau et al. (1994) advised the use of ketamine/xylazine, where rapid recovery is desired due to the availability of the xylazine reversal agent, yohimbine hydrochloride. The induction time for both tiletamine-zolazepam and ketamine/xylazine was 4.38 minutes, but if additional doses were required then induction time increased to 15.67 minutes (Andau et al. 1994). Recovery times were around 42 minutes for ketamine/xylazine and slightly longer for tiletamine-zolazepam.

In typical translocation operations, the orangutan was darted approximately 15 m up a tree. Both Telinject and Distinject™ systems were used along with 1- or 3-mL plastic or metal darts with 19- to 20-mm needles with retaining collars. The animals were allowed to fall naturally to the ground (the tangle of vines providing natural cushioning) or nets were used to catch the animal. Andau et al. (1994) reported no mechanical injuries from the capture, handling, and transport of animals, although the authors cautioned against darting animals at a height of over 30 m. Two fatalities were recorded. One was due to hyperthermia as a result of an immobilized animal remaining high in the nest fully exposed to the sun, and the other was a nursing infant that accidentally received the dart intended for its mother. The authors concluded that both tiletamine-zolazepam and ketamine/xylazine provided satisfactory immobilization to facilitate the capture and translocation of orangutans, although the need to provide additional



Figure 33.7 (a) Dr. Eddy Kambale Syaluha, Gorilla Doctors head veterinarian in DR Congo, removes a snare from infant mountain gorilla in Virunga National Park, 2017. (b) Dr. Fred Nizeyimana, Gorilla Doctors field veterinarian in Uganda, removes a snare from adult female mountain gorilla in Bwindi Impenetrable National Park, 2019. © Gorilla Doctors, printed with permission.

doses of drug in several animals suggested that a somewhat higher initial dose may be appropriate.

Medetomidine/tiletamine-zolazepam combination delivered intramuscularly to semicaptive or free-ranging orangutans provided rapid smooth induction, with recumbency within 1–7 minutes (Fahlman et al. 1999, 2006). It was considered favorable for remote drug delivery to free-ranging orangutans when compared with tiletamine-zolazepam alone due to low drug volume and more controlled descent from the trees. This combination resulted in the animals being able to grip branches during the descent down the tree, making the fall more gradual, with less risk for injury. This is in contrast with tiletamine-zolazepam alone, with which the animals rapidly became immobilized and fell unconscious from the tree. Adequate anesthetic depth with good muscle relaxation was also reported. Heart and respiratory rates and hemoglobin oxygen saturation remained stable, although occasional SpO_2 measurements were below 90% and significant declines in systolic blood pressure (below 80 mmHg in some cases) and body temperature were recorded. The authors recommended using IV fluids and oxygen supplementation to prevent these side effects. One orangutan developed hyperthermia and apnea during translocation, but was successfully resuscitated. The authors reported that additional doses of tiletamine-zolazepam were required during the orangutan translocations, and recommended further studies to determine optimal dosages in free-ranging orangutans. Atipamezole was administered intramuscularly at five times the dosage of medetomidine 23–54 minutes after injection of medetomidine/tiletamine-zolazepam or the last additional dose of tiletamine-zolazepam. First signs of recovery from anesthesia were noted on average approximately 10 minutes (range 3–27 minutes) after reversal. The recoveries were reported to be smooth and calm.

Returning confiscated and orphaned chimpanzees to native habitat is also an increasingly considered as well as controversial conservation strategy. Tutin et al. (2001) described the successful release of 20 wild-born chimpanzees, and the use of anesthesia to facilitate pre-release health examinations and transportation of the animals to the release site. Field immobilizations of chimpanzees have been described for health interventions in Uganda and Tanzania. Hyeroba et al. (2013) conducted field immobilizations of nine chimpanzees in Uganda with ketamine (4.74 mg/kg average dose) and medetomidine (0.04 mg/kg average dose) delivered by dart. In all cases medetomidine was reversed with atipamezole (0.21 mg/kg) IM. The authors report that induction was rapid and recovery smooth with no complications. Lonsdorf et al. (2014) reported immobilization of a habituated, wild chimpanzee in Gombe National Park. The severely ill adult male was induced with ketamine 250 mg (total dose) by hand injection. The animal recovered uneventfully after 1 hour.

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34

Canids

R. Scott Larsen and Anneke Moresco

Body Weight of Canids

The 36 species of nondomestic canids currently recognized by the International Union for Conservation of Nature Canid Specialist Group (https://www.iucnredlist.org/) are listed in Table 34.1.

Physical Restraint

Canids are strong, fast, and agile. Their teeth are large and sharp, their jaw muscles are strong, and most canids can bite through heavy leather gloves. Protective gloves may be worn to handle canids, not necessarily to protect the handler from bite injuries but to protect against scratches from the nails; however, gloves may restrict hand agility and decrease grip control, so some handlers prefer not to use gloves (Fig. 34.1).

Many noninvasive procedures can be performed without anesthesia in smaller species such as foxes (Brash 2003). Canids can be caught and temporarily restrained in large fishing nets, but substantial proficiency is needed to safely restrain large canids in this way (Fig. 34.2). Once in the net, animals can be pinned behind the head using a soft broom, forked stick, net, or catch pole. Canids should be pinned while injections are administered (Kreeger 1992). A towel or cloth should be placed over the eyes to decrease visual stimulation, calm the animal, decrease stress, and speed induction for chemical immobilization.

Small-to-medium-sized canids can be restrained from behind and held by the scruff (Brash 2003) or by holding around the neck, with the fingers closing underneath the jaws, taking care not to press or damage the trachea. At the same time that the neck is secured, the body is pushed firmly and gently against the ground by the handler or an assistant. Once in hand, a muzzle can be applied using a small rope, gauze bandage, or tape. Caution must be used with muzzles because they impair the animal's ability to pant and thus may hamper thermoregulation. If an animal appears overheated or distressed, the muzzle may need to be removed.

Drug Delivery Methods

Most canids are fast, elusive, and cunning, making them challenging to successfully immobilize if uncontained. Free-ranging canids are typically trapped before drugs are administered (Kreeger 1992), although field-darting occurs in some cases. Jackals have extremely fast reaction times to sound and can move out of the path of slow-moving darts (McKenzie & Burroughs 1993).

Injectable anesthetic drugs are most commonly administered intramuscularly by hand injection, pole syringe, or dart. Hand injection during physical restraint should be performed in smaller species to avoid errant needle placement and unnecessary tissue trauma. Larger canids can be safely darted with a blowpipe or dart gun.

Appropriately sized squeeze chutes can be used for any canid as long as the animal cannot get its mouth or legs through the spaces in the chute. Many canids in zoos can be trained to walk into a chute or to take voluntary injections.

Box traps, padded-jaw traps, or offset-jawed foothold traps are often used for initial containment of free-ranging canids. Although coyotes do not usually fight a trap for long (Kreeger 1992), other canids may fight against the trap frantically (especially when approached by humans) and may pull out of the trap and/or potentially severely injure themselves. Leg fractures may occur when steel-jawed traps are used to capture red foxes, but are not common (Kreeger et al. 1990a). Box traps may be used on naïve fox populations, but are ineffective on many red foxes. Leg snares may be useful for this species (Jessup 1982). Small leg snares will also capture coyotes and other canids.

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Table 34.1 Body weights of canids.

			Adult Body Weight (kg)		
Genus	**Species**	**Common Name**	**Female**	**Male**	**Combined**
Canis	*adustus*	Side-striped jackal	7–10	7–12	
Canis	*aureus*	Golden jackal	6.5–7.8	7.6–9.8	
Canis	*latrans*	Coyote	7.7–15	7.8–15	
Canis	*lupaster*	African wolf	7.4–8.8	8.4–9.6	
Canis	*lupus*	Gray wolf			23–60[a]
Canis	*mesomelas*	Black-backed jackal	6–10	6–12	
Canis	*rufus*	Red wolf	20–30	22–34	
Canis	*simiensis*	Ethiopian wolf	11–14	14–19	
Cerdocyon	*thous*	Crab-eating fox			4.5–8.5
Chrysocyon	*brachyurus*	Maned wolf			21–30
Cuon	*alpinus*	Dhole	10–13	15–20	
Lycaon	*pictus*	African hunting dog	19–27	25–35	
Nyctereutes	*procyonoides*	Raccoon dog	3–13	3–12	
Otocyon	*megalotis*	Bat-eared fox	3.2–5.4	3.4–4.9	
Pseudalopex	*culpaeus*	Culpeo (Andean fox)	4–10	3.4–14	
Pseudalopex	*fulvipes*	Darwin's fox	1.8–3.7	1.9–4.0	
Pseudalopex	*griseus*	Chilla	2.5–5	3.1–4.9	
Pseudalopex	*gymnocercus*	Pampas fox	3.0–5.7	4.0–8.0	
Pseudalopex	*sechurae*	Sechuran fox			2.6–4.2
Pseudalopex	*vetulus*	Hoary fox	3.0–3.6	2.5–4.0	
Speothos	*venaticus*	Bush dog			5–8
Urocyon	*cinereoargenteus*	Gray fox	2.0–3.9	3.4–5.5	
Urocyon	*littoralis*	Island gray fox	1.3–2.4	1.4–2.5	
Vulpes	*bengalensis*	Indian fox	>1.8	2.7–3.2	
Vulpes	*cana*	Blanfords fox	0.8–1.5	0.8–1.4	
Vulpes	*chama*	Cape fox	2.0–4.0	2.0–4.2	
Vulpes	*corsac*	Corsac fox	1.9–2.4	1.6–3.2	
Vulpes	*ferrilata*	Tibetan sand fox	3.0–4.1	3.8–4.6	
Vulpes	*Lagopus*	Arctic fox	2.4–4.8	2.7–5.1	
Vulpes	*macrotis*	Kit fox	1.6–2.2	1.7–2.7	
Vulpes	*pallida*	Pale fox			2.0–3.6
Vulpes	*rueppelli*	Sand fox	1.1–1.8	1.1–2.3	
Vulpes	*velox*	Swift fox	1.6–2.3	2.0–2.5	
Vulpes	*vulpes*	Red fox	3.6–6.5	4.4–7.6	
Vulpes	*zerda*	Fennec fox	1.0–1.9	1.3–1.7	

[a] Data from Kreeger et al. (2023).
Data from Gutema et al. (2018).
All other data from information compiled in Sillero-Zubiri et al. (2004).

Leg snares are more likely to result in compromise of blood supply and edema of the paw, but are less likely than jawed traps to cause crushing, contusions, lacerations, or fractures. In colder climates, snares may result in frostbite-type lesions and should not be used. Always check for trap injuries when such means of capture are employed. A restraint pole and double leather gloves can be used to remove animals from traps (Jessup 1982).



Figure 34.1 A weakened wild coyote pup can be held by placing hands behind the head and by the mandible to prevent its ability to open its mouth and bite. Photo credit: A. Moresco.



Figure 34.2 Ideally a variety of sizes of nets are available for net capture in the smaller canids.

Animals in traps are sometimes administered oral medication through "tranquilizer tabs" (Balser 1965). The device is attached to the jaw of the trap and the tablet is ingested when the animal bites at the trap, resulting in sedation. Such sedation may decrease the chance of the animal injuring itself, but is insufficient for handling (Jessup 1982). This technique was originally described in coyotes using high doses of powder-form diazepam (48–96 mg/kg) wrapped in semirotten cloth; ataxia often lasted 18–36 hours and sedation could last days (Balser 1965). Some deaths were reported using this technique, but it is unknown what effect the drug has had on mortality as compared with other factors (Balser 1965). Modifications to these "tranquilizer tabs" have since been made; one device includes a balloon with 3 mL of petroleum jelly, covered by two layers of gauze (Jessup 1982). If the trap may get wet, the tabs can be sealed by dipping them repeatedly in a melted mixture of 25% refined beeswax and 25% paraffin wax (Balser 1965). Tablets of diazepam (6–7 mg/kg), midazolam (3–4 mg/kg), or acepromazine (5 mg/kg) have been used. When using tablets, doses are relatively high because of the likely loss of drug during chewing (Jessup 1982), but these doses may result in long recovery if completely ingested. More recently, propiomazine has been used, to good effect, in gray wolves (Sahr & Knowlton 2000). Gray wolves in traps with propiomazine had less trap-associated trauma on their legs than those that received no tranquilizers; no mortality was associated with use of this drug, even when doses of 1000 mg were consumed by wolf pups or smaller nontarget species (Sahr & Knowlton 2000).

Gray wolves can be relatively safely pursued and darted from helicopters because they are large and inhabit areas with open country. For this type of procedure, a pilot and a shooter are typically needed. Rapid projectile dart rifles are needed to insure accurate dart placement. Complications of helicopter darting may include pneumothorax secondary to inadvertent thoracic dart placement (Kreeger et al. 1995), hyperthermia, or overexertion. Coyotes have also been effectively captured in this manner (Baer et al. 1978), as well as with helicopter-launched net guns, although the impact of the net may cause mortality (Gese et al. 1987).

African painted dogs can be darted from a vehicle at a range of 15–30 m (van Heerden 1993) and should be darted in the upper hind leg. Wild dogs can also be captured by using a helicopter to chase a pack into a funnel-shaped boma. Jackals have occasionally been darted from vehicles to which they have been habituated, but trapping is a much more practical method of capturing these animals (McKenzie & Burroughs 1993). Small animals such as foxes will not normally approach to within darting distances. These animals have small muscle masses and damage to vital organs is likely, even with light darts (McKenzie & Burroughs 1993). Bat-eared foxes may retreat into burrows if darted; they also have a bushy coat that makes accurate dart placement difficult, so darting is not recommended (McKenzie & Burroughs 1993). In some cases, capture collars (Wildlink Capture Collar, Advanced Telemetry Systems, Isanti, Minnesota 55040, USA) have been used to facilitate immobilization through the automated injection of drugs using a remote signal (Federoff 2001).

Vascular Access

Arterial and venous access sites are comparable with those of domestic dogs. If medetomidine or dexmedtomidine are used, venipuncture and catheterization should be done as soon as possible after induction because alpha-2 agonists often cause vasoconstriction and may predispose to vasospasm, particularly when more than 20 minutes have elapsed since injection. Typical sites for phlebotomy are the jugular, cephalic (brachial), and lateral saphenous veins. Venous catheters are typically placed in the cephalic or saphenous veins. For blood gas analysis, arterial samples are readily obtained from the femoral artery (Larsen et al. 2002).

Endotracheal Intubation

Intubation of the anesthetized canid is not always essential, but should be performed during prolonged procedures (especially if inhalant anesthetics are used), if animals are hypoxemic, if they are hypoventilating, or if they have preexisting health conditions. Intubation is as described for domestic dogs. Endotracheal sizes increase in proportion to the size of the animals: 3–4 mm for adult fennec foxes, 5–6 mm for adult red foxes (Bertelsen & Villadsen 2009), 9–10 mm for adult red wolves (Sladky et al. 2000), and 10–12 mm for adult gray wolves.

Sedation/Tranquilization Techniques

Dissociative Agents

The dissociative anesthetic ketamine is a mainstay of canid anesthesia. Tiletamine is also used commonly, but this drug is only available in combination with zolazepam (in Telazol® or Zoletil®) and recoveries are typically long. Ketamine has been used alone to immobilize African painted dogs, gray wolves, coyotes, red foxes, gray foxes, and kit foxes (Ebedes & Grobler 1979; Jessup 1982; Kreeger & Seal 1986a). Induction times are rapid (3–6 minutes), but immobilization times are short (18–22 minutes) relative to recovery times (50–90 minutes) (Kreeger & Seal 1986a). Only light anesthesia is typically achieved, but heart rate and respiratory rate are stable (Ebedes & Grobler 1979). Increasing doses do not decrease induction times or substantially increase immobilization times, but recoveries are longer (Jessup 1982).

If used alone, dissociative agents induce rough inductions and recoveries, hyperthermia, skeletal muscle hypertonicity, muscle spasms, uncontrolled head movements, ptyalism, and convulsions (Jessup 1982; Kreeger 1992) so they are typically combined with alpha-2 agonists, benzodiazepines, and/or opioids. Dissociatives cannot be antagonized; if they are given with other agents that can be antagonized, the antagonists should be administered after most of the dissociative has been metabolized. Early reversal may result in convulsions, tremors, hyperthermia, or rough recoveries due to residual ketamine. A 45-minute wait generally appears adequate.

Alpha-2 Adrenoceptor Agonists

Alpha-2 agonists, including xylazine, medetomidine, and dexmedetomidine, are potent, reversible sedatives that are commonly used to smooth induction and recovery, while also improving muscle relaxation. Alone, alpha-2 agonists can heavily sedate canids to the point of relatively safe handling, but these animals may also be aroused with stimulation and can be capable of directed attack. For these reasons, it is usually preferable to combine an alpha-2 agonist with at least one other drug.

Xylazine

Xylazine has been used alone in wolves, coyotes, red foxes, gray foxes, and kit foxes (Jessup 1982; Philo 1978), but is only suitable for short, nonstimulatory procedures. Initial effects occur in 2–3 minutes, animals are sternal in 4–10 minutes, and maximal effect is in 15 minutes (Philo 1978). Induction is no quicker with higher doses, but respiration is more depressed (Philo 1978). Vomiting and low heart rates are common (Jessup 1982; Philo 1978). Animals can be approached and safely handled if there are no loud noises and contact with the animal is not abrupt (Kreeger et al. 1988). Xylazine sedation typically lasts 30–60 minutes, but complete recovery takes 2–3 hours without reversal (Kreeger et al. 1988; Philo 1978). Recovery typically occurs 4–6 minutes after intravenous (IV) administration of yohimbine (Kreeger et al. 1988).

Medetomidine

Medetomidine is more potent and specific than xylazine; high doses can effect complete immobilization in relatively calm canids. Complete immobilization was achieved in farmed Arctic foxes using 0.1 mg/kg medetomidine (Jalanka 1990); similarly, calm, habituated gray wolves have been induced with 0.05 mg/kg (Kreeger et al. 1996). Medetomidine alone has even been effective in field settings with coyotes (0.12 mg/kg) and red foxes (0.14 mg/kg) (Baldwin et al. 2008), although it should be noted that only noninvasive and minimally stimulating procedures could be accomplished. At high doses of medetomidine, there is better muscle relaxation and less chance of spontaneous

recovery, but oxygenation may be poor (as low as 74% blood oxygen saturation), respiration may be impaired, and mucous membranes may be cyanotic (Kreeger et al. 1996). Second-degree atrioventricular heart blocks are common with the use of medetomidine and occur with increased frequency at higher doses. Atropine has been administered to relieve bradycardia; although the anticholinergic drug may double the heart rate, oxygen saturation does not necessarily improve. Without administration of reversal agents, immobilization with medetomidine lasts about 60 minutes (Kreeger et al. 1996). Recoveries are quick (2–5 minutes) with the administration of atipamezole (0.25 mg/kg IV) and are slower if yohimbine (0.2 mg/kg IV) is used (Kreeger et al. 1996). Although some sources advocate IV administration of atipamezole, we do not. IV atipamezole appears to effect extremely rapid changes in cardiovascular parameters, with potentially deleterious consequences; such changes are not as rapid with intramuscular (IM) atipamezole or IV yohimbine (Ambrisko & Hikasa 2003). Intramuscular administration also provides personnel with a few additional moments to safely leave the recovery area.

Dexmedetomidine

Medetomidine is composed of equal parts of the optical entantiomers dexmedetomidine and levomedetomidine. Most of the pharmacologic effects of medetomidine are considered to be due to the dexmedetomidine enantiomer. Dexmedetomidine has become widely available as a significantly more potent alternative to medetomidine, with more selective alpha-2 agonist effects. Reports often describe that dexmedetomidine should be used at about 50% of the dosage of medetomidine; however, in clinical experience, it may be more appropriate to use 30–50%. There are a few descriptions of the use of dexmedetomidine in nondomestic canids, with similar immobilization protocols and results to those using medetomidine (Feng et al. 2015; Gutema et al. 2018; Lescano et al. 2018). However, we do not know of any controlled studies comparing the two drugs directly.

Phenothiazine Derivatives

The phenothiazine derivative acepromazine is a tranquilizer that is occasionally used alone orally to calm canids that are trapped (5 mg/kg; McKenzie 1993). Since acepromazine interferes with thermoregulation, it should not be used if ambient temperatures are high or low; if used, traps must be checked frequently. Acepromazine is not effective alone as an immobilizing agent, but has occasionally been used successfully for South American canids in combination with ketamine (Pessutti et al. 2001).

Opioids

Some opioids can be useful in combination with other drugs for sedation, immobilization, and anesthesia. Butorphanol is used most often as it has relatively mild respiratory effects and is readily absorbed via IM injection. By itself, butorphanol has produced "apathetic sedation" in wolves (Kreeger 1992). Anesthesia can be achieved when butorphanol is combined with an alpha-2 agonist, but these combinations work best on calm, captive animals and are not potent enough to anesthetize free-ranging or otherwise highly excited canids (Kreeger 1992).

Ultrapotent opioids (etorphine, carfentanil, sufentanil) have been used historically in large canids, but the human and animal hazards of these drugs, along with the availability of safer options, make it unlikely that they would be used for canids today (Kreeger & Seal 1990).

Benzodiazepines

Benzodiazepines, such as diazepam, midazolam, and zolazepam, are useful sedatives for facilitating muscle relaxation and preventing convulsions, particularly in combination with dissociative agents. Both diazepam and midazolam have been used with ketamine; zolazepam is sold as a combination with tiletamine (Telazol®). Benzodiazepines are reversible with flumazenil; however, benzodiazepine reversal is probably not necessary in most situations because benzodiazepines have minimal adverse cardiorespiratory effects and residual sedation is the most commonly observed occurrence post immobilization. Flumazenil administration may be warranted in animals that are going through cardiorespiratory decompensation or when animals are to be immediately released into the wild after immobilization.

Ketamine-Xylazine

Ketamine-xylazine combinations were the standard protocols used for many canid species for several years, and still are used in countries where medetomidine and dexmedetomidine are not readily available. Large canids generally need smaller doses (mg/kg) of ketamine than small canids, but doses for xylazine tended to remain constant for different body weights. Some have advocated administration of xylazine 10 minutes prior to administration of ketamine (Cornely 1979), but this is impractical in the field setting and it is our experience that temporal separation of the drugs is not needed and may even lead to unnecessary excitation. Lower doses of ketamine with higher doses of xylazine result in quicker recoveries by taking advantage of alpha-2 antagonist sedation while minimizing the amount

of ketamine that persists. With lower doses of ketamine, quick recoveries often occur even without reversal (Kreeger & Seal 1986b). In coyotes, if the dose of ketamine is decreased from 4 to 2 mg/kg, the recovery time is shortened from 2–3 hours to <60 minutes (Kreeger & Seal 1986b).

Induction with ketamine-xylazine is variable, occurring in 2–20 minutes; faster inductions occur when using relatively high doses of ketamine and relatively low doses of xylazine. Working times are typically 20–40 minutes and complete recovery occurs in 1–2 hours (Cornely 1979; Kreeger & Seal 1986b). Heart rate may be either slowed or elevated: tachycardia is seen with high doses of ketamine and bradycardia is seen with high doses of xylazine (Kreeger & Seal 1986b). Premature ventricular contractions may occur occasionally, but do not typically cause clinical problems (Kreeger & Seal 1986b). These arrhythmias are less common if atropine is administered (Fuller & Kuehn 1983), but severe sustained hypertension is also more common (Kreeger & Seal 1986b). Since atropine may exacerbate hypertension without improving oxygenation, its use is usually contraindicated. Oxygenation with ketamine-xylazine is typically stable, but may be lower than desired (83–94%; Osofsky et al. 1996). Respiratory rate is often elevated (Sladky et al. 2000). Canids immobilized with ketamine-xylazine have poor thermoregulatory ability and hyperthermia is frequently observed (Fuller & Kuehn 1983), although temperatures tend to decrease over the course of the immobilization (Fuglei et al. 2002; Sladky et al. 2000).

The xylazine component can be antagonized with yohimbine (0.1–0.2 mg/kg), tolazoline (8 mg/kg) (Kreeger et al. 1986, 1990b) or atipamezole. With yohimbine, arousal occurs in 1–8 minutes, sternal recumbency in 5–6 minutes, and uncoordinated ambulation in 10–25 minutes (Kreeger & Seal 1986b). Doses of yohimbine higher than 0.2 mg/kg do not improve or hasten reversal, but instead cause ataxia, tachycardia, and hypersalivation (Kreeger et al. 1990b). Yohimbine may be given IV, IM, or a percentage by both routes (Osofsky et al. 1996). Some immobilization-associated deaths have been reported with ketamine-xylazine, but the reasons for these deaths were not clear (Fuller & Kuehn 1983).

Ketamine-Medetomidine

Clinicians have largely switched from using ketamine-xylazine to ketamine-medetomidine. Much is similar about the two protocols; however, medetomidine is more potent and specific than xylazine, so lower doses of ketamine are effective and reversal with atipamezole is quicker and more complete. For canids, in our experience, slightly higher doses of ketamine (4–6 mg/kg) can be safely combined with lower doses of medetomidine (0.02–0.04 mg/kg) to provide effective immobilization with fewer adverse cardiopulmonary effects.

Animals are typically ataxic in 1–5 minutes, recumbent in 5–10 minutes, and induced in 10–15 minutes. Inductions may be much faster in captive animals that are accustomed to handling than in less acclimated individuals (Fuglei et al. 2002; Jalanka 1990). Animals should be kept as calm as possible during induction to avoid excitement and overriding the effects of the alpha-2 agonist. Vomiting occasionally occurs (Arnemo et al. 2013, 1993; Fuglei et al. 2002; Holz et al. 1994), particularly if animals have not been fasted. Animals that are acclimated to handling and people may have stable body temperatures, but hyperthermia is common and temperatures tend to decrease over time (Arnemo et al. 2013, 1993; Jalanka 1990; Sladky et al. 2000). Decline in body temperature may be substantial in raccoon dogs that are anesthetized during the winter when they hibernate; this decrease may critically affect their metabolism and will affect recovery, so special care to body temperature should be paid in this species (Arnemo et al. 1993).

Heart rate may increase or decrease over time in canids (Aguirre et al. 2000; Arnemo et al. 1993; Fuglei et al. 2002; Sladky et al. 2000). Heart rate is increased by atropine administration (Holz et al. 1994), but use of this drug is not typically warranted for the reasons described for ketamine-xylazine. Oxygenation is typically stable but may be somewhat low. Arctic fox pups anesthetized with ketamine-medetomidine had SpO_2 values of 78–95% (Aguirre et al. 2000), while mean values were 92–94% in red wolves (Sladky et al. 2000). Respiratory rate tends to increase over time (Aguirre et al. 2000; Jalanka 1990; Sladky et al. 2000). Raccoon dogs anesthetized with ketamine (5 mg/kg) and medetomidine (0.1 mg/kg) exhibited intermittent apnea and tachypnea, but breathing became more regular as time went on (Arnemo et al. 1993); these respiratory effects may have been due to the relatively high dose of medetomidine that was used.

Ketamine-medetomidine immobilization typically lasts approximately 60 minutes after initial injection, although individual animals may rouse more quickly (Jalanka 1990) and some animals do not regain corneal or pedal reflexes until >120 minutes (Arnemo et al. 1993). Recovery is usually rapid, with animals standing 5–20 minutes post antagonist and fully recovered 10–35 minutes post antagonist (Aguirre et al. 2000; Arnemo et al. 1993; Jalanka 1990). Without antagonist agents, complete recovery occurs in about 3 hours (Arnemo et al. 1993). Medetomidine is typically antagonized with atipamezole (5 mg/mg medetomidine [5:1]). For most species, high doses of atipamezole are contraindicated; foxes given 0.25 mg/kg atipamezole were reported to be nervous, over-alert, and developed muscle

fasciculations (Jalanka 1990). However, it is important to note that raccoon dogs were not effectively antagonized when given 5:1 atipamezole:medetomidine; for these animals, 10:1 was needed instead (Arnemo et al. 1993). Although this dose is higher than for any other canid, it did not cause raccoon dogs to be excited or overly alert (Arnemo et al. 1993). Antagonism may be quicker with IV administration of atipamezole than with IM delivery, but may cause adverse effects and the difference in recovery time is only a matter of 2–5 minutes. In blue foxes, IV atipamezole caused a 200% increase in heart rate 1.5 minutes post administration (Jalanka 1990). Given the rapid and dramatic changes in blood pressure and cardiovascular output that occur when atipamezole is given IV, this route of administration poses unnecessary risks and should not be performed. Theoretically, yohimbine may also be used to antagonize medetomidine, but even in domestic dogs, there is sparse literature about dosing.

Unexplained mortalities have been seen with the use of ketamine-medetomidine. Of 20 Arctic foxes anesthetized with ketamine (3 mg/kg)-medetomidine (0.5 mg/kg) for implantation of heart-rate transmitters, two died 30–35 minutes into surgery (Fuglei et al. 2002). The cause of death was not explained so surgical factors cannot be discounted. The use of ketamine (6–8 mg/kg)—medetomidine (0.1–0.2 mg/kg) administered to grey wolves via dart from helicopter resulted in a high complication rate, including several mortalities, so this combination is not recommended under those conditions (Arnemo et al. 2013).

Ketamine-Dexmedetomidine

As dexmedetomidine has become available, this drug has often been used as a replacement for medetomidine due to either preference or availability. Dexmedetomidine can often be used as a substitute for medetomidine, but at dosages that are one-third to one-half that of medetomidine. It has been used effectively in African wolves, Andean fox, and Sechuran fox (Chirife et al. 2020; Gutema et al. 2018; Lescano et al. 2018).

Xylazine-Butorphanol

Butorphanol (0.4 mg/kg) has been combined with xylazine (2 mg/kg) to heavily sedate gray wolves (Kreeger et al. 1989). Animals were induced in 12 minutes; bradycardia, respiratory depression, and normotension were observed. Immobilization was rapidly antagonized with yohimbine and naloxone. After antagonists were administered, heart rate and respiratory rate rapidly increased (Kreeger et al. 1989).

Medetomidine-Butorphanol

Butorphanol has also been combined with medetomidine in canids; this drug combination can be fully antagonized, with few side effects, but requires visual and auditory stimulation to be minimized to be effective as neither is a true anesthetic. Medetomidine (0.04 mg/kg) with butorphanol (0.4 mg/kg) was successfully used to immobilize 23 of 24 red wolves (Larsen et al. 2002). Induction times were 5–15 minutes. Some wolves received supplemental diazepam (0.2 mg/kg IV) immediately following induction, others received ketamine (1 mg/kg IV) 30 minutes post induction, and others received no additional anesthetics. A few red wolves experienced bradycardia (<40 beats per minute); heart rate and blood pressure increased when ketamine was given. Second-degree heart block and sinus arrhythmia were observed, but there were no other cardiac arrhythmias. Initial blood pressure values were high (98–194 mmHg) but decreased over time. Oxygenation was initially poor in a few animals but improved over time and was generally good (SpO_2 > 93%). Effects of the medetomidine-butorphanol lasted 30–40 minutes; longer recumbency times were achieved with addition of diazepam or ketamine. Antagonism with atipamezole (0.2 mg/kg)-naloxone (0.02 mg/kg) effected quick recovery times (~7 minutes). When low doses of glycopyrrolate were added, there appeared to be a threshold effect on heart rate and blood pressure. At low doses (0.0025–0.005 mg/kg), heart rate and blood pressure did not change, but at higher doses (0.0075–0.0175 mg/kg), acute tachycardia and severe sustained hypertension occurred (Larsen et al. 2001).

Xylazine-Fentanyl

Similar to xylazine-butorphanol, xylazine (1 mg/kg)-fentanyl (0.1 mg/kg) has been used successfully to immobilize canids (de Villiers et al. 1995; Hattingh et al. 1995). This combination can be antagonized with yohimbine (0.125 mg/kg) and naloxone (1.2 mg/animal). For African painted dogs, animals were ataxic in 1.5–3 minutes and recumbent in 5–7.5 minutes (Hattingh et al. 1995). If approached too soon, animals would respond to touch by standing and running in an uncoordinated fashion. With any alpha-2 agonist-opioid combination, canids should be left as undisturbed as possible until 10 minutes post darting. Immobilization with xylazine-fentanyl typically lasts 45–60 minutes. During this time, canids are normoxemic, but hypercapnic (blood partial pressure of carbon dioxide [pCO_2] = 64 mmHg) and acidemic (blood pH = 7.18–7.28) (Hattingh et al. 1995). Supplementation with small doses of xylazine-fentanyl can extend the immobilization by 45–60 minutes. Once antagonists are administered (IV), complete reversal occurs within

1–2 minutes (Hattingh et al. 1995). Detomidine-fentanyl has been used in African painted dogs in a similar manner (Hattingh et al. 1995; Langan & Jankowski 2019).

Ketamine-Medetomidine-Butorphanol

This combination takes advantage of the properties of each agent while minimizing their side effects by decreasing the needed dose of each drug. In red wolves, hypertension was not as severe and recoveries were shorter and smoother than with ketamine-xylazine, ketamine-medetomidine, or ketamine-medetomidine-acepromazine, although all combinations were effective (Sladky et al. 2000).

A recent study reported minimal hypertension with mild cardiac changes (first- and second-degree atrioventricular blocks, sinus arrhythmia, and depressed left ventricular systolic function) using a combination of ketamine (2 mg/kg)-medetomidine (0.03 mg/kg)-butorphanol (0.2 mg/kg)-acepromazine (0.02 mg/kg)-isoflurane (1–2%) in gray wolves (Valerio et al. 2005). However, this report did not measure blood pressure or assess arrhythmias until 35 minutes post injection and recovery times were not reported so it is difficult to compare these results with other investigations (Guglielmini et al. 2006; Valerio et al. 2005).

Ketamine-Midazolam

Use of ketamine-midazolam has been reported in red foxes, induction times of 4–6 minutes and head-up times of 14–23 minutes; when compared with other drug regimens, inductions were longer and there were more spontaneous recoveries (Kreeger et al. 1990b). Ketamine-midazolam has not been a combination that has been extensively investigated for wild canids, probably because of the availability, low cost, and safety margin of Telazol®.

Tiletamine-Zolazepam

Tiletamine-zolazepam (Telazol®) is relatively inexpensive, has a wide margin of safety, can be reconstituted at higher concentrations to decrease drug volumes, and used in a wide variety of species. It can be especially useful for field captures, where accurate dosing may be compromised and quick induction is essential. Induction times were the same in gray wolves using 5 mg/kg or 10 mg/kg Telazol® (5–8 minutes), but arousal time was twice as long with the higher dose (Kreeger et al. 1990c). However, for helicopter captures, doses over 10 mg/kg may need to be used in order for wolves to be adequately induced (Ballard et al. 1991). Telazol® has also been effectively combined with xylazine in gray wolves (Kreeger et al. 1995).

High stepping is often the first drug response, followed by disoriented gait, loss of use of hind legs, licking lips, loss of use of forelegs, loss of head and neck movement, nystagmus, and loss of tongue movement (Ballard et al. 1991). Many maned wolves anesthetized with 3 mg/kg tiletamine-zolazepam had compulsive licking, excessive salivation, muscle twitching, or muscle tremors (Furtado et al. 2006). In other canids, extreme salivation may occur and mild seizures are not uncommon (Ballard et al. 1991; van Heerden et al. 1991). Within reason, differences in Telazol® do not seem to have substantial effects on heart rate, respiratory rate, blood pressure, or body temperature. Working times are typically 60–90 minutes at these doses and recovery time is highly variable (25–300 minutes) (Ballard et al. 1991). Complete recovery times have been reported to be as long as 5–6 hours with 5 mg/kg Telazol® and some wolves have very rough recoveries with ataxia, paddling, falling backward, and severe mutilation (Kreeger et al. 1990c). If only using injectable drugs, canids induced with Telazol® can be supplemented with ketamine, rather than more Telazol®, to provide additional working time without excessively prolonging recovery (Kreeger et al. 1990c).

Tiletamine-Zolazepam-Medetomidine

Quality of recovery and anesthesia may be much improved with lower doses of Telazol® combined with medetomidine. When tiletamine-zolazepam (2 mg/kg) was administered to red foxes in combination with medetomidine (0.04 mg/kg), the anesthetic quality and recovery times (6 minutes) were similar to those for procedures performed using ketamine-medetomidine (Bertelsen & Villadsen 2009). Other cardiorespiratory changes also appear to be similar to ketamine-medetomidine as initial tachycardia gradually decreased during anesthesia, initial moderate hypertension decreased over time, and an initially low respiratory rate gradually increased to normal.

Medetomidine-Midazolam

Medetomidine (0.06 mg/kg)-midazolam (0.5 or 1 mg/kg) has been used successfully in red foxes (Shilo et al. 2010) with faster induction times in animals given 1 mg/kg midazolam than those given 0.5 mg/kg midazolam (Table 34.2). Recovery times were similar between the two doses and were approximately 10 minutes after atipamezole administration. In that study, mild hypertension was noted and blood pressure values were similar between animals given ketamine-medetomidine and those given medetomidine and 0.5 mg/kg midazolam. Interestingly, foxes given medetomidine and 1 mg/kg midazolam had higher blood pressure values than animals given ketamine-medetomidine.

Table 34.2 Injectable immobilization drug dosages for canids. Drugs or drug combinations are listed in order in which they are recommended.

Species	Drug Combination	Reversal	Comments	Reference
Atelocynus microtis (short-eared dog)	Telazol® (10 mg/kg)			Kreeger et al. (2023)
Canis audustus, Canis aureus, Canis mesomelas (jackals)	Medetomidine (0.09 mg/kg)-midazolam (0.5 mg/kg)	Atipamezole (0.45 mg/kg)		King et al. (2008)
Canis audustus, Canis aureus, Canis mesomelas (jackals)	Ketamine (2 mg/kg)-medetomidine (0.11 mg/kg)	Atipamezole (0.55 mg/kg)		King et al. (2008)
Canis audustus, Canis aureus, Canis mesomelas (jackals)	Ketamine (5–8 mg/kg)-xylazine (0.5 mg/kg)			McKenzie & Burroughs (1993)
Canis audustus, Canis aureus, Canis mesomelas (jackals)	Telazol® (3–4 mg/kg, 6–8 mg/kg if not enclosed)			McKenzie & Burroughs (1993)
Canis latrans (coyote)	Medetomidine (0.06–0.12 mg/kg)	Atipamezole (0.6 mg/kg)		Baldwin et al. (2008); Miller et al. (2009)
Canis latrans (coyote)	Ketamine (4 mg/kg)-xylazine (2 mg/kg)	Yohimbine (0.15 mg/kg)		Kreeger & Seal (1986b)
Canis latrans (coyote)	Telazol® (10–11 mg/kg)			Gray et al. (1974); Kreeger et al. (2023)
Canis lupaster (African wolf)	Ketamine (8–10 mg/kg)-dexmedetomidine (0.2 mg/kg)	Atipamezole (2 mg/kg)		Gutema et al. (2018)
Canis lupus (grey wolf)	Ketamine (3–4 mg/kg)-medetomidine (0.06–0.08 mg/kg)	Atipamezole (0.3–0.4 mg/kg IM)	Not recommended for helicopter captures	Holz et al. (1994); Kreeger et al. (2023); Arnemo et al. (2013)
Canis lupus (grey wolf)	Medetomidine (0.05 mg/kg)	Atipamezole (0.25 mg/kg IM)		Kreeger et al. (1996)
Canis lupus (grey wolf)	Xylazine (2 mg/kg)-butorphanol (0.4 mg/kg)	Yohimbine (0.125 mg/kg IV)-naloxone (0.05 mg/kg IV)		Kreeger et al. (1989)
Canis lupus (grey wolf)	Ketamine (4–10 mg/kg)-xylazine (1–3 mg/kg)	Yohimbine (0.15 mg/kg IV)		Kreeger (1992); Kreeger et al. (1987)
Canis lupus (grey wolf)	Xylazine (2 mg/kg captive, 3–4 mg/kg wild)	Hohimbine (0.15 mg/kg IV)		Kreeger et al. (1988); Philo (1978)
Canis lupus (grey wolf)	Telazol® (10 mg/kg)-xylazine (1.5 mg/kg)			Kreeger et al. (2023)
Canis lupus (grey wolf)	Telazol® (3–10 mg/kg, 10–13 mg/kg for helicopter captures)			Ballard et al. (1991); Boever et al. (1977); Kreeger et al. (1987)
Canis rufus (red wolf)	Medetomidine (0.04 mg/kg)-butorphanol (0.4 mg/kg), supplement with diazepam 0.2 mg/kg IV) or ketamine (1 mg/kg IV)	Atipamezole (0.2 mg/kg)-naloxone (0.02 mg/kg) ± flumazenil (0.02 mg/kg)		Larsen et al. (2001)
Canis rufus (red wolf)	Ketamine (2 mg/kg)-medetomidine (0.02 mg/kg)-butorphanol (0.2 mg/kg)	Atipamezole (0.2 mg/kg)		Sladky et al. (2000)
Canis rufus (red wolf)	Ketamine (2 mg/kg)-medetomidine (0.04 mg/kg)	Atipamezole (0.2 mg/kg)		Sladky et al. (2000)

(*Continued*)

Table 34.2 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
Canis rufus (red wolf)	Ketamine (8–10 mg/kg)-xylazine (2 mg/kg)	Yohimbine (0.1 mg/kg)		Kreeger et al. (2023); Sladky et al. (2000)
Canis rufus (red wolf)	Telazol® (10 mg/kg)			Kreeger et al. (2023)
Canis simiensis (Ethiopian wolf)	Telazol® (2–7 mg/kg)			Sillero-Zubiri (1996)
Cerdocyon thous (crab-eating fox)	Ketamine (12 mg/kg)-midazolam (0.5 mg/kg)			Souza et al. (2011)
Cerdocyon thous (crab-eating fox)	Ketamine (8–10 mg/kg)-xylazine (0.5–2 mg/kg)			Pessutti et al. (2001); Curi & Talamoni (2006)
Cerdocyon thous (crab-eating fox)	Ketamine (12 mg/kg)-acepromazine (0.1 mg/kg)			Souza et al. (2011)
Cerdocyon thous (crab-eating fox)	Telazol® (7 mg/kg)			Souza et al. (2011)
Chrysocyon brachyurus (maned wolf)	Ketamine (2.5 mg/kg)-medetomidine (0.08 mg/kg)	Atipamezole (0.4 mg/kg)		Kreeger et al. (2023)
Chrysocyon brachyurus (maned wolf)	Telazol® (1.2–5 mg/kg)		Supplement with ketamine (25–50 mg) or isoflurane	Deem & Emmons (2005); Estrada et al. (2009); Furtado et al. (2006); Norton (1990)
Chrysocyon brachyurus (maned wolf)	Ketamine (6–9 mg/kg)-xylazine (0.5–2 mg/kg)	Yohimbine (0.1–0.2 mg/kg)	Supplement with 5 mg of propofol boluses IV	Norton (1990); Pessutti et al. (2001); Guimarães et al. (2013)
Cuon alpinus (dhole)	Ketamine (6–8 mg/kg)-xylazine (1 mg/kg)			Muliya et al. (2016)
Cuon alpinus (dhole)	Telazol® (4 mg/kg)			Acharya et al. (2010); Grassman et al. (2006)
Lycaon pictus (African painted dog)	Medetomidine (0.04 mg/kg)-butorphanol (0.2 mg/kg)-midazolam (0.3 mg/kg)	Atipamezole (3 mg)-naltrexone (10 mg)-flumazenil (0.2 mg)		Fleming et al. (2006)
Lycaon pictus (African painted dog)	Ketamine (2–3 mg/kg)-medetomidine (0.02–0.04 mg/kg) ± midazolam (0.1–0.2 mg/kg) ± butorphanol (0.1–0.2 mg/kg)	Atipamezole (0.1–0.2 mg/kg) ± flumazenil (0.01–0.05 mg/kg) ± naloxone (0.02 mg/kg)		Langan & Jankowski (2019)
Lycaon pictus (African painted dog)	Ketamine (3–5 mg/kg)-medetomidine (0.05–0.1 mg/kg)	Atipamezole (0.15 mg/kg)		Cirone et al. (2004); van Heerden (1993)
Lycaon pictus (African painted dog)	Ketamine (2–4 mg/kg), midazolam (0.2–0.3 mg/kg), butorphanol (0.3–0.4 mg/kg)	± Flumazenil (0.01–0.05 mg/kg) ± naloxone (0.02 mg/kg)		Langan & Jankowski (2019)
Lycaon pictus (African painted dog)	Ketamine (3 mg/kg)-dexmedetomidine (0.03 mg/kg)-midazolam (0.2 mg/kg)	Atipamezole (0.1–0.2 mg/kg) ± flumazenil (0.01–0.05 mg/kg)		Langan & Jankowski (2019)
Lycaon pictus (African painted dog)	Ketamine (1.6 mg/kg)-xylazine (2.2 mg/kg)	Yohimibine (0.2 mg/kg IV/IM)		Osofsky et al. (1996)

Table 34.2 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
Lycaon pictus (African painted dog)	Xylazine (0.7–1.1 mg/kg)-fentanyl (0.1 mg/kg), supplement with xylazine (10 mg)-fentanyl (0.5 mg)	Yohimbine (0.1 mg/kg)-nalxone (0.04 mg/kg)		de Villiers et al. (1995); van Heerden (1993)
Lycaon pictus (African painted dog)	Telazol® (1–4 mg/kg)		Wild African painted dogs are more sensitive than captive ones	Hattingh et al. (1995); van Heerden (1993)
Nyctereutes procyonoides (raccoon dog)	Ketamine (5 mg/kg)-medetomidine (0.1 mg/kg)	Atipamezole (1 mg/kg)		Arnemo et al. (1993)
Nyctereutes procyonoides (raccoon dog)	Dexmedetomidine (0.02 mg/kg)-midazolam (0.4 mg/kg)-butorphanol (0.2 mg/kg)-atropine (0.04 mg/kg)	No reversal agents reported, but presumably similar dosages as for other canids		Feng et al. (2015)
Nyctereutes procyonoides (raccoon dog)	Ketamine (10 mg/kg)-xylazine 2 mg/kg			Oh et al. (2012)
Nyctereutes procyonoides (raccoon dog)	Telazol® (7 mg/kg)			Gray et al. (1974)
Otocyon megalotis (bat-eared fox)	Ketamine (5–8 mg/kg)-xylazine (0.5 mg/kg)			McKenzie & Burroughs (1993)
Otocyon megalotis (bat-eared fox)	Telazol® (5 mg/kg)			McKenzie & Burroughs (1993)
Pseudalopex culpaeus (South American fox)	Ketamine (3–4 mg/kg)-dexmedetomidine (0.05–0.06 mg/kg	Atipamezole (0.5–0.6 mg/kg)		Chirife et al. (2020)
Pseudalopex culpaeus, *P. griseus* (South American foxes)	Ketamine (2.5 mg/kg)-medetomidine (0.05 mg/kg)	Atipamezole (0.25 mg/kg)		Acosta-Jamett et al. (2010)
Pseudalopex culpaeus, *P. griseus* (South American foxes)	Ketamine (13 mg/kg)-xylazine (1.6–3 mg/kg)			Acosta-Jamett et al. (2010)
Pseudalopex culpaeus, *P. griseus* (South American foxes)	Telazol® (5 mg/kg)			Acosta-Jamett et al. (2010)
Pseudalopex gymnocercus (pampas fox)	Ketamine (11 mg/kg)-xylazine (1 mg/kg)			Vidal et al. (2014)
Pseudalopex gymnocercus (pampas fox)	Telazol® (8 mg/kg)			Vidal et al. (2014)
Pseudalopex sechurae (Sechuran fox)	Ketamine (2–5 mg/kg)-dexmedetomidine (0.02–0.03 mg/kg)	Atipamezole (0.1 mg/kg)		Lescano et al. (2018)
Pseudalopex vetulus (hoary fox)	Ketamine (3–5 mg/kg)-xylazine (0.6–0.8 mg/kg)			Pessutti et al. (2001)
Speothos venaticus (bush dog)	Ketamine (11 mg/kg)-xylazine (2 mg/kg)			Mol et al. (2015)

(*Continued*)

Table 34.2 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
Speothos venaticus (bush dog)	Telazol® (10 mg/kg)			Pessutti et al. (2001)
Urocyon cineoereoargenteus (grey fox)	Ketamine (11–15 mg/kg)-xylazine (2–3 mg/kg)			Jessup (1982)
Urocyon cineoereoargenteus (grey fox)	Telazol® (9 mg/kg)			Smith et al. (2017)
Vulpes spp.	Telazol® (10 mg/kg)			Kreeger (1992)
Vulpes bengalis (Indian fox)	Ketamine (13 mg/kg)-xylazine (2 mg/kg)			Belsare & Vanak (2013)
Vulpes chama (Cape fox)	Ketamine (5–8 mg/kg)-xylazine (0.5 mg/kg)			McKenzie & Burroughs (1993)
Vulpes chama (Cape fox)	Telazol® (5 mg/kg)			McKenzie & Burroughs (1993)
Vulpes lagopus (Arctic fox)	Ketamine (2.5 mg/kg)-medetomidine (0.05 mg/kg)	Atipamezole (0.3 mg/kg)		Aguirre et al. (2000); Jalanka (1990)
Vulpes lagopus (Arctic fox)	Medetomidine (0.025–0.1 mg/kg)			Jalanka (1990)
Vulpes velox (swift fox)	Ketamine (10 mg/kg)-xylazine (1 mg/kg)	Yohimbine (0.125 mg/kg)		Telesco & Sovada (2002)
Vulpes vulpes (red fox)	Ketamine (2–4 mg/kg)-medetomidine (0.02–0.07 mg/kg) ± butorphanol (0.04 mg/kg)	Atipamezole (0.1–0.3 mg/kg)		Bertelsen & Villadsen (2009); Brash (2003); Shilo et al. (2010)
Vulpes vulpes (red fox)	Medetomidine (0.14 mg/kg)	Atipamezole (0.80 mg/kg)		Baldwin et al. (2008)
Vulpes vulpes (red fox)	Medetomidine (0.04 mg/kg)-midazolam (0.3 mg/kg)-butorphanol (0.1 mg/kg)	Atipamezole (0.15 mg/kg)		Bertelsen & Villadsen (2009)
Vulpes vulpes (red fox)	Medetomidine (0.07 mg/kg)-midazolam (0.8 mg/kg)	Atipamezole (0.35 mg/kg)		Shilo et al. (2010)
Vulpes vulpes (red fox)	Dexmedetomidine (0.03–0.05 mg/kg)-midazolam (0.4 mg/kg) ± butorphanol (0.2 mg/kg)	Atipamezole (0.2 mg/kg)		Diao et al. (2017)
Vulpes vulpes (red fox)	Ketamine (25–30 mg/kg)-midazolam (0.6 mg/kg)			Kreeger & Arnemo (2007); Kreeger et al. (1990b)
Vulpes vulpes (red fox)	Ketamine (10–23 mg/kg)-xylazine (1–2 mg/kg)	Yohimbine (0.15 mg/kg)		Gilbert et al. (2018)
Vulpes vulpes (red fox)	Telazol^{R} (2 mg/kg)-medetomidine (0.04 mg/kg)	Atipamezole (0.2 mg/kg)		Bertelsen & Villadsen (2009)
Vulpes vulpes (red fox)	Telazol® (4–10 mg/kg)			Boever et al. (1977); Brash (2003); Kreeger et al. (1990b)

IM, intramuscular; IV, intravenous.

Medetomidine-midazolam has been similarly effective in golden-backed jackals (King et al. 2008). In that study, recovery times were slightly longer than with ketamine-medetomidine but were also smoother. It is notable that medetomidine doses were particularly high (0.09 ± 0.02 mg/kg), but bradycardia was not observed and hypertension was not severe.

Medetomidine-Midazolam-Butorphanol

Medetomidine-midazolam-butorphanol has been used in red foxes, but with lower doses of medetomidine (0.04 mg/kg) and midazolam (0.3 mg/kg) than with medetomidine-midazolam (Bertelsen & Villadsen 2009). Induction times with this protocol were slower (9 minutes) compared with combinations that included ketamine or Telazol® (3–4 minutes); similarly, recovery times were longer post atipamezole than with combinations that included ketamine or Telazol®. More important to note is that inductions and recoveries with medetomidine-midazolam-butorphanol were more variable, with some animals becoming arousable before atipamezole was administered and others still sedated long after atipamezole administration (Bertelsen & Villadsen 2009). Medetomidine-midazolam-butorphanol has also been used with success in free-ranging African painted dogs (Fleming et al. 2006).

Dexmedetomidine-Midazolam-Butorphanol

In the same way that dexmedetomidine has been substituted for medetomidine in ketamine-medetomidine combinations, dexmedetomidine has also been substituted in medetomidine-midazolam combinations. Dexmedetomidine-midazolam-butorphanol has been effective in raccoon dogs (Feng et al. 2015) and red fox (Diao et al. 2017). Cardiopulmonary parameters and recovery characteristics are as typical for medetomidine-based combinations.

Butorphanol-Azaperone-Medetomidine

A commercially available premixed drug preparation is available in the United States of butorphanol (27.3 mg/mL)-azaperone (9.1 mg/mL)-medetomidine (10.9 mg/mL), referred to as BAM. Doses of 0.1 mL per Arctic fox or red fox and 0.5 mL per wolf have been provided by Wildlife Pharmaceuticals as suggested dosages (Kreeger et al. 2023). Antagonism in foxes was listed at 0.2 mL of 25 mg/mL atipamezole + 0.5 mL of 50 mg/mL naltrexone; antagonism in grey wolves was listed as 1 and 0.5 mL of these products, respectively. Without additional information on inductions, anesthetic efficacy, or recoveries, BAM has not been listed in the table of drug options but is included here for reference.

Drug Choice

As with any group of animals, drugs of choice for immobilization of canids will vary by species and situation, as well as the preferences and experience of personnel.

For small or very young canids, induction and maintenance with isoflurane or sevoflurane (Crawshaw et al. 2007) is an easy way of quickly providing anesthesia from which animals can rapidly recover. Animals can either be manually restrained and induced via face cone or induced in a chamber. However, animals larger than 5 kg may be challenging to safely restrain in this way and injectable induction protocols are more appropriate for larger canids. Chamber induction can occur in purpose-built plastic induction chambers or by placing a plastic bag around a transport kennel. When using these devices, the patient must be closely monitored to ensure that the animal does not have complications, become overanesthetized, or become recumbent in a position that impedes respiration. Animals can become overheated in induction chambers, so these devices should not be used if ambient temperature cannot be controlled. Some people prefer to use clear bags when placing plastic bags around kennels so that the animals can be observed throughout induction. By using inhalant anesthetics for induction, there is increased risk of anesthetic exposure of personnel.

Isoflurane can be used for maintenance of anesthesia or supplementation. Animals may be maintained with a face mask over the mouth or through an endotracheal tube after intubation. There will be less environmental release of gas anesthetic if an endotracheal tube is used. Intubation is recommended for animals with complications or for any prolonged immobilization procedure to facilitate assisted ventilation. Sevoflurane can probably be used with equal efficacy and safety, inductions and recoveries tend to be quicker than with isoflurane in other taxonomic groups, but there is less comparative experience with this drug in nondomestic canids (Crawshaw et al. 2007).

Injectable anesthetic drugs are particularly appropriate for larger canids. Recommended doses from the literature are given in Table 34.2 based on literature reports, current drug availability, and personal experience.

For many routine procedures on young healthy animals in controlled environments, medetomidine-butorphanol can be used for immobilization if the patients are closely monitored for signs of recovery or reactiveness. This combination provides profound sedation and 45–60 minutes of working time for many canids. Induction times with medetomidine-butorphanol are typically 5–15 minutes; this is not an appropriate combination for situations where the animals are uncontained, such as darting from a helicopter, or for procedures that are more invasive than small

skin biopsies. It should also be noted that there will be a subset of the canid population that will not be adequately immobilized with this combination. For reactive animals and more invasive procedures, another agent, such as ketamine, diazepam, or midazolam, may be needed. If ketamine is used, atipamezole-naloxone should not be administered for 30–45 minutes to give time for the ketamine to be metabolized.

In less-controlled situations, such as emergency captures, Telazol®, ketamine-medetomidine, ketamine-dexmedetomidine, or ketamine-xylazine may be more appropriate since there is a lower volume of drug with these regimens and induction is rapid. Induction with medetomidine-butorphanol is often 10–15 minutes, whereas induction with Telazol® is typically <5 minutes. Due to a high number of capture-related mortalities, ketamine-medetomidine may not be appropriate for helicopter darting of wild canids (Arnemo et al. 2013).

In geriatric or ill animals, the use of alpha-2 agonists should be carefully evaluated, particularly if cardiac or respiratory disease is suspected. Although these agents can be rapidly antagonized, their effects on blood pressure, heart rate, and respiration may make them risky in compromised patients. For these animals, inhalant induction may be the safest option, but the stress of handling also needs to be considered and with larger canids, inhalant induction may not be a safe option for personnel. Injectable combinations such as ketamine-midazolam, ketamine-midazolam-butorphanol, or Telazol® can also be used.

Complications and Other Considerations

Anticipation and avoidance of potential complications are key points in preparation for canid anesthesia. Respiratory depression is a common complication for immobilized canids and can be induced by alpha-2 agonists or opioids. Respiratory depression often manifests as hypoxemia and hypercapnia. Hypoxemia can be addressed by providing supplemental oxygen via the nares or an endotracheal tube. Hypopnea and hypercapnia may be corrected through intubation and assisted ventilation (Fig. 34.3).

Opioids and alpha-2 adrenoceptor agonists may be antagonized, but the animal may not remain anesthetized and there may be adverse effects from residual dissociative agents unless the animal has been placed on gas anesthetics. A respiratory stimulant, such as doxapram, may increase respiratory rate and ventilation, at least transiently.

Prolonged exertion may result in hyperthermia and exertional myopathy, which needs to be treated immediately. When under a warm sun, heavily furred animals can become hyperthermic even with cold ambient temperatures



Figure 34.3 Instrumentation: capnography, pulse oximeter, and esophageal thermometer.

(Fig. 34.4). Most canids dissipate heat through panting, which is often compromised during immobilization. Hyperthermia should be suspected if rectal temperature is >40°C and treatment is mandatory if the temperature is >41°C. Hyperthermic animals should be moved out of direct sunlight. Cooling measures may be warranted such as spraying the body with water, packing with ice packs, application of isopropyl alcohol to proximal legs and ears, cold water enemas, and administration of cool IV fluids. These cooling methods should be adjusted as body temperature starts to decline to prevent hypothermia.

Hypothermia occasionally occurs under cold conditions, during prolonged immobilizations in small canids with use of inhalant anesthesia, and in animals with hair loss or debilitated body condition. Warm water containers, warm blankets, heat pads, heat lamps, warm IV fluids, and hand warmers can be used to increase body temperature. Recovery will be slowed if the animal remains below normal body temperature.



Figure 34.4 Especially with species from cold climates, environmental conditions are important to prevent overheating. Arctic fox. Photo credit: A. Moresco.

Severe sustained hypertension may be seen with concurrent use of dissociative agents and alpha-2 agonists. Ketamine-medetomidine-induced hypertension can be particularly severe, but this can also be seen with ketamine-xylazine or with alpha-2 agonists in the absence of a dissociative agent (Kreeger et al. 1986; Larsen et al. 2002; Sladky et al. 2000). Blood pressure typically declines over time and hypertension is less severe in calm animals. Anticholinergics should be used sparingly and judiciously to avoid exacerbating hypertension.

Vomiting may occur and can result in aspiration of stomach contents. To prevent this problem, captive animals should be fasted 12–24 hours prior to immobilization; water can typically be withheld for up to 12 hours in advance, but 2 hours is usually sufficient. Vomiting on recovery is typically less hazardous than at induction because the animal has control of its glottis and is less likely to aspirate. If an animal vomits when anesthetized, it should be placed in sternal recumbency with the neck extended and the nose pointed down. Proper endotracheal intubation and cuff insufflation also decrease the likelihood of aspiration during vomiting episodes.

Seizures may occur with the use of dissociative anesthetics, although they may be seen with less frequency at lower doses of dissociatives and when benzodiazepines are used as part of immobilization combinations. If the animal only experiences one or two short seizures, treatment is not necessary, but if more seizures occur, or if seizures are sustained, diazepam or midazolam should be administered IV or IM. Remember to administer diazepam over 10–20 seconds IV to prevent cardiac arrest from the propylene glycol in diazepam formulations.

Wounds are common in canids and should be treated with appropriate medical care. All anesthetized canids should be checked for wounds from traps, darts, needles, and conspecifics. Removal of hair should be minimized if the coat is needed for thermoregulation.

Gastrointestinal dilation (bloat) may sometimes occur in larger canids, particularly in animals that have recently eaten (and especially if the food ingested was rotten). Although rare, gastrointestinal dilation and volvulus may also occur. Care should be taken to avoid unnecessary rolling of animals, particularly over their backs.

There is much discussion in the literature regarding the stress of capture and immobilization of African painted dogs, with speculation that handling-induced stress contributed to mortality in this species through elevated corticosteroids and recrudescence of latent viruses. The evidence for this is scant and analysis of the pertinent data suggests that handling does not increase the likelihood of disease in this species (de Villiers et al. 1995).

The immobilized animal should not be left unattended until it has fully recovered, unless it is in captivity or held such that it can be kept away from other animals and hazards (e.g., in a transport crate). Monitoring should intensify when hazards such as water and precipices are in the immediate area. For these reasons, anesthetic combinations that can be antagonized are ideal. Yohimbine may be given IV to rapidly antagonize xylazine; similarly naloxone or naltrexone may be given IV to antagonize butorphanol. Some authors advocate IV atipamezole for reversal of medetomidine or dexmedetomidine, but this may put undue strain on the cardiovascular system due to the drug's potent and specific nature. Atipamezole IM appears to result in acceptably swift recovery times, especially if the animal has not become hypothermic. Once antagonists are administered, the animal should be left undisturbed in a shaded quiet area; if moved after antagonists are administered, the animal may become agitated and tend to stand and run before having fully recovered. Free-ranging animals can also be maintained in transport crates until fully recovered and then released.

Many canids are pack animals. Reintroduction after prolonged separation (>12 hours) may result in extensive fighting so animals should be kept with the pack as much as possible. Even if it is necessary to perform frequent immobilizations on an individual, it is generally preferable to perform procedures as quickly as possible and return the animal to the pack each time, rather than separating the animal and then attempting reintroduction (Kreeger 1992).

Analgesia and Analgesic Techniques

Analgesic therapy for nondomestic canids is generally considered similar to analgesia for domestic dogs; given the similarity in anatomy and physiology, use of dosages and techniques designed for domestic dogs should generally be effective. Although there are sparse prospective studies on analgesia in nondomestic canids, there are occasional case reports describing these techniques. For example, a juvenile red fox (*V. vulpes*) received an epidural injection of lidocaine (2.5 mg/kg), bupivacaine (0.625 mg/kg), and morphine (0.1 mg/kg) in the lumbosacral junction using a 22-gauge, 2.5-cm spinal needle by way of the "hanging drop" technique employed for domestic dogs (Anagnostou et al. 2015). Meloxicam (0.1–0.2 mg/kg IV, 0.3 mg/kg IM), butorphanol (0.2 mg/kg IM), morphine (0.05 mg/kg IV), and ketoprofen (2 mg/kg IM) have all been used for analgesia, as has regional infiltration of 0.5% bupivacaine and a 75 ug/h fentanyl patch (Crawshaw et al. 2007; Lee et al. 2014; McNulty et al. 2000; Moriarty et al. 2015). Lidocaine 4% gel and subcutaneous infiltration of lidocaine injectable solution has been administered

to perform skin biopsies (Moriarty et al. 2015). Postoperative pain has been treated with carprofen (4.4 mg/kg for 3 days; Lee et al. 2014).

Species-specific locations for regional dental nerve blocks have recently been described in both maned wolves (*Chyrsocyon brachurus*) and bush dogs (*Cerdocyon thous*) (de Souza et al. 2013, 2016). These studies provide detailed descriptions of the mandibular anatomy of these species to facilitate infusion of local anesthetics to provide regional anesthesia, but as investigations were in cadaver specimens, verification of the efficacy of the anesthetics was not performed (de Souza et al. 2013, 2016).

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35

Bears

Nigel Caulkett and Jon M. Arnemo

Body Weight

Body weights of bear species can be very variable within and between species. Body weight will also vary significantly over the course of the year. Weight ranges are included in Table 35.1.

Physical Restraint

Physical capture techniques are often employed to capture wild bears. The two most common methods in North America are culvert traps and snares. Bears captured in culvert traps may experience hemoconcentration (Cattet et al. 2003a). Brown bears captured with snares demonstrated a stress leukogram, hemoconcentration, and muscle damage, evidenced by elevations in serum muscle enzymes (Cattet et al. 2003a). Snared bears often exhibit increased serum myoglobin, and pathological lesions indicative of capture myopathy have been observed (Cattet et al. 2008a,b). Fractures and soft tissue injuries may also be encountered in snared animals. If used, snares should be checked frequently to minimize time spent in the snare, and snared animals should be closely examined to identify and treat snare-related injuries.

Drug Delivery Method

Drug delivery systems must be reliable and accurate. Systems that have low-impact energy and deliver drugs at a low velocity are generally preferable (Cattet et al. 2006). Captive bears may be injected with a pole syringe or blow dart. Volume limitations with blow darts necessitate the use of potent drug combinations for large bears.

It is advisable to dart free-ranging bears from a safe distance. Dart rifles will facilitate drug delivery in these situations. Many bear species will demonstrate seasonal variation in fat distribution. Black bears and brown bears will deposit a thick layer of fat over the hindquarters in fall, and the thigh is the preferred location for dart placement. In spring, these animals can be darted in the hindquarters. Polar bears may have a thick layer of fat at any time of the year and the shoulder or neck is often targeted.

Vascular Access

Venous blood can be sampled from the jugular, cephalic, or medial saphenous vein. Intravenous (IV) catheters may be placed in the jugular or cephalic vein (Fig. 35.1). The femoral pulse can easily be palpated in the groin for collection of arterial blood samples for blood gas analysis. A pulsating flow confirms insertion of the needle into the femoral artery. Firm pressure must be applied to the arterial sample site for a minimum of 2 minutes post sampling to avoid development of a hematoma.

Endotracheal Intubation

Intubation of bears is not difficult if the bear is in a sufficient plane of anesthesia. The oral and pharyngeal anatomy is similar to that of a canid. Intubation is easiest with the bear positioned in sternal recumbency. A long laryngoscope and a light source will facilitate visualization of the glottis prior to intubation (Fig. 35.2). Endotracheal tube size is dependent on the size of the bear. We typically carry size 8–14 tubes (internal diameter in millimeters) for black bears and 8–18 tubes for brown bears.

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Table 35.1 Recommended drug combinations for immobilization of bears.

Species	Drug Combination	Reversal	Comments	Reference
Polar bear (*Ursus maratimus*) 150–300 kg (F) 300–800 kg (M)	Zolazepam-tiletamine 8 mg/kg	None	Prolonged recoveries	Caulkett et al. (1999)
	Medetomidine 0.06 mg/kg + zolazepam-tiletamine 2.2 mg/kg	Atipamezole at five times the medetomidine dose		Caulkett et al. (1999); Cattet et al. (1999b)
	Xylazine 2 mg/kg + zolazepam-tiletamine 3 mg/kg	Yohimbine 0.1–0.2 mg/kg or atipamezole 0.1 mg/kg		Cattet et al. (2003b)
Brown bear (*Ursus arctos*) 100–325 kg	Medetomidine 0.08 mg/kg Zolazepam-tiletamine 4.1 mg/kg	Atipamezole at five times the medetomidine dose	Dose for wild bears; can be reduced in hypometabolic or captive animals	Fahlman et al. (2011); Painer et al. (2012); Evans et al. (2016)
	Xylazine 2.5 mg/kg Zolazepam-tiletamine 3.8 mg/kg	Yohimbine 0.1–0.2 mg/kg or atipamezole 0.1 mg/kg		Cattet et al. (2003c)
	Dexmedetomidine 0.057 mg/kg Zolazepam-tiletamine 4.87 mg/kg	Atipamezole at 10 times the dexmedetomidine dose	Dose for wild bears; can be reduced in captive animals	Fandos Esteruelas et al. (2017)
American black bear (*Ursus americanus*) 92–140 kg (F) 115–270 kg (M)	Medetomidine 0.05 mg/kg Zolazepam-tiletamine 2 mg/kg	Atipamezole at five times the medetomidine dose		Caulkett & Cattet (1997)
	Butorphanol 0.6 mg/kg Azaperone 0.2 mg/kg Medetomidine 0.2 mg/kg	Atipamezole 1.5 mg/kg and naltrexone 0.8 mg/kg		Williamson et al. (2018)
	Nalbuphine 0.9 mg/kg Azaperone 0.2 mg/kg Medetomidine 0.2 mg/kg	Atipamezole at five times the medetomidine dose Naltrexone at 1.3 times the nalbuphine dose		Wolfe et al. (2019)
	Dexmedetomidine 0.008 mg/kg Zolazepam-tiletamine 3.4 mg/kg	Atipamezole 0.04 mg/kg		Coltrane et al. (2015)
Asiatic black bear (*Ursus thibetanus*) 65–90 kg (F) 110–150 kg (M)	Zolazepam-tiletamine 8 mg/kg			Kreeger et al. (2023)
	Medetomidine 0.03–0.05 mg/kg + zolazepam-tiletamine 1.5–2.3 mg/kg	Atipamezole at five times the medetomidine dose		Jeong et al. (2017)
Sloth bear (*Melursus ursinus*) 55–145 kg	Xylazine 2 mg/kg Ketamine 5 mg/kg			Shanmugam, et al. (2011)
	Zolazepam-tiletamine 6 mg/kg			Kreeger et al. (2023)
	Medetomidine 0.014 mg/kg + zolazepam-tiletamine 1.49 mg/kg + ketamine 1.64 mg/kg	Atipamezole at five times the medetomidine dose	Used for induction of anesthesia with various maintenance techniques; noted emesis and ptyalism in some animals	McEntire et al. (2020)
Sun bear (*Ursus malayanus*) 50–73 kg	Medetomidine 60–80 µg/kg Ketamine 2–3 mg/kg			Kreeger et al. (2023)
	Medetomidine 0.05 mg/kg Zolazepam-tiletamine 2 mg/kg	Atipamezole at five times the medetomidine dose		Onuma (2003)

Table 35.1 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
Spectacled bear (*Tremarctos ornatus*) 60–140 kg	Zolazepam-tiletamine 6 mg/kg			Kreeger et al. (2023)
	Medetomidine 0.015 mg/kg + zolazepam-tiletamine 1.49 mg/kg + ketamine 1.92 mg/kg	Atipamezole at five times the medetomidine dose	Used for induction of anesthesia with various maintenance techniques; noted emesis and ptyalism in some animals; occasional seizure-like activity	McEntire et al. (2020)
Giant panda (*Ailuropoda melanoleuca*) 75–160 kg	Xylazine 0.4 mg/kg Ketamine 5 mg/kg			Kreeger et al. (2023)
	Dexmedetomidine 0.008 mg/kg Zolazepam-tiletamine 2 mg/kg	Antagonized with atipamezole at five times the dexmedetomidine dose	Consider a higher dose of atipamezole in free-ranging bears	Jin et al. (2016)
	Medetomidine 0.018 mg/kg + zolazepam-tiletamine 1.50 mg/kg + ketamine 1.36 mg/kg	Atipamezole at five times the medetomidine dose	Used for induction of anesthesia with various maintenance techniques; noted emesis and ptyalism in some animals; occasional seizure-like activity	McEntire et al. (2020)

F, female; M, male.
Body masses are referenced from Kreeger et al. (2023).



Figure 35.1 Grizzly bear, with intravenous catheter placed in the cephalic vein.

Sedation/Tranquilization/Anesthesia Techniques

The following section deals with drug combinations that can be used to anesthetize bears. Mean doses of recommended combinations can be found in Table 35.1.



Figure 35.2 Intubation of a spectacled bear.

Xylazine-Ketamine

This combination may be suitable for short procedures in small bears, but the risk of sudden arousal limits its utility in larger, more aggressive bears. Xylazine can be antagonized with atipamezole or yohimbine, but since a high

dose of ketamine is required, the adverse effects of the ketamine (rigidity, convulsions, hyperthermia) are unmasked. Bears anesthetized with this combination should be monitored closely for signs of arousal.

Medetomidine-Ketamine and Medetomidine-Ketamine-Guaifenesin

The major advantage of medetomidine-ketamine over xylazine-ketamine is that a smaller dose of ketamine is required with the more specific alpha-2 agonists. As the ketamine dose is lower, reversal of the effects of medetomidine with atipamezole is less likely to induce rigidity or convulsions due to ketamine residual effects. The delivery volume of medetomidine-ketamine is also lower. Medetomidine-ketamine may be useful for small bears, but should not be used in larger, potentially aggressive bears. Sudden recoveries have occurred in brown bears and polar bears (Caulkett & Arnemo 2024). This combination should only be used by experienced personnel for short procedures, and depth of anesthesia should be closely monitored. A recent study described a maintenance anesthetic protocol for use in black bears following induction with medetomidine-ketamine. The authors administered a constant rate infusion (CRI) of a solution containing 50 mg/mL guaifenesin, 1 mg/mL ketamine, and 0.01 mg/mL medetomidine, delivered at an infusion rate of 1 mL/kg/h. This resulted in a CRI dose of 50 mg/kg/h guaifenesin, 1 mg/kg/h of ketamine, and 0.01 mg/kg/h medetomidine (Siegal-Willet et al. 2019). This approach should allow for longer procedures and can be titrated to adjust the depth of anesthesia when needed.

Medetomidine-Azaperone-Butorphanol and Medetomidine-Azaperone-Nalbuphine

A combination of (mean doses) 0.3 mg/kg butorphanol, 0.25 mg/kg azaperone, and 0.10 mg/kg medetomidine has been used to successfully anesthetize 16 captive yearling black bears and five wild black bears. The combination produced a rapid, reliable induction and a rapid, smooth recovery following antagonism of medetomidine with atipamezole at five times the medetomidine dose. Butorphanol was antagonized in the wild bears with naltrexone at a ratio of five times the butorphanol dose. Recovery time was approximately 13 minutes in the captive bears and 9 minutes in the wild bears (Wolfe et al. 2008). The rapid recovery times are a major advantage over dissociative-based combinations, where recoveries are often prolonged. Williamson et al. (2018) compared butorphanol-azaperone-medetomidine (BAM), with a higher medetomidine dose, to xylazine ketamine. This study demonstrated that animals recovered more rapidly from the BAM combination following antagonism of the medetomidine and butorphanol when compared to antagonism of xylazine in the xylazine-ketamine-treated bears.

Given that butorphanol is a controlled substance in the USA an alternative combination (NalMed-A) has been developed to enable distribution to non-veterinarians. This combination has been administered at a dose of 0.88 mg/kg nalbuphine HCl, 0.22 mg/kg azaperone tartrate, and 0.22 mg/kg medetomidine HCl. Mean induction time was 16.2 minutes and mean recovery time was 19 minutes following antagonism of medetomidine with atipamezole at five times the medetomidine dose. Three bears required supplemental drug administration, most likely due to inaccurate weight estimation (Wolfe et al. 2016). An additional study in captive black bears demonstrated the benefit of supplemental inspired oxygen with this combination (Wolfe et al. 2019).

Zolazepam-Tiletamine (Telazol®, Zoletil®)

This drug combination produces reliable anesthesia in bears. Recovery is usually slow, smooth, and predictable. Zolazepam-tiletamine produces minimal adverse effects on the respiratory or cardiovascular systems, therefore it has a high margin of safety (Caulkett et al. 1999). The major disadvantages of zolazepam-tiletamine are lack of analgesia (Caulkett et al. 1999) and lack of reversibility (Caulkett et al. 1999; Cattet et al. 1999a). Recovery can be prolonged, particularly in large bears and if repeated doses are administered.

Medetomidine-Zolazepam-Tiletamine

This combination can be delivered in small volumes, which increases its utility in large polar bears or brown bears. Medetomidine-zolazepam-tiletamine (MZT) provides better analgesia than zolazepam-tiletamine alone (Caulkett et al. 1999). The major advantage of this combination is that it is partially reversible with atipamezole administered intramuscularly at five times the medetomidine dose. The major disadvantages of MZT are hypertension and hypoxemia (Caulkett & Cattet 1997; Caulkett et al. 1999; Fahlman et al. 2011). Hypoxemia can be offset by the provision of supplemental oxygen (Fahlman et al. 2010). MZT has been used in black bears (Caulkett & Cattet 1997), polar bears (Cattet et al. 1999a), and brown bears (Fahlman et al. 2011; Painer et al. 2012; Evans et al. 2016). Ketamine may be added to this combination to reduce the dose requirements of tiletamine-zolazepam. A recent study described the use of this protocol for induction of anesthesia in sloth bears, Andean bears, and giant pandas (McEntire et al. 2020).

Xylazine-Zolazepam-Tiletamine

Xylazine-zolazepam-tiletamine (XZT) has many of the same characteristics as MZT (Cattet et al. 2003b,c). It provides analgesia and can be delivered at approximately half the volume of zolazepam-tiletamine alone. XZT produces hypertension and hypoxemia (Cattet et al. 2003b). Hypoxemia is generally not severe and responds well to supplemental inspired oxygen. XZT will produce effective immobilization. It is important to note that the quality of anesthesia is different to zolazepam-tiletamine alone, and head lifting or limb movement may immediately precede arousal. This combination is partially reversible with yohimbine or atipamezole, whereas tolazoline appears to be ineffective. Recovery is not as rapid as with medetomidine-ketamine or MZT

Dexmedetomidine-Zolazepam-Tiletamine

This combination has been described in brown bears and giant pandas. Since dexmedetomidine is approximately twice as potent as medetomidine it can be administered at a reduced dose. In helicopter-darted brown bears a dose rate of 2.06 mg/kg of tiletamine, 2.06 mg/kg of zolazepam, and 10.1 μg/kg dexmedetomidine induced anesthesia in 5.6 minutes. The combination appeared to induce less impairment of oxygenation than reported doses of medetomidine-zolazepam-telazol. Atipamezole is typically recommended to be administered at a ratio of 10:1 with dexmedetomidine. The authors administered atipamezole at either a 10:1 or 5:1 ratio IV in the study. They found a recovery time of 25 ± 8 minutes that did not differ between doses. The authors reported that recovery appeared to be more complete at the 10:1 ratio and recommended the use of this dose (Teisberg et al. 2014). Fandos Esteruelas et al. performed a comparative study of dexmedetomidine-zolazapam-tiletamine and medetomidine-zolazapam-tiletamine in brown bears. The study used approximately equipotent doses of the two combinations and observed no advantage of one combination over the other (Fandos Esteruelas et al. 2017).

In giant pandas dexmedetomidine was administered at a dose of 8.4 μg/kg and tiletamine-zolazepam was administered at a dose of 2 mg/kg. Pandas were anesthetized in approximately 8 minutes and maintained for 55 minutes. Atipamezole was administered at a dose of five times the dexmedetomidine dose, recovery was smooth in six of seven pandas, and recovery to standing was observed 51 minutes following intramuscular (IM) administration of atipamezole (Jin et al. 2016). The authors caution about the use of this lower ratio of atipamezole and recommend further studies with extended monitoring of the recovery period to determine if adverse effects occur.

Volatile Anesthesia

Volatile anesthesia may be required for invasive or prolonged procedures. The bear is induced with one of the above injectable drug combinations, intubated, and maintained on volatile anesthesia delivered via an appropriately sized circuit. Bears under 150 kg body weight may be maintained on a small animal circle system. A large animal machine should be used for heavier animals. Isoflurane is a good choice for maintenance of anesthesia. Isoflurane-induced vasodilation tends to offset the hypertension that can result from administration of potent alpha-2 agonists. The major side effects of isoflurane are hypotension and respiratory depression. It is advisable to monitor blood pressure and end-tidal or arterial CO_2 in bears anesthetized with isoflurane.

Recovery from isoflurane is generally smooth. Alpha-2 agonist drugs should be antagonized at the termination of surgery to hasten recovery.

Complications and Other Considerations

Anesthetic Depth

Depth of anesthesia should be closely monitored as some drug combinations have proven to be unreliable in bears. Sudden recoveries have been encountered with xylazine-ketamine and medetomidine-ketamine (Caulkett & Arnemo 2024; Cattet et al. 1999a). These combinations are best avoided in most situations. Factors that increase the risk of sudden arousal include loud noise, particularly distress vocalization of cubs. Other factors that can induce arousal include movement of the bear, i.e. changing the body position or location of the anesthetized animal (Cattet et al. 1999b), or painful stimuli, such as tooth extraction. Local anesthesia should be considered whenever possible to decrease pain-related stimulation during painful procedures.

Techniques for monitoring depth of anesthesia will depend on the agent used. Zolazepam-tiletamine {Telazol®, Zoletil® [ZT]} used alone will produce reliable anesthesia with predictable signs of recovery. Lightening of anesthesia is evidenced by rapid spontaneous blinking, increased jaw tone, chewing, and paw movement. As the depth of anesthesia further decreases, animals will demonstrate head movement. Animals anesthetized with ZT alone with significant head movement generally require a top-up of tiletamine-zolazepam or ketamine unless they are to be left to recover. Top-up doses of tiletamine-zolazepam can significantly prolong recovery and should only be used if >30 minutes of additional anesthetic time is required. Ketamine is a better choice if 5–20 minutes of additional time is needed.

In xylazine-ketamine or medetomidine-ketamine anesthetized bears, head lifting or limb movement signal that the bear's depth of anesthesia is extremely light and it should not be approached or manipulated. Increased intensity of the palpebral reflex or nystagmus are early indicators that the bear is light.

With both XZT and MZT, head lifting should be absent before the bear is approached. The palpebral reflex can be used to determine depth of anesthesia. Lightly anesthetized bears will begin to breathe deeply and may sigh. They may start to lick, and will develop a spontaneous palpebral and an increased jaw tone. Head lifting or paw movement should be a sign to be extremely cautious, as the bear may soon rouse.



Figure 35.3 Brown bear receiving supplemental inspired oxygen.



Figure 35.4 Oscillometric cuff placement for indirect blood pressure measurement in a black bear.

Pulmonary Function

Hypoxemia can occur in bears during anesthesia with different drug protocols, as demonstrated by arterial blood gas studies in brown bears, black bears, and polar bears (Fahlman et al. 2011; Caulkett et al. 1999; Caulkett & Cattet 1997). Both free-ranging and captive brown bears anesthetized with MZT developed hypoxemia, despite lower drug doses used in the captive bears (Fahlman et al. 2011).

Oxygenation can be monitored with a pulse oximeter, with the probe placed on the tongue. Pulse oximetry readings may be difficult to achieve in bears lightly anesthetized with ZT, as they tend to chew. A hemoglobin saturation below 85% is indicative of hypoxemia, which can generally be treated with supplemental inspired oxygen (Fahlman et al. 2010, 2012) (Fig. 35.3). It is important to note that pulse oximetry may not reliably indicate hypoxemia or normoxemia. Inconsistent pulse oximetry values have been reported in polar bears anesthetized with ZT and in brown bears anesthetized with MZT (Cattet et al. 1999b; Fahlman et al. 2010). Since pulse oximeters tend to overestimate saturation at lower ranges of partial pressure of arterial oxygen (PaO_2), hypoxemia can be missed if arterial oxygenation is evaluated only by pulse oximetry.

Cardiovascular System

The cardiovascular system should be closely monitored. Polar bears, black bears, and brown bears anesthetized with ZT commonly have heart rates of 70–90 beats per minute (bpm). Heart rate is slightly lower with XZT and MZT, 50–70 bpm. Bradycardia is common with medetomidine-ketamine, and heart rates of 30–40 bpm are not uncommon in polar bears. The femoral artery is the best location to palpate a pulse, but the brachial artery can also be used.

Blood pressure can be measured directly from the femoral artery. Oscillometric monitors can be useful in smaller bears. The cuff width should be approximately 0.4 times the limb circumference (Fig. 35.4). Mean arterial pressure in polar bears anesthetized with ZT was approximately 150 mmHg (Caulkett et al. 1999). Polar bears anesthetized with MZT are hypertensive (mean arterial pressure >200 mmHg) (Caulkett et al. 1999). Black bears are also hypertensive with this combination (Caulkett & Cattet 1997).

Thermoregulation

Rectal temperature should be closely monitored. Rectal temperature tends to decrease over time with ZT, whereas it tends to increase with XZT and MZT. In hot ambient temperatures, after intense physical activity, and in stressed animals, body temperature can increase to dangerous levels (>40°C). Effective treatment of hyperthermia may include cooling the animal with snow or water, fanning, IV drip, cold water enema, and intranasal oxygen (Ozeki et al. 2015). In extreme situations termination of the procedure and administration of an alpha-2 antagonist can also be considered as this will tend to normalize body temperature (Ozeki et al. 2015).

Supportive Care

The eyes should always be lubricated, and caution must be exercised to avoid corneal abrasions or ulceration. A blindfold should be placed to protect the eyes and decrease visual stimuli.

Bears can be positioned in sternal or lateral recumbency, but can also be positioned in dorsal recumbency with few adverse effects.

When possible, anesthesia should be reversed in free-ranging animals. This is particularly important for sows with cubs, and in areas where high concentrations of bears are present.

Translocation of bears in cargo nets by helicopter can result in mortality (Cattet et al. 1999b). Slinging in a cargo net can induce hypertension and hypoxemia (Cattet et al. 1999b). Ideally, these bears should be transported or weighed with their head and neck extended and their body extended (Cattet et al. 1999b). We have used a stretcher-type sling or a wooden board to facilitate this positioning. If bears are to be relocated in culvert traps, they should be awake before transport.

Species-Specific Considerations

Refer to Table 35.1 for dose recommendations.

Polar Bear (Ursus Maritimus)

Polar bears can have substantial fat deposits throughout the year. The shoulder and neck are often used for drug delivery, but care must be taken to avoid hitting the thorax. Male polar bears can be large and heavy. Potent drug combinations are required to keep drug volume and dart size to a minimum. Polar bears should be positioned carefully to avoid excessive pressure on limbs, which could result in compartment syndrome. In areas where large numbers of polar bears congregate, reversible anesthetic protocols should be considered. This will decrease the risk of predation from other bears. Reversible protocols should also be considered for mother bears with cubs.

Zolazepam-tiletamine will produce reliable immobilization, but can also result in prolonged recoveries (Caulkett et al. 1999). Volume requirements are high, which will necessitate the use of large darts, and this can result in excessive tissue trauma.

Xylazine-zolazepam-tiletamine can be delivered at approximately half the volume of zolazepam-tiletamine alone. Although potentially reversible with yohimbine or atipamezole, reversal of this mixture is not reliable. This is probably due to residual zolazepam-tiletamine sedation. Animals immobilized with this mixture will benefit from supplemental inspired oxygen (Cattet et al. 2003b).

Medetomidine-zolazepam-tiletamine will produce reliable immobilization. This combination will produce rapid onset of immobilization, can be delivered in a small volume, and is readily reversible with atipamezole, administered at five times the medetomidine dose. Animals will benefit from supplemental inspired oxygen (Caulkett et al. 1999).

Brown Bear (Ursus Arctos)

A variety of techniques can be used to anesthetize brown bears. Drug combinations should be reliable and potent. Reversible combinations are desirable in certain situations, particularly in free-ranging sows with cubs. Brown bears enter a hypometabolic state in the winter. Drug requirements are greatly decreased at this time (Evans et al. 2012, 2016).

Zolazepam-tiletamine is routinely used for management of brown bears in North America. Zolazepam-tiletamine will produce reliable immobilization, but also results in prolonged recoveries. High volume requirements necessitate the use of large darts, which can produce excessive tissue trauma.

Xylazine-zolazepam-tiletamine is potentially reversible with yohimbine or atipamezole. Reversal of this mixture is not reliable. This is probably due to residual effects of zolazepam-tiletamine. Animals immobilized with this mixture will benefit from supplemental inspired oxygen (Cattet et al. 2003c).

Medetomidine-zolazepam-tiletamine will induce a rapid onset of immobilization and can be delivered in a small volume. It is partially reversible with atipamezole, administered at five times the medetomidine dose. MZT is the drug combination of choice used for immobilization of brown bears in Scandinavia (Fahlman et al. 2011; Arnemo & Evans 2017). Doses and physiological evaluation of capture and MZT anesthesia in brown bears have been described in detail (Fahlman et al. 2011; Arnemo & Evans 2017).

Low doses of MZT + ketamine (MZTK) can be used for anesthesia of free-ranging brown bears during hibernation in the wild (Evans et al. 2012, 2016). Two- to 4-year-old bears were darted in their dens with medetomidine at 0.02–0.6 mg/kg, ZT at 0.9–2.8 mg/kg, and ketamine at 1.1–3.0 mg/kg. Hypoxemia was corrected with intranasal oxygen therapy. One bear that was darted with the higher dose of MZTK developed apnea and was intubated followed by manual ventilation with a bag valve mask.

American Black Bears (Ursus Americanus)

These bears have a more placid nature than brown bears, and dose requirements are lower with zolazepam-tiletamine. A variety of drugging techniques can be used. Black bears are frequently immobilized for management purposes in North America. The bear may be snared or captured in a culvert trap prior to drug administration. Physical capture of the bear will facilitate drug administration and limit mobility on induction. Free-ranging bears are often treed prior to drug administration. This will also facilitate drug administration and decrease mobility on induction. Ideally, a coniferous tree should be picked, as the boughs will help to break the bear's fall on induction. Air-filled bags or mattresses can be placed at the base of the tree to soften the landing. Bears that remain in the tree, after induction, may need to be placed in a sling and lowered with ropes.

Zolazepam-tiletamine will produce reliable immobilization and can be delivered at a relatively low volume in most bears. Prolonged recovery is the major limitation of this technique. Dexmedetomidine-zolazepam-tiletamine has been described in black bears with minimum impairment of respiratory function and good reversibility (Coltrane et al. 2015).

Medetomidine-zolazepam-tiletamine will induce a rapid onset of immobilization, can be delivered in a small volume, and is readily reversible with atipamezole, administered at five times the medetomidine dose. Animals will benefit from supplemental inspired oxygen (Caulkett & Cattet 1997).

Butorphanol-azaperone-medetomidine or nalmefene-azaperone-medetomidine have been successfully used in black bears. These combinations offer good reversibility and low volume requirements. Supplemental oxygen should be considered to treat hypoxemia (Wolfe et al. 2008)

Xylazine-ketamine can be used, cautiously, in black bears. It is important to monitor the bear closely for signs of arousal. Rapid nystagmus and brisk tongue withdrawal are signs of light anesthesia. An IV top-up of xylazine-ketamine at one-third of the original dose may be considered, or procedures may be terminated.

Sloth Bear (Melurus Ursinus), Sun Bear (Ursus Malayanus), Asiatic Black Bear (Ursus Thibetanus), Spectacled Bear (Tremarctos Ornatus), and Giant Panda (Ailuropda Melanoleucia)

Zolazepam-tiletamine, in combination with medetomidine and ketamine, has been used in sloth bears, spectacled bears, and giant pandas. The combination was used for induction prior to maintenance with volatile or injectable anesthesia. The most common side effect was nausea and ptyalism. Occasional seizure-like activity was noted in a small number of spectacled bears and pandas (McEntire et al. 2020). Sloth bears are commonly anesthetized with xylazine-ketamine (Shanmugam et al. 2011). Sun bears have been anesthetized with medetomidine-ketamine (Kreeger et al. 2023) or medetomidine-zolazepam-tiletamine (Onuma 2003). Giant pandas have been anesthetized with ketamine-xylazine (Kreeger et al. 2023). One study described the use of dexmedetomidine combined with zolazepam-tiletamine in wild giant pandas (Jin et al. 2016). The combination was found to be effective in these animals and may be a good alternative to some of the older combinations still being used in this species.

Analgesia and Analgesic Techniques

There is not a great deal of information available in the literature concerning analgesia in bears. Meloxicam has been used for postoperative pain control at a dose of 0.1–0.2 mg/kg subcutaneous (SC) or per os (PO) in Asiatic black bears and brown bears (Bourne et al. 2010). Tramadol has been administered to Asiatic black bears at a dose of 4–6 mg/kg PO twice daily.

Opioid analgesics can be considered for intraoperative analgesia. Butorphanol may be administered at a dose of 0.2 mg/kg IM. The author (Caulkett) has used hydromorphone at a dose of 0.1 mg/kg IM for analgesia in black bears. Local anesthetic techniques should be considered for painful procedures. Local anesthetics can be administered via infiltration of surgical sites, and many specific nerve blocks may be extrapolated from canine techniques (Fig. 35.5).

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Figure 35.5 Administration of an infraorbital block in a spectacled bear.

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36

Procyonids and Mustelids

Noha Abou-Madhi

Introduction

Recent phylogenic studies have reconfigured the taxonomy of these small to medium-sized carnivoran mammals and the superfamily Musteloidea now encompasses the families of Mustelidae, Mephitidae, Procyonidae, and Ailuridae (Wesley-Hunt & Flynn 2005; Yu et al. 2011). Despite their variable natural history and species-specific characteristics, they generally have an elongated body and long tails, and share susceptibility to important infectious diseases. Protocols and challenges for physical restraint and chemical anesthesia are in many ways similar to those encountered with domestic and wild species but the metabolic impact of stress associated with restraint, capture, and general anesthesia is often underestimated. Ferrets manually restrained showed significant increase in their plasma concentration of cortisol and adrenocorticotropic hormone and a decrease in alpha-melanocyte stimulating hormone (MSH), while isoflurane anesthesia resulted in a significant increase in plasma MSH directly after induction (Schoemaker et al. 2003). Preemptive treatment for exertional rhabdomyolysis and clostridial enterotoxemia should be considered when capturing or treating wild or refractory neartic otters. Applying the basic principles of restraint and anesthesia is essential to ensuring a successful outcome of emergency and routine procedures. Specialized equipment and supplies (small endotracheal tubes, special face masks, small intravenous and intraosseous catheters, and cannulas) should be on hand at the outset of the procedure. Additionally, emergency drug doses should be calculated and drawn up in labeled syringes or vials prior to beginning the anesthetic procedures. Attempting to calculate, draw up, and administer emergency drugs for a 50-g (1.8-oz) ermine can be problematic at the time of an anesthetic emergency. Drug dosages used are extrapolated from the dog or cat unless specific doses are available for species such as the ferret (Morrisey & Johnston 2018).

Species-Specific Physiology

Mustelidae and Mephitidae

The family of Mephitidae comprises 12 species, including the skunks and stink badgers. Skunks are widespread in the Americas and stink badgers are found in Southeast Asia. There are 56–60 species of mutelids, including the wolverine, fisher, nearctic otter, sea otter, polecat, marten, ferret, badger, tayra, and grison. Mustelids are distributed in all continents except Antarctica and Australia. The otters have the widest distribution, being found in North, Central, and South America as well as in Africa, Europe, and Asia. Mustelid habitats range from Arctic tundra to tropical rainforest and they are terrestrial, arboreal, fossorial, and found on the open seas, as with the sea otter. Many are small (<l kg or 2.2 lb), while some are relatively large (45 kg or 99 lb) when compared to members of other mammalian families. The smallest, the weasel, rarely exceeds 19 cm (7.5 inches) in length. The giant river otter is the longest mustelid, reaching a length of up to 190 cm (6.2 feet). All have five toes on each foot, with nonretractable claws. Sexual dimorphism is marked in most mustelids but is less apparent in badgers and otters. Male skull size may be 5–25% longer than that of females.

Prominent sharp canines, cutting carnassials, heavy premolars, and powerful jaws that are capable of crushing thick bones are common characteristics of these species. The dental formula varies within and between subfamilies. As examples, the European common weasel has the dental formula of I3/3, C1/1, P3/3, M1/2 = 36, whereas the dental formula of the wolverine is I3/3, C1/1, P4/4, M1/2 = 36.

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Mustelids and mephitids lack both a clavicle and an appendix. The otters, like other aquatic carnivores, have a multilobulated, reniculated kidney (Baitchman & Kollias 2000). The renal lobules are firmly compressed against each other, forming a somewhat solid kidney.

Musk is present in most species and produced by modified sebaceous glands, stored in perianal sacs, and in skunks these can deliver a powerful deterrent to perceived threatening situations. The composition of musk varies between species and is used for demarcation of territory, often for generations. In the case of skunks, musk is used for defense purposes. The reproductive biology of mustelids and mephitids also varies between species, with males and females of most species living separately the majority of the year. They are induced ovulators and require vigorous copulation for ovulation. Males have a baculum (os penis) and females an os clitoris. Delayed implantation, up to 10 months, is exhibited in 16/67 mustelid and mephitids species. The mediators of delayed implantation are largely unknown and may include environmental factors such as photoperiod. Delayed implantation can occur in semidormancy.

Procyonidae and Ailuridae

The Procyonidae are small- to medium-sized, long-bodied, and long-tailed mammals. There are 16 New World procyonid species including the raccoon, white-nosed coati, and the kinkajou. New World procyonids inhabit temperate, tropical, and neotropical regions. Procyonids are generally omnivores but are known to be opportunistic carnivores. The dental formula is I3/3, C1/1, P4/4, M2/2 = 40. An exception to this formula is the kinkajou, which has P3/3. The molars of all procyonids are large and well adapted to crushing. There is some interspecies variation in dentition, which relates to food preferences. Procyonids have highly specialized gastrointestinal systems with all members of the family lacking a cecum. The feet of procyonids have five toes and they walk partly or wholly on the soles of their feet (plantigrade). Claws are nonretractable, except the ring-tails, which have semiretractable claws on their front feet. All procyonids have agile front feet, which make them excellent climbers. Excepting the coati, procyonids are generally nocturnal or crepuscular. Females usually breed in the spring of their first year and males from their second year on. The small procyonids live 10–15 years in captivity. The authors are aware of a male kinkajou that lived until 32 years of age in a zoo. In the wild, it is unusual for procyonids to exceed 7 years of age.

Red pandas (family Ailuridae) are small (4–8 kg) herbivorous animals feeding mostly on bamboo in the wild. Their dental formula is I3/3, C1/1, P3/3-4, M2/2 = 36–38 teeth. As procyonids, they do not possess a cecum. The sole of their feet is covered with hair and has a central pad scent gland. The enlarged radial sesamoid bone (the "panda's thumb") helps grasp bamboo branches. Their thick pelage is adapted for cool environmental temperatures and red pandas may be prone to hyperthermia in hot and humid environments (Ramsay 2015).

Preanesthetic Preparation

Depending on the circumstances surrounding a procedure, preanesthetic preparation may be limited to the acquisition of the proper equipment or may include preanesthetic fasting, basic blood work (ferrets), and/or sedation prior to induction. Due to their high metabolic rate, potential to develop perianesthetic hypoglycemia, and their fast gastrointestinal transit time, ferrets are usually fasted for less than 4 hours (Hawkins & Pascoe 2012). Premedication with gastro-protectants and prokinetic agents may be indicated to avoid postanesthetic nausea and vomiting in ferrets (maropitant 1 mg/kg per os [PO], subcutaneous [SC] once every 24 hours, odansetron 1 mg/kg PO every 12 hours, famotidine 0.25–0.5 mg/kg SC, PO, intravenous [IV] once every 24 hours) (Hoefer et al. 2012). If preanesthetic administration is not an option, some of these drugs can be given parenterally under anesthesia.

Physical Restraint

In captive Musteloidea, operant conditioning training can facilitate the administration of drugs via hand injections.

Animals may be habituated to station in narrow tunnels or enter squeeze cages or small cages for a more controlled administration of induction drugs (Fig. 36.1). This reduces the level of stress, optimizes the effect of the drugs, and overall facilitates a smoother anesthesia and recovery.



Figure 36.1 Operant condition facilitates the administration of parenteral drugs when animals are habituated to station in these "tunnels".

Physical restraint may be possible for short and nonpainful procedures in selected captive laid-back or smaller individuals. Nets, towels, and heavy gloves are necessary for the protection of the handlers; basic procedures may be performed in awake animals but may also be associated with an unacceptable level of stress. Manual restraint in free-ranging animals is often used for very brief procedures (release of an animal from a trap, transfer to a cage) and extreme caution is exercised to avoid bite wounds and anal gland discharges. In general, chemical restraint is indicated for the benefit of the handlers and the animals.

General Anesthesia

Injectable Drugs

Delivery of injectable agents to procyonids and mustelids, as with other wild mammals, often requires some form of restraint (physical or with restraint equipment, less frequently using remote delivery systems), and specialized supplies and equipment. Squeeze cages or boxes and transfer boxes greatly facilitate the delivery of injectable drugs and help to minimize stress while maximizing the quality of induction, immobilization, and recovery of procyonids and mustelids. As an example, recently captured nearctic river otters (*Lontra canadensis*) are transferred from their holding cages to a small squeeze cage and injected with ketamine (10–15 mg/kg) and midazolam (0.3–0.4 mg/kg), the squeeze cage is covered with a drape or towel and minimal environmental noise occurs, and the otters are consistently immobilized in 10–12 minutes and remain so for 35–45 minutes. Following a complete administration of induction drugs, it is essential to maintaining a quiet and dark environment to allow the otters to reach an acceptable level of anesthesia. Complications such as hyperthermia may occur due to excessive movement, and, similarly, stormy recoveries with hyperkinesis, vocalization, and disorientation will ensue if the animal is stimulated (Kollias 1999).

Premedication may be used in calmer and habituated individuals (e.g., in ferrets, using butorphanol, midazolam), but more often a single administration of induction drugs is preferred to avoid multiple restraints in fractious animals. Numerous general and specific single drugs or drug combinations have been reported for chemical restraint, immobilization, and anesthesia for various species and are summarized in Table 36.1. Species-specific variations are noted, especially when comparing field anesthesia of free-ranging individuals to the chemical restraint of captive animals (Thornton et al. 2005).

The combinations of ketamine/midazolam or ketamine/medetomidine (or dexmedetomidine) with or without midazolam, provide safe and rapid induction, stable anesthesia, and rapid recovery. In most balanced anesthetic combinations, midazolam has now replaced diazepam and the addition of a potent alpha-2 agonist leads to faster recoveries since a smaller dose of ketamine is often required and reversal agents are available. Supplemental oxygen should be provided when injectable drugs are used, and especially when an alpha-2 agonist is included in the anesthetic protocol. Excitement during recovery has been reported when atipamezole is used to reverse dexmedetomidine or medetomidine and strategic use of antagonistic agents is indicated (e.g., decreasing doses after prolonged procedures, adding a benzodiazepine if larger doses of ketamine were necessary). In the author's experience, the doses listed in Tables 36.1 and 36.2 are guidelines for use and often require modification when applied to specific individuals or collections of animals and whether they are used for captive, recently captured, or free-ranging individuals. Some of the combinations described are older but offer alternate options if the newer drugs are not available to the veterinarian.

Inhaled Anesthetics

Generally, induction of inhalation anesthesia is facilitated by prior administration of injectable agents (Tables 36.1 and 36.2) and as recommended in standard veterinary anesthesia texts for domestic dogs and cats (Muir & Hubbell 2007; Seymour & Gleed 1999). Isoflurane and sevoflurane have been shown to be safe and efficacious and are inhalant agents of choice in these species (Denver 2000; Gaynor et al. 1997; Schumacher 1996). Following administration of preanesthetic agents or parenteral drugs, some animals may still require restraint. They can be held in a towel or with gloves and the inhalant agent is provided via face mask or induction chamber. Alternatively, chamber induction with no prior injectable drugs may be achieved in smaller animals. This technique requires less handling of the animal but also increases the potential for human exposure to inhalant drugs when the box is opened. Once the animal loses its righting reflex, it is masked until it is intubated or maintained on a face mask. Nontraumatic instillation of a small amount of lidocaine (calculate less 1 mg/kg) directly on the glottis may facilitate intubation. With intubation or face-mask maintenance, inhalants should be administered using a nonrebreathing circuit (Ayre's T-piece or Bain system). Oxygen flow should be two to three times the minute ventilation (~200–350 mL/kg/min) (Cantwell 2001). For large species, a rebreathing system is selected. Anesthesia monitoring, including by

Table 36.1 Procyonidae and Ailuridae chemical restraint agent doses (IM).

Adult Weight Range	Agents and Doses	Reversal Agent	Comments	Reference
Coatimundi (*Nasua* spp.) 3–6 kg	Ketamine 20 mg/kg + xylazine 1 mg/kg	None reported		Seal & Kreeger (1987)
Coatimundi (*Nasua* spp.) 3–13 kg	Medetomidine 0.051–0.064 mg/kg + ketamine 2.5–7.7 mg/kg + butorphanol 0.34–0.36 mg/kg	Atipamezole 0.25 mg/kg half SC, half IM	Prolonged recovery in some cases with higher ketamine doses	Georoff et al. (2004)
Olingo (*Bassaricyon gabbii*) 0.9–1.5 kg	Tiletamine/zolazepam 5 mg/kg		Supplement with ketamine as needed if inhalation anesthetics are not available 5 mg/kg	Seal & Kreeger (1987)
Raccoon (*Procyon lotor*) 2–12 kg	Ketamine 5.5 mg/kg + medetomidine 0.055 mg/kg	Atipamezole 0.375 mg/kg		Kreeger & Arnemo (2018)
	Ketamine 20 mg/kg + xylazine 4 mg/kg	Yohimbine 0.15 mg/kg	Alternative choice	Kreeger & Arnemo (2018)
	Ketamine 20 mg/kg + acepromazine 0.1 mg/kg		Alternative choice 60 minutes handling time, 120 minutes to full recovery	Belant (2004)
	Tiletamine/zolazepam 3 mg/kg + xylazine 2 mg/kg		Alternative choice	Belant (2004)
Kinkajou (*Potos flavus*) 1.4–4.6 kg	Ketamine 5.5 mg/kg + medetomidine 0.1 mg/kg Tiletamine/zolazepam 10 mg/kg	Atipamezole 0.5 mg/kg	Wild/free-ranging kinkajous Alternative choice Alternative choice	Fournier et al. (1998); Belant (2004)
Ringtail (*Bassariscus astutus*) 0.8–1.3 kg	Tiletamine/zolazepam 10 mg/kg Ketamine 10 mg/kg + acepromazine 0.2 mg/kg			Seal & Kreeger (1987); Jessup (1982)
Red panda (*Ailurus fulgens)* 4–8 kg	Ketamine 6.6 mg/kg + medetomidine 0.08 mg/kg	Atipamezole 0.4 mg/kg		Ramsay (2015)
	Ketamine 6–9 mg/kg + xylazine 0.2–0.4 mg/kg	Yohimbine 0.125 IV, IM or SC	Alternate choice	Wolff et al. (1990)
	Tiletamine/zolazepam 4.5–6 mg/kg		Alternate choice	Wolff et al. (1990)

IM, intramuscular; IV, intravenous; SC, subcutaneous.

Table 36.2 Mustelid and mephitid chemical restraint doses (IM).

Adult Weight Range	Agents and Doses	Reversal Agent	Comments	Reference
Badger, European (*Meles meles*) 5.5–12.5 kg (mean 9.3 kg)	Ketamine 20 mg/kg	None	Recovery considered prolonged; mean HR 170 bpm	Thornton et al. (2005)
	Ketamine 15 mg/kg + midazolam 0.4 mg/kg	None given	Authors mentioned few advantages over ketamine alone; mean HR 150 bpm	Thornton et al. (2005)
	Ketamine 10 mg/kg + midazolam 1 mg/kg	None given	Authors mentioned few advantages over ketamine alone; mean HR 160 bpm	Thornton et al. (2005)
	Ketamine 5 mg/kg + medetomidine 0.08 mg/kg	Atipamezole (decimal error noted in doses listed by authors)	Best quality of maintenance of anesthesia; lower mean HR than with other agents used (mean = 100 bpm); mean arterial pressure higher than with other agents used (mean = 150 mmHg); early reversal with antipamezole may cause excitement	Thornton et al. (2005)
Badger, European (*Meles meles*)	Ketamine 5–10 mg/kg + medetomidine 0.05–0.1 mg/kg	Atipamezole 0.25–0.5 mg/kg	Preferred combination	Fernandez-Moran et al. (2001)
	Tiletamine/zolazepam 2.5 mg/kg + medetomidine 0.04 mg/kg	Atipamezole 0.2 mg/kg	Alternative combination	Fernandez-Moran et al. (2001)
Badger, European (*Meles meles*) 10–16 kg	Tiletamine/zolazepam 10 mg/kg		Supplement with ketamine (5 mg/kg)	Kreeger & Arnemo (2018)
	Ketamine 15 mg/kg + acepromazine 0.4 mg/kg			Kreeger & Arnemo (2018)
	Ketamine 16 mg/kg + xylazine 6 mg/kg			Kreeger & Arnemo (2018)
Badger, European (*Meles meles*) 5.5–12.5 kg $n = 93$ badgers were trapped and transported to a central holding station prior to anesthesia	Ketamine 2 mg/kg		Three combination protocols were compared to the administration of ketamine only. Ketamine alone provided rapid induction and adequate level of anesthesia but caused poor recovery in >50% of the animals. Quality of induction was similar (range 3–22 minutes, mean 6 minutes); mucous membranes were paler with combination protocols (vs. ketamine alone). Recovery (37–39 minutes) with no reversals; sudden arousal or recovery occurred in 14/93 (15%) of the badgers when combination protocols were used and was statistically linked to increasing rectal temperature.	McLaren et al. (2005a,b)
	Medetomidine 0.02 mg/kg + ketamine 0.04 mg/kg + butorphanol 0.08 mg/kg	None given		McLaren et al. (2005a,b)
	Medetomidine 0.02 mg/kg + ketamine 0.04 mg/kg + butorphanol 0.06 mg/kg	None given		McLaren et al. (2005a,b)
	Medetomidine 0.02 mg/kg + ketamine 0.06 mg/kg + butorphanol 0.04 mg/kg	None given		McLaren et al. (2005a,b)

(*Continued*)

Table 36.2 (Continued)

Adult Weight Range	Agents and Doses	Reversal Agent	Comments	Reference
Badger, ferret (*Melogale moschata*) 1–3 kg	Tiletamine/zolazepam 5 mg/kg		Supplemented with ketamine (5 mg/kg)	Kreeger & Arnemo (2018)
Badger, hog (*Arctonyx collaris*) 7–14 kg	Tiletamine/zolazepam 4.4 mg/kg		Supplemented with ketamine 2.2 mg/kg	Kreeger & Arnemo (2018)
Badger, honey (ratel) (*Mellivora capensis*) 7–13 kg	Tiletamine/zolazepam 2.2 mg/kg		Supplemented with ketamine 2.2 mg/kg	McKenzie & Burroughs (1993)
Badger, American (*Taxidea taxus*) 2–14 kg	Tiletamine/zolazepam 4.4 mg/kg Ketamine 15 mg/kg + xylazine 1 mg/kg		Supplemented with ketamine 4.4 mg/kg Alternative choice	Jessup (1982); Schwantje et al. (1998)
Ermine (*Mustela erminea*) 0.05–0.365 kg	Ketamine 5 mg/kg + medetomidine 0.1 mg/kg	Atipamezole 0.5 mg/kg half IV, half IM	Supplemented with ketamine 2.5 mg/kg	McKenzie & Burroughs (1993)
Ermine (*Mustela erminea*) 0.05–0.365 kg	Tiletamine/zolazepam 11–22 mg/kg			Fernandez-Moran et al. (2001)
Black-footed ferret (*Mustela nigripes*) 0.7–1.5 kg	Ketamine 3 mg/kg + medetomidine 0.075 mg/kg	Atipamezole 0.375 mg/kg half IV, half IM		Fernandez-Moran et al. (2001)
Black-footed ferret (*Mustela nigripes*) 0.7–1.5 kg	Ketamine 35 mg/kg + diazepam 0.2 mg/kg			Kreeger & Arnemo (2018)
Ferret (*Mustela putorius*) 0.6–1.2 kg	Ketamine 25 mg/kg + xylazine 2 mg/kg		Supplemented with ketamine 12 mg/kg	Kreeger & Arnemo (2018)
	Ketamine 25 mg/kg + acepromazine 1.1 mg/kg			Kreeger & Arnemo (2018)
	Tiletamine/zolazepam 15 mg/kg		Recovery may be prolonged	Kreeger & Arnemo (2018)
	Ketamine 5 mg/kg + medetomidine 0.1 mg/kg	Atipamezole 0.5 mg/kg		
	Ketamine 10–30 mg/kg in combination with xylazine 1–2 mg/kg, diazepam 1–2 mg/kg, or acepromazine 0.05–0.30 mg/kg			Fernandez-Moran et al. (2001)
	Ketamine 25–35 mg/kg + diazepam 2–3 mg/kg		Anesthesia; poor analgesia	Morrisey & Johnston (2018)

Medetomidine 0.08 mg/kg + butorphanol 0.1 mg/kg	Atipamezole 0.4 mg/kg	Anesthesia; monitor blood pressure and ventilation	Morrisey & Johnston (2018)
Ketamine 5 mg/kg + medetomidine 0.08 mg/kg	Atipamezole 0.4 mg/kg	Induction for inhalation of anesthesia	Evans & Springsteen (1998); Wolfensohn & Lloyd (1998)
Ketamine 5 mg/kg + medetomidine 0.08 mg/kg + butorphanol 0.1 mg/kg	Atipamezole for medetomidine reversal (0.40 mg/kg) Naloxone for butorphanol reversal (0.01–0.04 mg/kg)	Induction for inhalation anesthesia	Evans & Springsteen (1998); Wolfensohn & Lloyd (1998)
Ketamine 5–10 mg/kg + midazolam 0.25–0.5 mg/kg		Induction for inhalation anesthesia	Evans & Springsteen (1998); Wolfensohn & Lloyd (1998)
Propofol 5–8 mg/kg IV	None	Induction of anesthesia	Cantwell (2001)
Diazepam 0.5–3 mg/kg SC or IM		Premedication	Cantwell 2001
Butorphanol 0.1–0.5 mg/kg	Naloxone 0.01–0.04 mg/kg	Premedication and analgesia	Cantwell (2001)
Buprenorphine 0.01–0.03 mg/kg SC, IM, IV	Naloxone 0.01–0.04 mg/kg	Premedication and analgesia	Cantwell (2001)
Oxymorphone 0.05–0.2 mg/kg SC, IM, IV	Naloxone 0.01–0.04 mg/kg	Premedication and analgesia	Cantwell (2001)
Morphine 0.2–2.0 mg/kg SC, IM	Naloxone 0.01–0.04 mg/kg	Premedication and analgesia	Cantwell (2001)
Meperidine 5–10 mg/kg SC, IM	Naloxone 0.01–0.04 mg/kg	Premedication and analgesia	Cantwell (2001)
Atropine 0.02–0.05 mg/kg	None	Premedication to decrease secretion and maintain HR	Cantwell (2001)
Glycopyrrolate 0.01 mg/kg	None	Premedication to decrease secretion and maintain HR	Cantwell (2001)
Acepromazine 0.1 mg/kg + butorphanol 0.2 mg/kg + glycopyrrolate 0.01 mg/kg	Naloxone 0.01–0.04 mg/kg	Premedication will cause moderate to deep sedation	Cantwell (2001)
Midazolam 0.5 mg/kg + oxymorphone 0.1 mg/kg + glycopyrrolate 0.01 mg/kg	Naloxone 0.01–0.04 mg/kg	Premedication: will cause moderate to deep sedation	Cantwell (2001)
Acepromazine 0.05 mg/kg + butorphanol 0.1 mg/kg + ketamine 10 mg/kg	Naloxone 0.01–0.04 mg/kg	Premedication will cause moderate to deep sedation	Cantwell (2001)

(*Continued*)

Table 36.2 (Continued)

Adult Weight Range	Agents and Doses	Reversal Agent	Comments	Reference
Ferret, European or polecat (*M. putorius*) Males: 0.84–1.04 kg ($n = 11$) Females: 0.64 kg ($n = 1$)	Ketamine 10 mg/kg + medetomidine 0.2 mg/kg	Atipamezole (1.0 mg/kg IM) injected 28–54 minutes after ketamine/medetomidine injection; standing in 1.5–9.4 minutes; ambulatory in 10–25 minutes	Free-ranging polecats; captured for clinical examination; blood collection and placement of intra-abdominal radio transmitters; induction smooth and rapid (0.7–3.9 minutes); degree of anesthesia and muscle relaxation satisfactory in most individuals; all animals exhibited decreased heart rate, respiratory rate, and temperature; hypothermia was significant and was controlled/prevented by placing animals on a warmed plastic table (37°C)	Cantwell (2001)
Fisher (*Martes pennanti*) 2.6–5.5 kg	Tiletamine/zolazepam 11 mg/kg	None given	Wild caught/trapped	Mitcheltree et al. (1999)
	Ketamine 30 mg/kg + xylazine 3 mg/kg	Atipamezole 0.02–0.06 mg/kg half IM, half SC after 45 minutes of anesthesia	Wild caught/trapped; high dose range	Mitcheltree et al. (1999)
Fisher (*Martes pennanti*) Males: 4.7–5.8 kg Females: 2.3–2.9 kg	In males: ketamine 3.2–4.2 mg/kg + medetomidine 0.062–0.078 mg/kg In females: ketamine 3.3–3.9 mg/kg + medetomidine 0.063–0.077 mg/kg	None given	Recently wild caught; mean induction time 4.6 minutes; mean downtime 142 minutes; mean alert time 147 minutes; mean recovery time 200 minutes. Mild bradycardia and hypertension; deep plane of anesthesia; calm recovery; temperature ranged 38–40°C	Dzialak et al. (2002)
	In males: ketamine 16.9–20.5 mg/kg In females: ketamine 17–21.4 mg/kg		Mean induction time 4.5 minutes; mean down time 36.2 minutes; mean alert time 40.8 minutes; mean recovery time 81.1 minutes; increased muscle tone; light depth of anesthesia (adequate for short procedures); smooth and rapid recovery	Dzialak et al. (2002)
Fisher (*Martes pennanti*) 2.6–5.5 kg	Ketamine 4 mg/kg + medetomidine 0.08 mg/kg	Atipamezole 0.4 mg/kg	Supplement with ketamine 2 mg/kg	Kreeger & Arnemo (2018)
	Tiletamine/zolazepam 3 mg/kg + xylazine 2 mg/kg			Kreeger & Arnemo (2018)

Marten (*Martes americanus*) 0.5–1.5 kg	Ketamine 10 mg/kg + medetomidine 0.2 mg/kg	Atipamezole 1 mg/kg half IM, half SC	Prone to hyperthermia; supplement with ketamine 5 mg/kg if indicated	Kreeger & Arnemo (2018)
	Ketamine 18 mg/kg + xylazine 1.6 mg/kg	Atipamezole (0.02–0.06 mg/kg) or yohimbine (0.2–0.5 mg/kg)		Kreeger & Arnemo (2018)
Mink, European (*Mustela lutreola*) Males: 0.77–1.03 kg ($n = 6$) Females: 0.42–0.54 kg ($n = 8$)	Ketamine 10 mg/kg + medetomidine 0.2 mg/kg	Atipamezole (1 mg/kg) injected IM 28.1–54.0 minutes after ketamine/medetomidine injection; standing in 1.5–9.4 minutes; ambulatory in 10–25.7 minutes	Free-ranging mink captured for clinical examination, blood collection, and placement of intra-abdominal radio transmitters. Induction smooth and rapid (0.7–3.9 minutes); degree of anesthesia and muscle relaxation satisfactory in most individuals; all animals exhibited decreased heart rate and respiratory rate, and rectal temperature. Hypotermia was significant and was controlled/prevented by placing animals on a warmed plastic table (37°C).	
Otter, neartic (American river) (*Lontra canadensis*) Males: 2.9–9.3 kg (mean 5.64 kg) Females: 3.6–8 kg (mean 5.5 kg)	For males and females >4.5 kg: ketamine 15 mg/kg + midazolam 0.3 mg/kg or diazepam 0.5 mg/kg For males and females <4.5 kg: ketamine 20 mg/kg + midazolam 0.30 mg/kg or diazepam 0.5 mg/kg	None used	Supplemented with 20–30 mg total dose of ketamine or isoflurane (0.5–1%) delivered via face mask	Kollias (1999)
Otter, neartic (American river) (*Lontra canadensis*) Males and females combined (free-ranging); in some geographic locations, males may be 17% heavier than females Males and females combined (captive) 5.7–13 kg	Ketamine 10 mg/kg + midazolam 0.25 mg/kg	None given	Highly recommended	Petrini et al. (2001); Spellman (1999)
	Ketamine 2.5 mg/kg + medetomidine 0.025 mg/kg	Atipamezole 0.125 mg/kg	Avoid in hypothermic otters May need higher doses (ketamine 3.5 mg/kg + medetomidine 0.035 mg/kg) though respiratory depression is more likely	Petrini et al. (2001); Spellman (1999)
	Titelamine/zolazepam 4–8 mg/kg	Flumazenil 0.08 mg/kg	Recovery may be prolonged without flumazenil	Petrini et al. (2001); Spellman (1999)
	Ketamine 10 mg/kg	None	Expect muscle rigidity and variable duration of anesthesia	Petrini et al. (2001); Spellman (1999)
	Ketamine 10 mg/kg + diazepam 0.5–1.0 mg/kg	None given	Prolonged recovery when compared to ketamine and midazolam combination	Petrini et al. (2001); Spellman (1999)
	Ketamine 5–10 mg/kg + xylazine 1–2 mg/kg	Yohimbine 0.125 mg/kg	Variable effects from heavy sedation to immobilization Possible respiratory depression	Petrini et al. (2001); Spellman (1999)
	Azaperone 0.1 mg/kg + fentanyl 0.1–0.2 mg/kg	Naloxone 0.04 mg/kg	Not recommended: reports of fatal complications	Petrini et al. (2001); Spellman (1999)

(*Continued*)

Table 36.2 (Continued)

Adult Weight Range	Agents and Doses	Reversal Agent	Comments	Reference
Otter, Asian small clawed (*Aonyx cinerea*)	Ketamine 5 mg/kg + medetomidine 0.12 mg/kg	Atipamezole 0.6 mg/kg IM	Supplement with ketamine 2.5 mg/kg	Kreeger & Arnemo (2018)
	Ketamine 10 mg/kg + midazolam 0.3 mg/kg			Kreeger & Arnemo (2018)
	Tiletamine/zolazepam 5.5 mg/kg	Flumazenil 0.08 mg/kg IM		Petrini et al. (2001); Spellman (1999)
Otter, Asian clawless (*Aonyx capensis*) 10–12 kg	Tiletamine/zolazepam 5 mg/kg	None given	Supplement with ketamine (2.5 mg/kg) IM	Kreeger & Arnemo (2018)
	Ketamine 8 mg/kg + xylazine 1 mg/kg	Yohimbine 0.125 mg/kg IV		Kreeger & Arnemo (2018)
Otter, sea (*Enhydra lutris*) Males: 22–45 kg Females: 15–32 kg	Recommended combination: fentanyl 0.22 mg/kg + midazolam 0.07 mg/kg	Midazolam usually not reversed unless animal is debilitated Naltrexone is used at 1.5–2 times the dose of fentanyl	For induction of anesthesia Note: Ketamine has a narrower margin of safety in sea otters. Meperidine alone may cause diaphragmatic spasms and respiratory depression.	Haulena & Schmitt (2018)
	Alternative protocols used for sedation in captive sea otters (but unreliable effects in wild sea otters) Dexmedetomidine alone (375 μg/m^2) Dexmedetomidine 0.0075 mg/kg + midazolam 0.05 mg/kg + butorphanol 0.5 mg/kg Dexmedetomidine 0.01–0.02 mg/kg + butorphanol 0.2 mg/kg	For dexmedetomidine: atipamezole 0.075 mg/kg For butorphanol: naltrexone 0.08 mg/kg		Haulena & Schmitt (2018)
	Previously used combinations: fentanyl 0.05 mg/kg + azaperone 0.2 mg/kg		Recommended for field use	Haulena & Schmitt (2018); Williams (1986)
	Fentanyl 0.3 mg/kg + diazepam 0.1 mg/kg	Naltrexone 0.6 mg/kg		Kreeger & Arnemo (2018)
	Fentanyl 0.1 ± 0.02 mg/kg + azaperone 0.5 ± 0.02 mg/kg + diazepam 0.1 ± 0.01 mg/kg, $n = 61$	None used	Deeper sedation than fentanyl/diazepam and duration up to 2.5 hours	Sawyer & Williams (1996)
	Fentanyl 0.1 ± 0.006 mg/kg + azaperone 0.14 ± 0.01 mg/kg + diazepam 0.2 ± 0.01 mg/kg, $n = 32$	None used	Deeper sedation than fentanyl/diazepam and duration up to 2.5 hours	Sawyer & Williams (1996); Haulena & Schmitt (2018)

Otter, sea (*Enhydra lutris*) Males: average 25.6 kg ($n = 230$) Females: average 21.1 kg ($n = 367$)	Alternative protocols: For surgical procedures: fentanyl 0.33 mg/kg + diazepam 0.11 mg/kg For nonsurgical biological sample collection procedures: fentanyl 0.22 mg/kg + diazepam 0.07 mg/kg	Naltrexone administered at two times the total dose of fentanyl (half IV, half IM); renarcotization noted when using naloxone to antagonize fentanyl	Free-ranging otters ($n = 597$) immobilized for collection of biological samples and for surgical instrumentation; smooth induction with minimal need for supplemental anesthesia during procedures lasting 30–40 minutes. Only one anesthesia-related mortality. Reversal with naloxone has led to renarcotization. Reversal with naltrexone occurred in 1–3 minutes and no opioid recycling was observed with that antagonist. Tremor and rigidity reported.	Monson et al. (2001)
Otter, (European) Eurasian (*Lutra lutra*) Males and females: 3–8.7 kg (mean 5.3 kg) ($n = 38, 82$ procedures)	Ketamine 3.4–6.6 mg/kg + medetomidine 0.034–0.066 mg/kg Recommendation: ketamine 5 mg/kg + medetomidine 0.05 mg/kg	Atipamezole given 30–40 minutes after induction at 5 times the medetomidine dose. Animals were able to move in <5 minutes. Ataxia noted but no resedation Atipamezole 0.25 mg/kg	Translocation project Mean induction time (5.5 ± 3.2 minutes), mean HR 95 bpm, mean respiratory rate 32 respirations per minute, oxyhemoglobin saturation 93%. Bradycardia reported. May cause hypothermia in cold environments. Supplemented with ketamine (2.5 mg/kg) if needed	Fernandez-Moran et al. (2001)
Otter, (European) Eurasian (*Lutra lutra*) 3–14 kg	Ketamine 18 mg/kg + diazepam 0.4 mg/kg	None given		Kulken (1988)
Otter, spotted-necked (*Lutra maculicollis*) Average 4 kg	Tiletamine/zolazepam 5 mg/kg	None given	For free-ranging otters; supplement with ketamine (5 mg/kg)	McKenzie & Burroughs 1993
	Ketamine 5–8 mg/kg + xylazine 0.5–1.0 mg/kg	None given	Alternative combination	McKenzie & Burroughs (1993)
Skunk, hog nosed (*Conepatus leuconotus*) 2.3–4.5 kg	Tiletamine/zolazepam 10 mg/kg	None given	Supplement with ketamine (10 mg/kg)	Seal & Kreeger (1987)
	Ketamine 15 mg/kg + acepromazine 0.2 mg/kg	None given	Alternate combination	Seal & Kreeger (1987)
Skunk, hooded (*Mephitis macroura*) 0.7–2.5 kg	Tiletamine/zolazepam 10 mg/kg	None given	Supplement with ketamine 10 mg/kg	Seal & Kreeger (1987)
	Ketamine 15 mg/kg + acepromazine 0.2 mg/kg	None given	Alternate combination	Seal & Kreeger (1987)
Skunk, striped (*Mephitis mephitis*) 2–3 kg	Tiletamine/zolazepam 10 mg/kg	None given	Field immobilization of free-ranging skunks Supplement with 10 mg/kg ketamine	Larivière & Messier (1996)

(*Continued*)

Table 36.2 (Continued)

Adult Weight Range	Agents and Doses	Reversal Agent	Comments	Reference
Kits 0.8–1.9 kg (average 1.24 kg) ($n = 78$)	Ketamine 36.3–62 mg/kg, average 52.4 mg/kg	None	Field immobilization: scent gland removal; immobilization time 1–3 minutes, surgical anesthesia 10–15 minutes, recovery 60–90 minutes. One mortality due to aspiration.	Ramsden et al. (1976)
Kits 0.5–1.82 kg (mean 1.0 kg) ($n = 43$)	Ketamine 32.9–69 mg/kg, mean 36.8 mg/kg	None	Field immobilization: scent gland removal; immobilization time 2–4 minutes, surgical anesthesia 5–10 minutes, recovery 45–74 minutes	Ramsden et al. (1976)
Kits 0.6–2.5 kg (mean 1.1 kg) ($n = 13$)	Ketamine 39.2–107.7 mg/kg, average 73.3 mg/kg	None	Field immobilization: scent gland removal; immobilization 1–4 minutes, surgical anesthesia 35–90 minutes, recovery 60–120 minutes. Better muscle relaxation than above two groups.	Ramsden et al. (1976)
Tayra (*Eira barbata*) 4–6 kg	Tiletamine/zolazepam 3.3 mg/kg	None given	Used in captive Tayra	Fernandez-Moran et al. (2001)
Weasel, long tailed (*Mustela frenata*) 0.085–0.2 kg	Same as for ermine			
Wolverine (*Gulo gulo*) 7–32 kg	Recommended: In free-ranging wolverine: ketamine 7 mg/kg + medetomidine 0.3 mg/kg Reduce doses by 50% in captive wolverines	Atipamezole (5 times dose of medetomidine, 1.5 mg/kg, given half IV, half IM)	If not down in 15 minutes repeat full dose in wild wolverines	Kreeger & Arnemo (2018)
	Alternate combination: ketamine 20 mg/kg + acepromazine 0.2 mg/kg	None		Kreeger & Arnemo (2018)
	Alternate combination: etorphine 0.1 mg/kg + xylazine 1 mg/kg	Diprenorphine 0.2 mg/kg + yohimbine 0.15 mg/kg		Kreeger & Arnemo (2018)

bpm, beats per minute; HR, heart rate; IM, intramuscular; IV, intravenous; SC, subcutaneous.

stethoscope, pulse oximeter, Doppler flow monitor, thermometer, capnograph, ECG, etc. (Fig. 36.2), is used in these species. Active monitoring of body temperature is essential to prevent hypo- and hyperthermia. Intravenous catheterization (cephalic, saphenous veins) may be challenging in smaller species, especially those with shorter legs, but IV catheters provide prompt vascular access for fluid administration and resuscitation drugs (Figs 36.3 and 36.4).

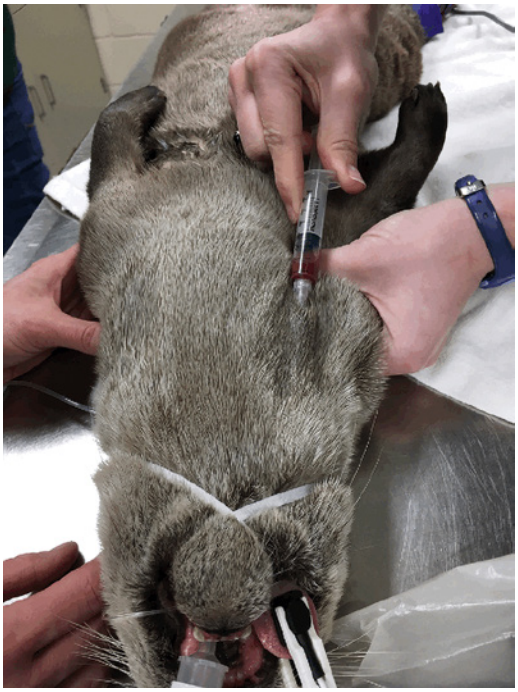


Figure 36.2 Blood collection in a North American river otter under general anesthesia. A pulse oximeter is placed on the tongue. The capnograph is connected to the endotracheal tube and a blood pressure cuff is attached to the pelvic limb.



Figure 36.3 Noninvasive blood pressure monitoring is achieved by placing the cuff on the tail or a limb (here a pelvic limb) to track trends.



Figure 36.4 Small (26-gauge) intravenous catheters can be placed in the lateral saphenous vein in ferrets. A Doppler flow monitor is placed on the ventral aspect of the base of the tail.

Recovery

Recovery from anesthesia is enhanced by using antagonists when appropriate. Atipamezole is used to antagonize medetomidine. The onset of action of atipamezole when given intramuscularly is 7–20 minutes and measures should be in place to recover the animal in a contained environment (small, dark cage). Administering half the dose of atipamezole intramuscularly and the other half subcutaneously may afford a smoother recovery. Although flumazenil can be used to reverse benzodiazepines in case of a delayed recovery, the latter is usually smoother when midazolam or zolazepam are allowed to bridge the period of time until ketamine or tiletamine are metabolized by the patient. In all cases, covering the cage of the animal and providing a quiet and protected environment will greatly enhance the quality of the recovery (Kollias 1999). Animals should be fully recovered prior to being reintroduced to their habitats and any companions.

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37

Viverrids and Herpestids

Anneke Moresco and James G. Johnson III

Body Weight

Viverrids and herpestids are small to medium-sized carnivores; these taxa include a large number of species but only a few species are regularly maintained at Association of Zoos and Aquariums (AZA) zoological institutions. This chapter will focus primarily on these species, referring to others when specific literature is not available for the species maintained in zoos. Body weights among viverrids and herpestids range from the dwarf mongoose (just over 200 g; Estes 1991) and the well-known meerkat (0.650–0.790 kg; Clutton-Brock et al. 2001) to the charismatic binturong (up to 30 kg; Moresco & Larsen 2003) and the fossa (formerly among the viverridae, now classified as Eupleridae) weighing up to 14 kg (Langer et al. 2013). There can also be variation within a species, for example females binturongs tend to be heavier than males (Moresco & Larsen 2003). Among the fossa, males are heavier than females (Langer et al. 2013). If estimating weights in meerkats, keep in mind that dominant females tend to be significantly heavier than subordinates (Clutton-Brock et al. 2001), and the dwarf mongoose male and female are similar in size (Sharpe et al. 2012).

Physical Restraint

Most viverrids and herpestid species are small enough that restraint with a net and/or leather gloves is possible, facilitating either hand injection or transfer to a crate. Loose skin, sharp teeth, and nails coupled with their feisty nature make manual restraint for induction potentially dangerous. Transfer into a carrier or closed container either from the net or by voluntary training is safer and less stressful to the animal. Once in a small carrier, waiting for the effect of injectable anesthetic or administration of gas induction is easy.

Drug Delivery Method

In zoo settings, anesthetic drug administration is most commonly done as chamber gas induction (Fig. 37.1). For this, animals are either restrained with a net and transferred to a crate or, ideally, are trained to enter a crate or other chamber that makes transportation from primary enclosure to hospital for gas administration easy. If injectable induction protocols are used, it is possible to administer via hand injection if the animal is restrained in a net or contained in a trap (fieldwork). Passive pole-syringes can also be used to inject animals in traps or in crates. Darting is not recommended in species smaller than binturongs because many are small and fast, and the probability of injury is high.

Vascular Access

In viverrids and herpestids the skin can be thick, the hair coarse, and subcutaneous tissue abundant (especially in obese zoo animals), all of which makes visualization of veins challenging.

Jugular Vein

The preferred site for phlebotomy is the jugular vein due to its accessibility and the possibility of obtaining a relatively large volume of blood (Fig. 37.2). The neck of viverrids and herpestids tends to be cylindrical, rather than cone-shaped. In binturongs the jugular vein can be small relative to body size and is located more laterally compared to dogs and cats, more similar to ferrets. In overweight animals, it is difficult to palpate or visualize the jugular vein unless the head of the animal is held slightly below the body by briefly extending the head and neck beyond the edge of the

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Figure 37.1 Chamber induction of a meerkat. Photo credit: J. Johnson/Saint Louis Zoo.



Figure 37.2 Jugular venipuncture in a banded mongoose. Photo credit: Scott Larsen.

examination table (the head should remain supported). This technique can put some additional pressure on the lungs, therefore it is important to evaluate the cardiorespiratory status of the animal using instrumentation such as observation of the mucous membranes and pulse oximetry prior to using this technique. If using anesthetic combinations that include alpha-2 agonists, veins are best visualized and accessed within 20 minutes after drug administration (Moresco & Larsen 2003). Liu et al. (2020) report using the cranial vena cava in several species of civets to obtain blood samples, but care should be taken when re-directing to avoid trauma to vital structures in the cranial thorax and neck.

Cephalic Vein

The cephalic vein is generally a valuable site for catheterization, but this may be difficult to achieve in smaller patients. In binturongs, the cephalic vein courses medially and is often large enough to place a 20-gauge ¾ or 1-inch intravenous catheter. This vein is visible after clipping hair and/or moistening with isopropyl alcohol.

Femoral Vein

Frequently, the femoral vein is not visible, but can be found adjacent to the easily palpable femoral artery. This site is useful for larger volumes but the artery can be inadvertently punctured, which may lead to formation of a large hematoma. The femoral vein is typically caudal and deep to the femoral artery; to avoid unintentional puncture of the femoral artery, direct the needle at a steep angle caudal to it to access the femoral vein. If the femoral artery is inadvertently punctured, bright-red blood with high pressure will fill the syringe; this blood sample is suitable for hematological analysis, but more prolonged pressure to the phlebotomy site will be necessary to prevent large hematoma formation from the artery.

Saphenous Vein

In binturongs, the saphenous vein can be accessed on the lateral aspect of the hind leg over the tarsus, similar to its location in dogs. It can vary considerably in size between individuals (Moresco, unpubl. data). In fossa, 10–12 mL of blood can be obtained with a 21-gauge butterfly catheter from this vein (Langer et al. 2013).

Coccygeal Vein

In some viverrids, the tail vein can be accessed for smaller amounts of blood, but it is not useful for drug administration or catheter placement. This vein can neither be seen nor palpated. The needle is inserted medially on the ventral aspect of the tail, perpendicular to the long axis; the needle is "walked" cranially, similar to the technique used in cattle. In binturongs, success is most likely when inserting the needle about 10 cm caudal to the tail base (Fig. 37.3). In most other viverrid or herpestid species, the coccygeal vein is too small to be a reliable venipuncture site.

Endotracheal Intubation

Endotracheal intubation of viverrids and herpestids is not specifically described in the literature, but it is generally straightforward because the mouth can be opened wide and the muzzle is relatively short. The glottis is usually easily visualized with an appropriately sized laryngoscope and endotracheal tube insertion is similar to that in cats (Fig. 37.4). In contrast to felids, binturongs have minimal laryngospasm, so topical lidocaine is generally not needed;



Figure 37.3 Coccygeal vein venipuncture. The binturong is in a dorsal position with the head to the right and the tail to the left. Photo credit: J. Johnson/Zoo Miami.

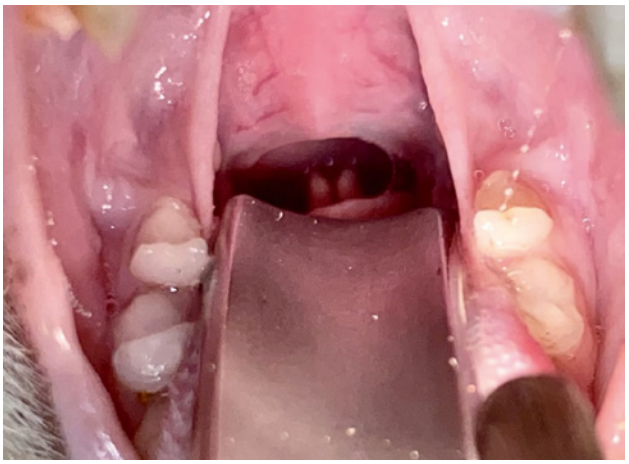


Figure 37.4 Meerkat glottis. Photo credit: J. Johnson/Saint Louis Zoo.

however, lignocaine was used to decrease laryngospasm in common palm civets to facilitate intubation in some individuals (Ahmad et al. 2019). Benzocaine-containing topical anesthetics such as Cetacaine® have been documented to cause methemoglobinemia in domestic dogs and cats (Davis et al. 1993; Krake et al. 1985) and presumptively in meerkats, and as a result are generally avoided in exotic feliform small carnivores (Gyimesi & Burns 2009). Due to the small patient size, it is important not to overinflate the cuff in order to avoid pressure necrosis. Since many viverrids and herpestids are small in size and require small-diameter endotracheal tubes, obstruction (with mucous secretions or blood) should be considered sooner when addressing ventilation problems. If intubation is not performed, nasal insufflation or a facemask may be used for oxygen supplementation (Fig. 37.5).

Sedation/Tranquilization Techniques

Haloperidol is a butyrophenone tranquilizer that has been used successfully for tranquilization in meerkats, especially when managing group dynamics and to prevent infanticide by the dam or conspecifics during the birth window and immediately post-partum. Haloperidol lactate has been used orally in meerkats at 0.2–2 mg/kg or 1.5 mg per animal (Johnson, unpubl. data).

Sedation and Anesthesia of Captive Viverrids and Herpestids

Most viverrids and herpestids are small enough that anesthesia can be successfully and quickly induced and maintained with gas anesthetics (isoflurane and sevoflurane).



Figure 37.5 Maintenance anesthesia. Left: Delivered via face mask (dwarf mongoose). Photograph credit J. Johnson/Saint Louis Zoo). Right: Delivered via endotracheal intubation (binturong). Photo credit: K. Backues.

Induction can also be achieved with injectable anesthetic drugs. The most commonly used combinations include a dissociative agent (ketamine or tiletamine) and either an alpha-2 adrenergic agonist (medetomidine, dexmedetomidine, or xylazine) or a benzodiazepine (diazepam, midazolam, or zolazepam) (Table 37.1). Although diazepam has been used intramuscularly, midazolam is preferable due to its more consistent absorption from the injection site and diazepam is recommended for intravenous use instead. An opioid or opioid agonist/antagonist (butorphanol) can be added to further reduce the need for doses of other drugs and would be useful for analgesia during and after a painful procedure (surgery, trauma/fracture repair).

Early on in wildlife medicine, the dissociative agent phencyclidine was successfully used in combination with promazine (a phenothazine) in a large number of viverrids: *A. binturong*, *A. trivirgata*, *C. ferox*, *G. genetta*, *H. derbyanus*, *N. binotata*, *P. hermaphroditus*, *P. larvata*, *P. linsang*, *V. civetta*, *V. indica*, and *V. zibetha* (Seal & Ericksson 1969). Although phencyclidine is no longer available in the United States, ketamine and tiletamine are other dissociative agents commonly used in viverrids. If dissociative agents are used alone, high muscle tone, persistent movement (paddling), rough inductions, and rough recoveries may occur (Seal & Ericksson 1969). These effects have been documented with phencyclidine and ketamine use in viverrids (Maddock 1989; Seal & Ericksson 1969), and with the use of other dissociatives in other carnivore species, therefore the use of dissociative agents by themselves is not recommended. Instead, it is recommended to use dissociatives in combination with a sedative or tranquilizer to improve muscle relaxation (see Table 37.2).

Ketamine (6 mg/kg) has been used in combination with a relatively high dose of xylazine (10 mg/kg) in the common genet (Palomares 1993). This combination requires much lower ketamine doses than that reported for ketamine alone (Maddock 1989).

Acepromazine has also been used in combination with ketamine in viverrids (Fuller et al. 1990; Maddock 1989). One study in Owston's palm civets (*Chrotogale owstoni*) and large Indian civets (*Viverra* zibetha) used ketamine-acepromazine-atropine as a combination mixed in the bottle prior to administration (King 2002). Acepromazine was chosen to decrease the risk of vomiting, which has been reported with the use of xylazine (Mudappa & Chellam 2001; Streicher 2001). Inductions were relatively quick (~7–9 minutes) and no vomiting was observed. This study only monitored body temperature, heart rate, and recovery. Body temperature did decrease substantially, heart rate averaged 154 beats per minute in the palm civets, and hyperthermia was noted in the Indian civets (King 2002). The main disadvantages of this combination are that acepromazine has a long duration of action and that none of the drugs used are reversible. Metoclopramide has been used in binturongs during ketamine-medetomidine immobilization to counter vomiting associated with medetomidine administration (Moresco, unpubl. data). Drugs such as maropitant (Cerenia®) and famotidine at feline dosages can also be considered to mitigate nausea and gastrointestinal upset associated with anesthesia in viverrids and herpestids.

Table 37.1 Recommended drug combinations for immobilization/anesthesia of viverrids and herpestids.

Species	Drug Combination	For Antagonist	Comments	Reference
Binturong (*Arctictis binturong*)	Ketamine (4 mg/kg), medetomidine(0.04 mg/kg), butorphanol (0.4 mg/kg)	Atipamezole (5 mg/mg medetomidine)	Slight hypertension	Moresco & Larsen (2003)
Banded mongoose (*Mungos mungo*)	Isofluorane (chamber induction 5%, then decrease for maintenance)	NA		Dzanic et al. (2021)
Meerkat (*Suricata suricatta*)	Isofluorane (chamber induction 5%, then decrease for maintenance)	NA		Naples et al. (2010)
Dwarf mongoose	Isofluorane (chamber induction 5%, then decrease for maintenance)	NA		Dzanic et al. (2021)
Common genet (*Geneta genetta*)	Ketamine (7 mg/kg) + xylazine (10 mg/kg) IM	Animals were not reversed	Yohimbine can be used to reverse xylazine	Palomares (1993)
Fossa (*Cryptoprocta ferox*)	Ketamine (2 mg/kg) + medetomidine (0.06 mg/kg)	Atipamezole (3 mg/kg)		Langer et al. (2013)

IM, intramuscular; NA, not applicable.

Table 37.2 Anesthetic combinations.

Species	Scientific Name	Anesthesia	For Antagonist	Reference
Civet, small-toothed	*Arctogalidia trivirgata*	Alfaxalone (5 mg/kg) and medetomidine (0.02 mg/kg)	Atipamezole (0.1 mg/kg)	Ahmad et al. (2012)
Civet, common palm	*Paradoxurus hermaphroditus*	Alfaxalone (5 mg/kg) and medetomidine (0.02 mg/kg)	Atipamezole (0.1 mg/kg)	Ahmad et al. (2012)
Civet, common palm	*Paradoxurus hermaphroditus*	Alfaxalone (5 mg/kg) and medetomidine (0.05 mg/kg)	Atipamezole (0.25 mg/kg)	Ahmad et al. (2012)
Mongoose, crab-eating	*Herpestes urva*	Isofurane 5% induction chamber, maintenance mask 2–2.5%		Liu et al. (2020)
Mongoose, banded	*Mungos mungo*	Isofurane 5% induction chamber, maintenance mask 2–2.5%		Dzanic & Moresco (unpubl. data)
Civet, masked palm	*Paguma larvata*	Isofurane 5% induction chamber, maintenance mask 2–2.5%		Liu et al. (2020)
Civet, Indian	*Viverricula indica taivana*	Isoflurane 5% induction chamber, maintenance mask 2–2.5%		Liu et al. (2020)
Meerkat, slender-tailed	*Suricata suricatta*	Isoflurane		Kvapil et al. (2018)
Meerkat, slender-tailed	*Suricata suricatta*	Mask isoflurane (4%)		Strike et al. (2017)
Meerkat, slender-tailed	*Suricata suricatta*	Mask sevoflurane (induction 6.5%, maintenance 4%)		Strike et al. (2017)
Meerkat, slender-tailed	*Suricata suricatta*	Ketamine (3–5 mg/kg) + dexmedetomidine (0.02 mg/kg) + midazolam (0.1 mg/kg)	Atipamezole (10× dexmedetmoidine dose), flumazenil (0.01 mg/kg)	Johnson (unpubl. data)
Civet, Formosan gem faced	*Paguma larvata taivana*	Dexmedetomidine (0.02–0.04 mg/kg)	Atipamezole (0.2 mg/kg)	
Mongoose, water or marsh	*Atilax paludinosus*	Ketamine (10.8–32.7 mg/kg)	NA	Maddock (1989)
Mongoose, slender	*Galerella sanguinea*	Ketamine (62.5–226.7 mg/kg)	NA	Maddock (1989)
Mongoose, large grey or Egyptian	*Herpestes ichneumon*	Ketamine (6.5–53.2 mg/kg)	NA	Maddock (1989)}
Fossa	*Cryptoprocta ferox*	Ketamine (2 mg/kg) + medetomidine (0.06 mg//kg)	Atipamezole (3 mg/kg)	Langer et al. (2013)
Binturong	*Arctitis binturong*	Ketamine (8 mg/kg) + medetomidine (0.02 mg/kg) $^{+}$ butorphanol (0.4 mg/kg)	Atipamezole (5 mg/mg medetomidine)	Moresco & Larsen (2003)
Binturong	*Arctitis binturong*	Ketamine (4 mg/kg) + medetomidine (0.04 mg/kg) + butorphanol (0.4 mg/kg)	Atipamezole (5 mg/mg medetomidine)	Moresco & Larsen (2003)
Binturong	*Arctitis binturong*	Ketamine (3.4 mg/kg) + dexmedetomidine (0.02 mg/kg) + butorphanol (0.2 mg/kg)	Atipamezole (0.2 mg/kg)	Thompson et al. (2016)
Fossa	*Cryptoprocta ferox*	Ketamine (3 mg/kg) + medetomidine (0.03 mg//kg) + diazepam (mg/kg)	Atipamezole (0.15 mg/kg)	Langer et al. (2013)
Genet, large spotted	*Geneta maculata*	Ketamine (31 mg/kg) + acepromazine hydrochloride (3 mg/kg)		Fuller et al. (1990)
Mongoose, small Indian	*Herpestes auropunctatus*	Ketamine (10 mg/kg) + xylazine (0.2 mg/kg)		Choudhary et al. (2013)
Civet, Indian palm	*Viverricula indica*	Ketamine (10 mg/kg) + xylazine (2 mg/kg)		Thirumurugan et al. (2004)

(*Continued*)

Table 37.2 (Continued)

Species	Scientific Name	Anesthesia	For Antagonist	Reference
Binturong	*Arctitis binturong*	Ketamine (10 mg/kg) + xylazine (2 mg/kg)	Not reversed	Grassman et al. (2005)
Genet, common	*Geneta genetta*	Ketamine (7 mg/kg) + xylazine (10 mg/kg)		Palomares (1993)
Civet, brown palm	*Paradoxurus jerdoni*	Ketamine (15 mg/kg) + xylazine (1.5 mg/kg)		Mudappa & Chellam (2001)
Mongoose, small Indian	*Herpestes auropunctatus*	Ketamine (20 mg/kg) + xylazine (1 mg/kg) + atropine sulfate (0.04 mg/kg)		Sethi et al. (2017)
Civets, Owston's palm	*Chrotogale owstoni*	Ketamine (17 mg/kg) + acepromazine (0.73 mg/kg) + atropine (0.04 mg/kg)		King (2002)
Civet, large Indian	*Viverra zibetha*	Ketamine (18 mg/kg) + acepromazine (0.77 mg/kg) + atropine (0.04 mg/kg)		King (2002)
Binturong	*Arctitis binturong*	Tiletamine-zolazepam (4–10 mg/kg)	NA	Grassman et al. (2005); Spriggs et al. (2007)
Fossa	*Cryptoprocta ferox*	Tiletamine-zolazepam (4 mg/kg)	NA	Libert et al. (2013)
Civet, common palm	*Paradoxurus hermaphroditus*	Tiletamine-zolazepam (5 mg/kg)	NA	Ahmad et al. (2019)

NA, not applicable.

Maintenance anesthesia can easily be performed in the hospital with inhalant anesthesia after intubation or via facemask for shorter procedures (Fig. 37.5). As previously mentioned, induction and maintenance with sevoflurane resulted in faster recoveries in meerkats (Strike et al. 2017). In small species a nonrebreathing system may greatly contribute to loss of heat. In the field, supplementation can be done with low doses of ketamine-medetomidine. Tiletamine-zolazepam can also be used, but this prolongs recovery times.

Alfaxalone is a neuroactive steroid with the properties of a general anesthetic. There is only one study in viverrids using this product (Ahmad et al. 2019). This study compared a combination of alfaxalone and medetomidine with tiletamine-zolazepam. Inductions were similar, but a better plane of anesthesia was reached with the alfaxalone-medetomidine combination and recoveries were shorter after reversal of medetomidine with atipamezole (Ahmad et al. 2019). However, this alfaxalone-medetodmidine combination did result in some degree of bradycardia and hypoxemia (Ahmad et al. 2019).

Immobilization of Free-ranging Viverrids and Herpestids

Much of the published injectable protocols pertain to field anesthesia for radio-collar placement, disease surveillance, and monitoring. Immobilization reports generally involve mechanical trapping followed by injectable protocols (Proulx et al. 2012). However, gas anesthesia is also occasionally used in the field, for example meerkats were mask induced with isoflurane to evaluate hemoglobin (Price 2012). These publications tend to include only scant information on physiologic parameters during anesthesia and rarely do they specifically compare different protocols.

Gas Anesthesia

Chamber induction can be safely achieved in small carnivores by covering a crate with a plastic bag or by transferring the patient into a smaller induction chamber (e.g., plexiglas box) with an intake and exhaust for gas and administering a mixture of oxygen and anesthetic gas to the chamber (Fig. 37.1). Initial concentrations of 5% isoflurane or 5–8% sevoflurane can be used for induction (Dzanic et al. 2021). One study in meerkats showed that induction with sevoflurane 6.5% and maintenance with sevoflurane 4% resulted in safe and effective anesthesia, better quality inductions, and faster recovery times than induction with sevoflurane 5% or isoflurane (Strike et al. 2017). However, both sevoflurane and isoflurane were found to be acceptable, with no difference in heart or respiratory rates (Strike et al. 2017). If animals are partially anesthetized or sick, induction can safely be completed via mask with manual restraint. Maintenance of

anesthesia can be achieved via mask or intubation and isoflurane can be decreased to a maintenance dose of 0.5–2% depending on the procedure and the condition of the patient. Full-mask inductions can potentially result in higher levels of stress due to the need to manually restrain the animals. However, this method tends to be quicker and use less gas anesthesia. Recoveries from gas anesthesia, especially sevoflurane, are generally short unless there is disease present. Facemask-only induction has been successful in meerkats suffering from acute pancreatitis (Naples et al. 2010).

Ketamine

Given the availability of several sedatives that can be used in combination with ketamine, the use of ketamine alone is not recommended because of muscle rigidity and unintentional leg movement (paddling); however, ketamine does have a high margin of safety (Maddock 1989). Ketamine alone was used in the rusty spotted genet (*Genetta tigrina*, current name *Genetta maculata*), the large grey mongoose or Egyptian mongoose (*Herpestes ichneumon*), the slender mongoose (*Galerella sanguinea*), and the water mongoose or marsh mongoose (*Atilax paludinosus*) (Maddock 1989). Some animals were dosed in excess of 100 mg/kg (maximum >226 mg/kg for one of the slender mongoose), which is extremely high compared to more recent use of ketamine, especially in combination with sedatives. Maddock notes that doses of 56 mg/kg were insufficient for full induction in spotted genets, while 36 mg/kg was sufficient for the Egyptian mongoose. Interestingly, although ketamine doses were in some cases 100-fold higher than ketamine doses currently used as part of various combinations, the time it took for the first signs of recovery to appear was only around 2–2.5-fold higher than the time seen with ketamine as part of a combination and lower dosing. Inductions were relatively long in some genets, but were short in small mongoose, probably owing to the relatively higher dosage. Several animals required supplemental anesthetics, temperature remained around 37°C, other physiologic values were not reported, and recoveries were long (Maddock 1989).

Ketamine-Xylazine

Ketamine-xylazine is a combination commonly used before the advent of medetomidine and now dexmedetomidine; the latter two are preferred over xylazine for their higher affinity for all the alpha-2 adrenergic receptors (Schwartz & Clark 1998). However, the ketamine-xylazine combination is still useful when medetomidine and/or dexmedetomidine is not readily available. Ketamine-xylazine has been used to immobilize the free-ranging brown palm civet (*Paradoxurus jerdoni*; Mudappa & Chellam 2001), the common palm civet (*P. hermaphroditus*; Thiangtum et al. 2004), the common genet (*Geneta genetta*; Palomares 1993), and the binturong (*Arctictis binturong*; Grassman et al. 2005). Doses of ketamine for these reports varied from 7 to 20 mg/kg and those of xylazine from 1.5 to 10 mg/kg. Reports did not include extensive comments on induction, anesthesia quality, patient monitoring and stability, or recovery.

Medetomidine-Dexmedetomidine

Medetomidine is the racemic mix of dexmedetomidine and levomedetomidine, the latter considered pharmacologically inactive. Domitor® (1 mg/mL medetomidine) is no longer sold in North America. Instead, Dexdomitor® (0.5 mg/mL dexmedetomidine, Zoetis), the active enantiomer of medetomidine, is available and this formulation makes accurate dosing in small patients easier than with the more concentrated formulations of medetomidine (20 mg/mL, ZooPharm, CO, USA; 10 and 20 mg/mL, Wildlife Pharmaceuticals, Mexico) currently sold for larger animals. The two sections below refer to the 0.5 mg/mL dexmedetomidine formulation; the medetomidine formulation mentioned is 1 mg/mL (Domitor®). Dexmedetomidine (0.02–0.04 mg/kg) was shown to maintain more stable effects and steady sedation in Formosan gem-faced civets (*Paguma larvata taivana*) as a sole agent, compared to xylazine, with the expected physiological effects of decreased heart rate, respiratory rate, and body temperature noted (Chongjun 2011). Reversal with atipamezole (0.2 mg/kg) was successful, with animals quickly returning to their normal demeanor (Chongjun 2011).

Ketamine-Medetomidine and Ketamine-Dexmedetomidine

A ketamine (2 mg/kg) and medetomidine (0.06 mg/kg) combination was used in fossa (*Cryptoprocta ferox*) with good inductions and recoveries, and atipamezole (0.3 mg/kg) was used to reverse the effects of medetomidine (Langer et al. 2013). The commercially available dexmedetomidine comes in a 0.5 mg/mL solution, making it easier to accurately dose small patients. Dexmedetomidine (0.02–0.03 mg/kg) has been used effectively in combination with ketamine (3–5 mg/kg) and midazolam (0.2 mg/kg) in meerkats and binturongs, and antagonized with atipamezole at 10 times the dexmedetomidine dose (Johnson, unpubl. data).

Ketamine-Medetomidine-Diazepam

A sufficiently deep plane of anesthesia was achieved for electroejaculation in male fossa (*Cryptoprocta ferox*) with a combination of ketamine (3 mg/kg), medetomidine (0.03 mg/kg), and diazepam (mg/kg); atipamezole (0.15 mg/kg) was used to reverse medetomidine (Langer et al. 2013). Midazolam is a good alternative to diazepam for intramuscular administration because it is water

soluble, resulting in more consistent bioavailability and effects than diazepam, which is oil-based.

Ketamine-Medetomidine-Butorphanol

The combination of ketamine-medetomidine-butorphanol has been successfully used for anesthetizing binturongs. Doses ranged from 2 to 8 mg/kg ketamine, 0.02 to 0.06 mg/kg medetomidine, and 0.2 to 0.5 mg/kg butorphanol; lower doses of ketamine were used with higher doses of medetomidine (Klaphake et al. 2005; Moresco & Larsen 2003). This combination worked well in binturongs, with good inductions, stable cardiopulmonary values, and fast, reversible recoveries. Inductions were shorter with higher doses of ketamine but were accompanied by slightly longer recoveries. High blood pressure values were seen in some of the animals with both high and low doses of medetomidine (Moresco & Larsen 2003). In one case report describing evaluation of a binturong for renal carcinoma, ketamine (3.4 mg/kg) and butorphanol (0.2 mg/kg) were used together with dexmedetomidine (0.02 mg/kg) and reversed with atipamezole (0.2 mg/kg), showing that ketamine-butorphanol can be used effectively with either medetomidine or dexmedetomidine in binturongs (Thompson et al. 2016).

Ketamine-Midazolam

Adequate anesthesia for surgical enucleation (to treat traumatic proptosis) in a common palm civet (*Paradoxurus hermaphrodites*) and a small Indian Civet (*Viverricula indica*) was achieved with a combination of ketamine (10 mg/kg) and midazolam (0.2 mg/kg). Induction times were 10 and 11 minutes and anesthesia was maintained with a supplemental dose of half the induction dose (Maruthi et al. 2015).

Tiletamine-Zolazepam (Telazol, Zoletil)

Tiletamine-zolazepam use at doses between 4 and 9 mg/kg has been reported in *N. binotata*, *C. civetta*, *H. derbyanus*, *V. indica*, *F. fossa*, *P. larvata*, *V. zibetha*, *P. hermaphroditus*, *V. tangalunga*, *Herpestes javanicus*, *Paradoxurus musangus*, and *Arctictis binturong* (Ahmad et al. 2019; Blanton et al. 2006; Colón 2002; Grassman et al. 2005; Kreeger 1999; Spriggs et al. 2007). Smaller species often require higher dosages, up to 12 mg/kg (McKenzie & Burroughs 1993). Tiletamine-zolazepam anesthesia is characterized by long recoveries, but tends to have a wide margin of safety.

Alfaxalone-Medetomidine

Alfaxalone is a neuroactive steroid and general anesthetic that is gaining more widespread use. Four small-toothed civets (*Arctogalidia trivirgata*) and 16 common palm civets (*Paradoxiurus hermaphroditus*) were anesthetized with alfaxalone (5 mg/kg) and medetomidine (0.02 mg/kg), which was sufficient for short procedures and intubation (Ahmad et al. 2012). A more complete study was later published by the same author comparing alfaxalone-medetomidine to tiletamine-zolazepam in the common palm civet ($n = 20$) (Ahmad et al. 2019). Alfaxalone (5 mg/kg) and medetomidine (0.05 mg/kg) had similar induction times, but recovery times were slightly shorter and body temperature was better maintained compared to tiletamine-zolazepam (5 mg/kg). Body temperature, heart rate, respiratory rate, and percentage hemoglobin saturation (SpO_2) were similar to those in animals anesthetized with tiletamine-zolazepam (Ahmad et al. 2019).

Complications and Other Considerations

Given the small size of most species in these taxa, hypothermia is much more common under anesthesia than hyperthermia, especially with gas anesthesia and the non-rebreathing systems used for small patients (Denver Zoo, unpubl. data). One complication in social carnivores is that of separating a specific animal and reintroducing it after anesthesia, as reintroduction can be accompanied by aggressive reactions by the group towards the animal being reintroduced. One way to address this is to keep procedures as short as possible and to schedule elective procedures on the same day for the whole group. Rubbing a different scent on each animal (e.g., herbs and spices) has worked well (Denver Zoo, unpubl. data) because each animal will have a novel odor and the aggression is not directed at only one individual.

Analgesia and Analgesic Techniques

There are no systematic studies on analgesics in small carnivores, but a variety of analgesics have been documented as part of surgical or medical case reports and case series (Table 37.3). These references tend not to specifically state if the drugs were effective or if any adverse effects were observed. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly reported class of drug, and trauma or surgery are the most common indications for treatment. Use of subcutaneous and intramuscular meloxicam (0.2–0.3 mg/kg for up to 3 days) has been published in meerkats, a small Indian mongoose (*H. auropunctatus*), a common palm civet (*Paradoxurus hermaphrodites*), and a small Indian civet (*Viverricula indica*) (Margalit Levi et al. 2017; Maruthi et al. 2015; Sethi et al. 2017). Oral meloxicam (0.2 mg/kg every 24 hours) has been used in the banded mongoose and dwarf mongoose for up to 7 days for arthritis and in a fossa for 3 days post-laparotomy (Denver

Table 37.3 Analgesics.

Species	Drug and Dosage	Comments	Reference
Civet, common palm (*Paradoxurus hermaphrodites*)	Meloxicam (0.2 mg/kg IM once), $n = 1$	Enucleation	Maruthi et al. (2015)
Civet, small Indian (*Viverricula indica*)	Meloxicam (0.2 mg/kg IM once), $n = 1$	Enucleation	Maruthi et al. (2015)
Meerkat (*Suricata suricatta*)	Meloxicam (0.2 mg/kg SC, frequency not reported), $n = 2$	Visceral pain from toxolplasmosis	Margalit Levi et al. (2017)
	Flunixin meglumine (10 mg/kg, IV), $n = 1$	Visceral pain from pancreatitis, used intraoperatively	Naples et al. (2010)
	Buprenorphine (0.02 mg/kg, SC), $n = 1$	Visceral pain from pancreatitis, used intraoperatively	Naples et al. (2010)
	Buprenorphine (0.03 mg/kg PO q12h, 3 days), $n = 4$	Visceral pain from gastroenterotomy	Hahn et al. (2013)
Mongoose, small Indian (*Herpestes auropunctatus*)	Meloxicam (0.3 mg/kg IM q24h, 3 days), $n = 1$	Visceral pain from evisceration repair	Sethi et al. (2017)
Binturong (*Arctictis binturong*)	Hydromorphone (0.04 mg/kg IV), $n = 1$	Hemilaminectomy, given preoperatively	Spriggs et al. (2007)
	Fentanyl (3 mg/kg, IV), $n = 1$	Hemilaminectomy, given preoperatively	Spriggs et al. (2007)

IM, intramuscular; IV, intravenous; PO, per os; q12h, every 12 hours; q24h, every 24 hours; SC, subcutaneous.

Zoo, unpubl. data). Flunixin meglumine was used intraoperatively in a meerkat with pancreatitis (Naples et al. 2010). There is a patent for transmucosal formulation of meloxicam, but to the authors' knowledge there have not been any publications documenting the use of this product in nondomestics (Heit et al. 2012).

Opioid agonist-antagonists have also been used intra- and postoperatively: buprenorphine was used in meerkats and mongoose subcutaneously and orally to treat visceral pain (Hahn et al. 2013; Naples et al. 2010). Hydromorphone and fentanyl were used as analgesia preoperatively for a hemilaminectomy in a binturong (Spriggs et al. 2007). Tramadol (1–1.5 mg/kg q12h) has been used orally for longer duration analgesia (arthritis) in banded and dwarf mongoose (Denver Zoo, unpubl. data)

Depending on the nature of the case, a multimodal approach to analgesia combining an NSAID with an opioid analgesic and incorporating an opioid analgesic in the anesthesia regimen for painful procedures is generally recommended for best control of pain.

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38

Hyenas

Nina Hahn, John M. Parker, Gregory Timmel, Mary L. Weldele, Wm. Kirk Suedmeyer, and Nigel Caulkett

Taxonomy and Biology Related to Anesthesia and Handling

Hyenas resemble large canids but because they belong to the suborder Feloidae (with cats and mongooses) they are more closely related to domestic cats (*Felis (sylvestris) catus*) than dogs (*Canis familiaris*). Reports of hyena anatomy and physiology indicate similarities to cats as well as dogs in terms of retinal anatomy (Calderone et al. 2003) and susceptibility to pathogens (Hahn et al. 2003; East et al. 2004; Troyer et al. 2005; Harrison et al. 2004; Ferroglio et al. 2003). Hyenas, however, are more cat-like in several ways, including dentition as well as physiological responses to xylazine and ketamine.

It is therefore appropriate that veterinarians utilize physical anesthetic techniques suitable for large dogs but rely on domestic cat references for drug choices and dosages. Suggested drug dosages can be found in Table 38.1.

Body Weights and Blood Values

Adult colony-born female spotted hyenas weigh 50 kg on average (range 49.5–90 kg). Adult males weigh slightly less than females, averaging 47.6 kg (range 44.5–54.5 kg). Brown hyenas average 37–43 kg and and aaardwolves average 9–14 kg. Serum chemistry, blood gas analysis, and complete blood counts are similar to both cats and dogs (Tables 38.2 and 38.3). Clot formation is frequently encountered in specimens treated with EDTA and therefore heparin is the preferred anticoagulant.

Vascular Access and Sample Collection Sites

Fore- and hindlimb veins are both readily accessible for catheterization (Figs 38.1 and 38.2). The venous anatomy as it pertains to catheterization of the forelimb is comparable to that of the domestic cat (Fig. 38.1). Catheterization of the cephalic vein can be performed with relative ease, as with a large dog. However, care should always be taken when positioning the catheter to avoid extensive branching and anastamoses of the superficial forelimb vessels (Fig. 38.1).

The jugular, cephalic, and saphenous veins are accessible for blood collection and cannulation. Sublingual vessels are prominent and can provide quick vascular access for electrolyte and blood gas analysis during anesthetic procedures. Arterial pulses can be palpated midline on dorsal metacarpi, but arterial cannulation has not been attempted by these authors. Cerebral spinal fluid can best be collected by cisternal puncture. The occipital protuberance, spinous process of axis, and wings of the atlas can palpated in an intubated hyena despite the thick neck muscles.

Endotracheal Intubation

Intubation of the hyena can be performed using a size 11–12 endotracheal tube with the same relative ease as in a large dog. The hyena is best intubated while in sternal recumbency. The larynx is easily visualized through the mouth using a large-bladed laryngoscope. Unlike cats, laryngeal spasm during intubation has not been observed.

Physical Restraint

Chemical restraint (anesthesia) is always necessary prior to performing any procedures on adult hyenas. Cubs less than 1 month old can be manually restrained for examination and minor procedures such as blood collection and vaccinations. Hyena cubs that are 2–6 months old may be placed in a "squeeze-back" cage for hand-injection with anesthetics, as described below.

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Table 38.1

Species	Drug Combination	Reversal	Comments	Reference
Spotted hyena (*Crocuta crocuta*)	Ketamine 4–6 mg/kg, xylazine 1 mg/kg, atropine 0.045 mg/kg	Yohimbine 0.11 mg/kg, maximum dose 6 mg	Dose for captive animals Diazepam 0.1–0.5 mg/kg intravenously may be needed to control muscle rigidity in low-weight animals	Hahn et al. (2003)
Spotted hyena (*Crocuta crocuta*)	Tiletamine-zolazepam 5–6.5 mg/kg	None	Recovery can be stormy, better combinations are available	Kock & Burroughs (2021)
Spotted hyena (*Crocuta crocuta*)	Tiletamine-zolazepam 1 mg/kg Medetomidine 0.05 mg/kg	Atipamezole at five times the medetomidine dose		Kock & Burroughs (2021)
Brown hyena (*Parahyaena brunnea*)	Ketamine 3–4 mg/kg Medetomidine 0.03–0.04 mg/kg	Atipamezole at five times the medetomidine dose	May require additional ketamine (30–40 mg intramuscularly) in the event of light anesthesia on approach	
Aardwolf (*Proteles cristatus*)	Ketamine 5–8 mg/kg Medetomidine 0.03–0.05 mg/kg	Atipamezole at five times the medetomidine dose		Kock & Burroughs (2021)

Table 38.2 Serum chemistry ranges for captive adult spotted hyenas under KXA anesthesia.

Serum Chemistry	Range	Units
Alkaline phosphate	14–136	U/L
ALT	65–162	U/L
AST	76–142	U/L
CK	149–419	U/L
GGT	1–7	U/L
Albumin	2.2–2.8	g/dL
Total protein	6.1–7.7	g/dL
Globulin	3.6–5.2	g/dL
Total bilirubin	0–0.2	mg/dL
Direct bilirubin	bilirubin	mg/dL
BUN	14–30	mg/dL
Creatinine	1.1–1.8	mg/dL
Cholesterol	165–300	mg/dL
Glucose	80–153	mg/dL
Calcium	9–10.9	mg/dL
Phosphorus	3.2–6.5	mg/dL
Chloride	106–118	mEq/L
Potassium	4.2–4.9	mEq/L
Sodium	140–149	mEq/L
A/G ratio	0.4–0.7	
B/C ratio	8.6–23.3	
Indirect bilirubin	0–0.1	mg/dL
Na/K ratio	29–35	
Anion gap	14–24	mEq/L
TCO_2	13–25	mEq/L

Notes: All parameters represent a 95% confidence interval of 210 samples collected from 103 animals over a 7-year period. All samples were treated with either heparin or EDTA. All analysis provided by IDEXX Laboratories Inc.
ALT, alanine transaminase; AST, aspartate aminotransferase; CK, creatine kinase; GGT, gamma-glutamyl transferase; BUN, blood urea nitrogen; A/G, albumin to globulin; A/C, albumin to creatinine; Na/K, sodium to potassium; TCO_2, total CO_2.

Table 38.3 Complete blood count ranges for captive adult spotted hyenas under KXA anesthesia.

Blood Value	Range	Units
WBC	7200–23,200	Thousands/mL
RBC	4.74–8.73	Million/mL
HCT	23–46.5	%
MCV	43–65	fl
MCH	14.4–22.5	pg
MCHC	32.3–35.4	g/dL
Neutrophils	42–85	%
Lymphocytes	5–48	%
Monocytes	0–7	%
Eosinophils	1–14	%
Basophils	0–3	%
Absolute neutrophils	3942–16,353	/mL
Absolute lymphocytes	512–7708	/mL
Absolute monocytes	0–1068	/mL
Absolute eosinophils	98–2440	/mL
Absolute basophils	0–504	/mL

Notes: All parameters represent a 95% confidence interval of 210 samples collected from <100 animals over 7-year period. All samples were treated with either heparin or EDTA. All analysis provided by IDEXX.
WBC, white blood cell; RBC, red blood cell; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration.

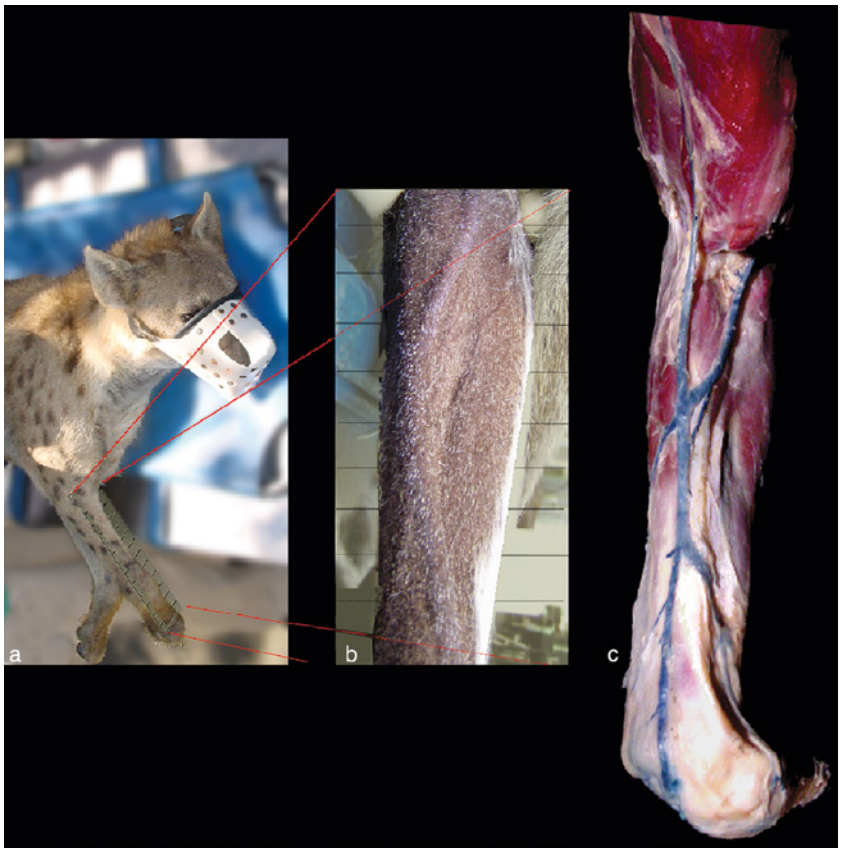


Figure 38.1 Three photographs of the spotted hyena forelimb. (a) A hyena in left lateral recumbency. Note the right antebrachium for panel orientation. (b) An *in situ* cranial-medial view from the level of mid elbow to proximal carpus. Note the prominent superficial veins (visualization aided by manual occlusion). (c) The venous anatomy *in situ*. Only the skin and superficial fascia have been removed in both panels. (b) and (c) Extensive anastomosis and bifurcations can be observed.



Figure 38.2 Catheter placement in the saphenous vein of a hyena.

Anesthesia and Immobilization

Captive Hyena Immobilization and Anesthesia

A breeding colony of spotted hyenas (*Crocuta crocuta*) was established at the University of California, Berkeley (UCB) in 1985 with wild cubs collected in Kenya. The spotted hyena was selected for research because of its unique morphological and behavioral characteristics. Female spotted hyenas are larger than and dominant to males. They lack an external vagina, and instead have a hypertrophied, penis-like clitoris through which they urinate, copulate, and give birth. This makes them a useful research model in which to study the general mechanisms of sexual differentiation, and the differential development of morphology and behavior.

Colony management has included annual physical examinations, which are always performed on anesthetized animals. Hyenas are also anesthetized for longer-term procedures, including dentistry, diagnostic imaging, and surgery. They are also routinely immobilized to collect blood and measurements essential to research. Nearly 2000 anesthetic procedures have been performed in the over 20 years that the UCB colony has been existent, and no mortality has resulted from anesthesia.

The anesthetic regime established 20 years ago at UCB remains the protocol of choice for captive hyenas. It consists of 4–6 mg/kg ketamine, 1 mg/kg xylazine, and 0.045 mg/kg atropine (KXA). The ketamine dose has been incorrectly reported as 10 mg/kg (Berger et al. 1992; Hahn et al. 2003). Hyenas that are 9 months of age and older are anesthetized using a reusable, air-charged dart/blow gun

system prior to handling. Telinject and Daninject systems have both been used successfully at UCB.

Prior to darting, it is usually best to isolate the hyena in a small enclosure. Hyenas are fasted overnight prior to anesthesia. Xylazine appears to be an emetic in hyenas, as in cats (Plumb 2005), and they frequently vomit after successful darting.

The hindquarters are the preferred anatomic site for dart placement. The excitement preceding darting often induces pronounced side-to-side whipping of the hyena's neck. This precludes the neck/shoulder region from being the preferred target site. Hyenas appear to undergo segmental anesthesia following KXA inoculation delivered into hindquarters; loss of function is first evident in the caudal region (lumbrosacral region, pelvic limbs, and tail).

Mature hyenas are anesthetized with KXA using 3-mL darts and drug preparations of 100 mg/mL ketamine, 100 mg/mL xylazine, and 15 mg/mL atropine. Dart preparation can be safely performed by first adding calculated doses of xylazine and atropine based on previous weights to the dart-syringe, then adding ketamine to fill the remaining 3-mL volume (2.2–2.4 mL). Heavier hyenas will therefore receive a lower dose and will often need supplemental doses of ketamine (1–2 mg/kg) for full sedation. In contrast, low-weight animals often require supplemental sedatives to counter the side effects associated with ketamine, such as rigidity and twitching. Intravenous diazepam (0.1–0.5 mg/kg) is commonly used for this purpose. When supplementing KXA anesthesia, diazepam causes a transient respiratory depression evident by prolonged periods of apnea. Subadult animals may not require the amount of ketamine needed to fill the dart to capacity. Less-concentrated preparations of xylazine (20 mg/mL) and atropine (0.54 mg/mL) should be used for small cubs. Hyena cubs can be either hand or squeeze-cage restrained and drugs can be delivered via hand-injection. Additionally, cubs generally require approximately 80% of the weight-calculated adult ketamine and xylazine doses. The previously stated adult dose of atropine, however, is used for cubs.

Hyenas must be muzzled on immobilization and, when applicable, remained muzzled for the duration of the procedure when maintained on injected anesthetics. The bite response is not as readily abolished by ketamine anesthesia as it is with dogs, cats, and primates. Jaw tone should be cautiously and properly assessed prior to endotracheal intubation.

Yohimbine (0.11 mg/kg) up to a maximum dose of 6 mg is administered intramuscularly to reverse the xylazine at the conclusion of the procedure, at least 20 minutes after the last injection of ketamine. The time delay and route of administration decreases the likelihood of negative reaction due to the presence of ketamine.

Telazol® (5 mg/kg) has been used successfully to anesthetize "ketamine reactors" (see below) but was associated with a rough, prolonged recovery in the captive colony and therefore is not recommended.

Anesthetic Maintenance

For long-term and major surgeries, hyenas are catheterized, intubated, and maintained on isoflurane anesthesia (1–2%) after darting with KXA as described above. Yohimbine given after isoflurane stabilization may help prevent xylazine-induced adverse effects such as bradycardia, respiratory depression respiratory, and loss of thermoregulation, as described below.

Complications

Xylazine frequently induces emesis, pronounced bradycardia, and loss of thermoregulation in hyenas. Atropine is included to reduce salivation typical of ketamine and offset bradycardia associated with xylazine administration. Aspiration of regurgitate was noted on necropsy in one geriatric animal (21 years old) with biliary carcinoma following immobilization with KXA, but aspiration following KXA administration has never been a clinical problem in hyenas. As a precaution, however, hyenas are always fasted prior to immobilization.

Hyenas' eyes remain open after ketamine administration, as do cats' eyes (Plumb 2005), and should always be treated with ophthalmic lubricant (e.g., Lacri-lube®). Prolonged apnea is noted infrequently following bolus diazepam and ketamine-diazepam administration, as occurs in cats.

Hyperthermia in response to KXA administration has been observed. Care is taken to avoid darting during hot weather, but hyperthermia has been noted on days when ambient temperature is not a contributing factor. Hyperthermia has been attributed to agitation and increased activity prior to darting, but this may be a response to ketamine, as has been observed in cats (Plumb 2005). Xylazine causes loss of thermoregulation in many animal species (Plumb 2005) and this may also contribute to hyperthermia in anesthetized hyenas.

Very rarely, respiratory depression after KXA administration is noted. Reversal of the xylazine with yohimbine will correct this. Heart rates as low as 48 beats per minute are often observed, but as clinical outcome for these animals is no different from animals with higher heart rates, this has been attributed to the effects of xylazine and considered normal. Systolic heart murmurs have been occasionally identified during physical examination under KXA

anesthesia. Follow-up cardiac ultrasound examinations identified a decrease in ventricular myocardial contractility in the three animals examined. This was attributed to the xylazine component of the anesthetic combination and not considered clinically significant.

There are two types of adverse reaction to KXA anesthesia that have been observed. Some hyenas display tonic-clonic-like movements and extensor rigidity after KXA administration. This response is not uncommon in male hyenas. Male hyenas weigh on average less than female hyenas and therefore may receive the high end of the 4–6 mg/kg ketamine range when following the UCB KXA protocol. The adverse ketamine reaction observed in these hyenas may be due to the ensuing relatively high ketamine to xylazine ratio. This reaction may be similar to what has been described in captive macaque monkeys (*Macaca mulatta*), who undergo frequent exposure to ketamine anesthesia. In macaques ketamine causes varying degrees of muscle rigidity in susceptible individuals. These animals may have a tonic-clonic or psychotomimetic response to the administration of ketamine (UC Davis Veterinary School, Clinical Medical Primatology lecture notes). Cats also demonstrate "myoclonic jerking and/or tonic/clonic convulsions" (package insert of Ketaset®) with ketamine administration.

Two male hyenas (brothers with the same parents but from different litters) developed generalized seizures after KXA administration. They both had been anesthetized with KXA numerous times. Both of these animals developed generalized seizures when anesthetized with KXA in their fourth year. Prior to having seizures, neither of these two animals demonstrated the tonic-clonic movements as described above. Hyenas at the UCB colony are routinely immobilized for research purposes: seven times in the first year, four times in the second year, twice in the third year, and yearly thereafter. Seizures have been reported to occur in 20% of cats anesthetized with therapeutic doses of ketamine (Plumb 2005). Ketamine is known to be epileptogenic (Plumb 2005), and there may be individual susceptibility to the effects of ketamine in hyenas, but the mechanisms of both the seizure activity and tonic-clonic movements are purely speculative.

Diazepam (0.5–1 mg/kg intravenously to effect) will eliminate seizures as well as tonic-clonic muscle activity in hyenas. Diazepam should always be kept close at hand when anesthetizing hyenas.

Recovery

Hyenas are placed in a straw-bedded, enclosed cage for post-surgical recovery. Animals are allowed to fully recover from anesthesia prior to being reintroduced to cage-mates. After short-term procedures using xylazine reversal this can generally be within 1–2 hours of anesthesia. In longer-term or major surgical procedures when xylazine reversal is not used, or if opioid analgesics are used, hyenas are allowed overnight recovery prior to reintroduction to cage-mates. After laparotomy hyenas are kept separate from cage-mates for up to 2 weeks.

Disease Issues (Affecting Anesthesia)

Acute and peracute pain has dramatic effects on dosage requirements and induction time. Beyond this there are no known disease issues that affect anesthesia in hyenas.

Field Anesthetic Techniques

The anesthetic procedures described for anesthesia in captive spotted hyenas (see the section on captive hyena immobilization and anesthesia) are also used in the field (Berger et al. 1992; Place et al. 2002). The most commonly used agent for immobilization in the field, however, is a combination of tiletamine hydrochloride and zolazepam hydrochloride (Telazol®; A.H. Robbins, Richmond Virginia, USA), given at an estimated dose 6.5 mg/kg (K. Holekamp, pers. comm.; Van Horn et al. 2004). For field use in hyenas, Telazol® (500-mg vial) is reconstituted with 2.5 mL of diluent instead of the label-recommended 5 mL. The resulting solution provides 86.2 mg/mL of each of tiletamine and zolazepam (combined 172.4 mg/mL of Telazol®). Adult hyenas receive 1.8–2.0 mL, subadults 1.4–1.6 mL, and cubs approximately 1 mL of this solution. The actual dose used is probably less than 6.5 mg/kg, and 5 mg/kg Telazol® is recommended for captive hyenas. Hyenas can be darted with either a blow-pipe or a CO_2-powered rifle. The blow pipe is only useful at distances of 1–5 m and only practical for animals that are very comfortable around a vehicle. It is always preferable to use the CO_2 rifle since it is silent and allows the dart to hit the animal with a smaller, less traumatic impact. Hyenas are darted in the early morning hours. They are allowed to recover in the shade and are attended until able to walk. The Telazol® dose for field use has also been reported as 2.5 mg/kg (Harrison et al. 2004; Holekamp & Sisk 2003), but this is likely an error. The tiletamine-zolazepam dose can be significantly reduced and recovery times shortened if 1 mg/kg tiletamine-zolazepam is combined with medetomidine at a dose of 0.05 mg/kg. This combination has been used in brown and spotted hyenas, and it can be partially antagonized with atipamezole at five times the medetomidine dose (Fig. 38.3) (Kock & Burroughs 2021). A combination of butorphanol 0.1 mg/kg, midazolam 0.1 mg/kg, and medetomidine 0.03–0.05 mg/kg has been



Figure 38.3 Wild spotted hyena (*Crocuta crocuta*) immobilized at night with medetomidine-tiletamine-zolazepam. In this situation a reversable combination is desirable as a prolonged recovery will place the animal at risk of injury or predation.



Figure 38.4 A GPS collared brown hyena (*Hyaena brunnea*) inadvertently disturbed from its daytime den. Brown hyenas are rarely observed during daylight hours.

used successfully in Kruger National Park. This combination can be antagonized with naltrexone at twice the butorphanol dose and with atipamezole at five times the medetomidine dose (Kock & Burroughs 2021). Butorphanol-azaperone-medetomidine has been used in hyenas but spontaneous arousals have been described so it must be used with caution; blindfolds and hobbles are recommended (Kock & Burroughs 2021).

Field Immobilization of the Brown Hyena (*Hyaena brunnea*) in Namibia

Few references for field immobilization techniques of the brown hyena are reported in the literature. An understanding of its natural history and habits facilitates successful capture. Health assessment, placement of tracking devices, evaluation of reproductive status, and morphometric measurements are only accomplished by immobilization.

The brown hyena is a nocturnal, cautious, silent, solitary forager (Fig. 38.4) (Nowak 1991; Estes 1992; Mills 2003). However, large carcasses will attract several hyenas. As opposed to the spotted hyena (*Crocuta crocuta*), brown hyenas generally feed singly, rather than as groups, even on larger carcasses; individuals will wait patiently in the distance until a conspecific finishes. In most instances, black-backed jackals (*Canis mesomelas*) will arrive at the site first; vocalization and activity of larger groups of jackals may attract hyenas to the location. Jackals will commonly telegraph a hyena's approach by nervously looking in the direction of the approaching animal. In some areas, hyenas disperse jackals from the site, whereas in other locations, jackals antagonize hyenas from the carcass. Use of camouflage, a low-profile silhouette, and absolute stillness are paramount to success. The field marksman should be in place prior to sunset as brown hyenas are very aware of movement and changes in the environment. Utilization of enhanced lighting in the form of infrared technology facilitates darting during moonless nights. Dart placement is key to efficient immobilization. Commercially available remote delivery systems work well. A well-aimed dart placed in the shoulder or neck affords consistent success. Patience is necessary to predict the stance of the hyena while feeding. Carcasses should be placed in a position that encourages the hyena to present a lateral profile. Use of a centrally located, secured carcass with a peripheral, spoke-wheeled scent trail improves the chances of success. The strength of hyenas should not be underestimated. Adult hyenas have been observed carrying entire carcasses of freshly killed Cape fur seal pups (*Arctocephalus pusillus*) (Wiesel 2010), and removing springbok (*Antidorcas marsupialis*) and large carrion from dart sites. Carcasses must be secured with 1–2 m posts driven deeply into the ground. Hyenas will carry carcasses to more secure locations if they can.

A combination of 3–4 mg/kg ketamine hydrochloride with 0.03–0.04 mg/kg medetomidine hydrochloride provides effect within 3 minutes and recumbency within 7 minutes on average. It is advisable to use either telemetry darts and/or allow several minutes before attempting to locate the immobilized animal as brown hyenas are prone to running for extended distances if startled. The initial response is a sudden gallop from the dart site, followed by circling back to the general area as the drugs take effect. In most instances, the hyena can be located less than 50 m from the initial site. On occasion, an anesthetized hyena

may require 30–40 mg of supplemental ketamine hydrochloride given intramuscularly to facilitate complete recumbency. This combination provides good muscle relaxation, stable heart rate and rhythm (although bradycardia is commonly encountered, heart rates average 40–60 beats per minute), slight to moderate pytalism and 40–50 minutes of stable anesthesia. Rectal body temperatures with this combination average 38°C.

Atropine sulfate should not be utilized to control ptyalism because it counters the alpha-adrenergic effects on peripheral vasoconstriction and can lead to complications. Initial hypoxia (<75% pulse oximetry) is routinely observed but improves over time. In most instances, brown hyenas achieve pulse oximetry readings of >90% after 20–30 minutes of anesthesia. Supplemental oxygen should be provided if available. Application of a bland ophthalmic ointment protects the eyes during times of blowing sand. Covering the eyes and placing plugs in the ear canal also lessens ocular and aural stimulation, which in turn provides consistent recumbency (Fig. 38.5). Reversal is achieved with atipamezole hydrochloride at five times the milligram dose of medetomidine induction. Atipamezole given intramuscularly produces smooth, reliable recovery within 5–10 minutes (Fig. 38.6). Blepharospasm, followed by purposeful movement of the head and cervical spine, is a prelude to rapid recovery to standing within minutes.

In general, the hyena stands, then canters away with mild ataxia, which rapidly resolves to normal ambulation within an additional 3–5 minutes. It is advisable to remotely monitor the response to full recovery as black-backed jackals can antagonize and injure the hyena unless it is fully recovered (Fig. 38.7).

Use of ketamine-medetomidine produces safe, reliable, and predictable results in the brown hyena in field situations and may be a suitable combination for captive anesthetic approaches.



Figure 38.5 A brown hyena (*Hyaena brunnea*) anesthetized with ketamine HCl and medetomidine HCl in Namibia. Note the aural plugs, pulse oximetry, and substrate barrier.



Figure 38.6 A brown hyena (*Hyaena brunnea*) shortly after reversal without atipamezole. Note the position of the head and cervical spine just prior to standing.



Figure 38.7 An anesthetized brown hyena (*Hyaena brunnea*) immediately after reversal with atipamezole. Note the encroachment by a black-backed jackal (*Canis mesomelas*), which can injure recumbent hyenas.

Analgesia

Analgesia is always provided following major surgeries and dental procedures. Buprenorphine (0.01 mg/kg subcutaneously or intramuscularly) is administered at the time of intubation and repeated following the end of surgery. If additional analgesia is indicated, 10 mg/kg etodolac (Etogesic®) is administered orally once daily in food. No ill-effects have been observed in any hyena receiving etodolac, including one hyena given 9 mg/kg daily for a month. Meloxicam (0.2 mg/kg SQ) has been used for endodontic procedures. It is given once at the completion of the procedure.

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39

Felids

Andrew Cushing

Introduction

Felidae is a family of mammals comprising 39 species of extant felidae, including the domestic cat (*Felis catus*). Anatomically and physiologically, they often exhibit retractile claws, powerful bites, and slender bodies, and are often incredibly agile. These characteristics provide challenges to captivity, requiring high fences or roofed enclosures and, for the larger species in particular, extreme caution when in contact. Despite these challenges, nondomestic felids are often displayed in zoological collections, and inevitably require anesthesia or heavy sedation for most procedures. Table 39.1 shows the more commonly kept captive felid species.

Handling and Restraint

Physical Restraint

Physical restraint of nondomestic felids is primarily limited to young animals, depending on their temperament. Nets can be used to allow hand-injection in fractious young animals or smaller species. Squeeze cages can be used for slightly larger animals, but should be designed for the size of animal they are intended to be used for. Fig. 39.1 shows an adult cheetah restrained in a squeeze box, which allows access to the medial saphenous vein and to administer injections as required.

Vascular Access

Some animals may be trained to allow blood collection from the tail. Lateral tail veins are located just dorsal to the 3 o'clock and 9 o'clock positions on the tail. They can be difficult to sample large volumes from, especially in a fully conscious animal. There is also venous access in the ventral tail, located midline. This is most easily accomplished at the level of the first one to two tail vertebrae. However, cats are usually reactive to sampling in this area.

In sedated or fully anesthetized animals the medial saphenous vein, cranial to the hock, is the most accessible. The jugular veins are large and suitable for blood draws or placement of intravenous catheters in a fully anesthetized animal. This vein is relatively mobile and positioning the cat with a rolled towel underneath the neck, with the legs pulled caudally and the head extended all aids in immobilization of the vessel.

Cephalic veins are usually not easily visualized, but can be accessed using anatomical knowledge. In the author's experience, in tigers the cephalic vein often lies at or close to the demarcation of orange and white fur on the leg.

Lingual veins, on the ventral surface of the tongue, allow for small samples or placement of up to a 25-gauge venous catheter. Using a butterfly strip and staples, this can be affixed to the base of the tongue and an extension set used to provide access outside the oral cavity. Positioning a catheter in this location provides extra security for intravenous emergency access, as saphenous or jugular catheters can be lost during positioning or transport.

Arterial access, for blood gas analysis or catheterization for invasive blood pressure monitoring, is most easily performed using the dorsal pedal artery. The femoral artery can also be used.

Anesthetic Pre-considerations

Prior to consideration of drug protocols clinicians must consider a number of factors related to the planned procedure. Anesthetic procedures are not without some degree of risk to both animals and personnel, so thought must be given to the benefits of a planned procedure and if these potential benefits outweigh the known risks. Clearly, a full preanesthetic assessment is difficult to perform, but

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Table 39.1 Commonly kept felid species in zoological institutions.

Genus	Species	Current Holding Number*
Panthera	Tiger (*P. tigris*)	>500
	Lion (*P. leo*)	>500
	Leopard (*P. pardus*)	>500
	Jaguar (*P. onca*)	480
	Snow leopard (*P. uncia*)	440
Neofelis	Clouded leopard (*N. nebulosa*)	308
Leptailurus	Serval (*L. serval*)	>500
Caracal	Caracal (*C. caracal*)	210
Leopardus	Ocelot (*L. pardalis*)	272
Lynx	Bobcat (*L rufus*)	314
	Eurasian lynx (*L. lynx*)	>500
Acinonyx	Cheetah (*A. jubatus*)	>500
Puma	Cougar (*P. concolor*)	454

* The current holding number is only for facilities worldwide using the Zoological Information Management Software as of August 2020. Search numbers are limited to 500 individuals.



Figure 39.1 Cheetah restrained in a squeeze box.

obtaining a full history from husbandry staff may indicate specific health problems. Additionally, it may be possible to collect urine or fecal samples, achieve a good visual



Figure 39.2 Hand-injection of tiger.

examination, or record an accurate bodyweight. A review of anesthetic records for a specific animal may indicate previous issues under anesthesia. Planning nonemergent procedures with knowledge of local weather and temperature can help prevent hypo- or hyperthermia. Fasting for 12–24 hours is recommended (Gunkel & Lafortune 2007).

The route of administration is usually via remote injection, using a 30–40-mm needle, ideally via the gluteal musculature. However, the use of behavioral conditioning or, for smaller species, a squeeze cage or net may allow hand-injection. In the author's practice, the vast majority of anesthetic drugs are delivered by hand-injection, using a 3-mL syringe with a 1.5-inch 18-gauge needle, administered rapidly through the bars of a rolling cage or den (Fig. 39.2). There is minimal literature on intravenous administration of sedation drugs, but it may be possible in trained animals. Doses via this route are likely to be lower than those given intramuscularly and the time to effect more rapid.

Sedation

Safety when working around nondomestic felids should be of paramount importance, given the ability of many of these animals to cause mortal harm. There exist some circumstances when a heavy sedation, i.e. without the use of a

dissociative anesthetic drug, is all that is required for a procedure. The use of these protocols for short procedures has been primarily investigated in the cheetah (Semjonov et al. 2019; Woc Colburn et al. 2017; Lafortune et al. 2004) and showed promising results regarding rapid induction and recovery due to full antagonism. However, unexpected arousals were noted (Lafortune et al. 2004; Woc Colburnet al. 2017). Butorphanol-medetomidine-midazolam combinations have also been used in wild African lion (Wenger et al. 2010), again showing rapid and smooth recoveries. The potential for unexpected arousal in lions was guarded against with hobbles and blindfolds, but no arousal was observed (Bush et al. 2012; Wenger et al. 2010).

In the author's experience, the use of midazolam (0.2 mg/kg) and medetomidine (0.02 mg/kg) in lions and tigers produces moderate to heavy sedation that allows for careful extension and extraction of a limb or tail for blood sampling from a caged area, followed by a rapid recovery with antagonism of the sedatives. Urine samples have also been obtained this way, via catheterization of the urethra. However, mild arousal, ranging from limb retraction to moving of the head, is commonly seen and entry into confined areas with this combination should be avoided. For urinary catheterization, particularly in females, application of topical lidocaine instilled around the entry to the urethra appears to significantly decrease reactions during placement of the catheter.

Acepromazine maleate, a phenothiazine derivative, has been used to provide moderate sedation or as an anxiolytic in nondomestic felids (Armando et al. 2004). Another alternative, short-acting sedative drug is gabapentin. The author has used this drug in margay (*Felis wiedii*) at a dose of 60 mg/kg administered orally to obtain blood samples under manual restraint.

Anesthesia

A principal requirement for anesthesia is the use of safe and effective dosages. Allometric scaling of basal metabolic rate, using ketamine-xylazine doses from domestic cats and applying them to nondomestic felids, has bene shown to be inconsistent (Carregaro et al. 2016). Numerous studies and reports have demonstrated the use of a wide range of anesthetic regimes, each of which has aspects to consider before use.

General anesthesia is commonly performed due to the safety risks of working around conscious or sedated nondomestic felids. Depending on the situation, drugs can be administered in a staged approach, to achieve sedation before anesthesia, or administered as a single dose. In either case, *N*-methyl-D-aspartate (NMDA) receptor antagonists (ketamine or tiletamine) and/or an inhalant anesthetic (e.g., isoflurane or sevoflurane) are commonly employed.

NMDA Receptor Antagonists

Ketamine hydrochloride is the most commonly utilized immobilization drug, and has been shown to be both safe and efficacious in a wide range of species. Its use as a sole anesthetic agent is not recommended because of higher dosage requirements and the occurrence of significant side effects: seizures, muscle rigidity, and rough recoveries. These side effects can be drastically reduced when used in conjunction with an alpha-2 adrenoreceptor agonist, opioid, benzodiazepine, or a combination of these (Wildt et al. 1988; Epstein et al. 2002; Taylor et al. 1998). The anesthetic effects of ketamine are relatively short lived, up to approximately 45 minutes, although this can vary with route of administration, dose, and, possibly, species (Hanna et al. 1988). In bobcats and South Chinese tigers, females have been reported to require higher dosages of ketamine than male counterparts (Beltrán & Tewes 1995; Armstrong 1996), therefore clinicians relying primarily on ketamine should be ready to administer supplemental intramuscular or intravenous doses of approximately 1 mg/kg (Miller et al. 2003; Quigley et al. 2001). Alternatively, volatile anesthetics can be used to prolong the anesthesia time for extended procedures.

Tiletamine, another NMDA receptor antagonist, is available for use. It is sold in conjunction with a benzodiazepine, Zolazepam, as a powder for reconstitution. This is sold as Telazol or Zoletil. Labelling recommends reconstitution of the product with 10 mL of sterile water to produce a Telazol concentration of 100 mg/mL made up of 50 mg/mL tiletamine and 50 mg/mL zolazepam. However, to produce smaller volumes for injection, which can facilitate either darting or hand-injection, a reduced volume of sterile water can be used to reconstitute a more concentrated solution. Further to this, anesthetic drugs can be used in place of sterile water to enhance the potency of the solution further, for example ketamine and xylazine in cheetah (Lewandowski et al. 2002), ketamine with jaguars (author's experience), and, unusually, thiafentanil in rhea (*Rhea americana*) (Ter Beest et al. 2012). It should be noted that none of these off-label formulations have been assessed for longevity in solution.

Telazol has been previously perpetrated as contraindicated in tigers, a dogma that persists to this day. Initial reports included a proceedings from 1980, where a Siberian tiger had prolonged incoordination. A newsletter in 1990 then described post-capture symptoms of central nervous system disease, following immobilization of

tigers with Telazol. This progressed to a statement that "Zoletil is contraindicated in tigers" in a peer-reviewed journal (Vogelnest 1999), before appearing in published textbooks (Wack 2002; Gunkel & Lafortune 2007). A review into anesthetic-related deaths in tigers demonstrated a 1.3% mortality rate, similar to other combinations, leading to the conclusion that the use of Telazol in tigers poses no more of an anesthetic risk than other regimens (Kreeger & Armstrong 2010).

Alpha-2 Agonists

Alpha-2 agonists are commonly used in conjunction with ketamine. The availability of alpha-2 antagonists allows the effects of these drugs to be reversible, allowing for rapid, smooth recoveries. The use of alpha-2 adrenoreceptor agonists has been shown to have significant effects on cardiac systolic function, when assessed using echocardiography, and can significantly decrease renal blood flow (Rodriguez et al. 2018; Lawrence et al. 1996). Due to vasoconstriction and significant reductions in cardiac output, alpha-2 adrenoreceptor agonists are not recommended for use in domestic cats with renal disease (Ter Beest et al. 2012). Reducing the dose of alpha-2 agonists in cheetah (*Acinonyx jubatus*), and replacing the removed dosage with midazolam, has been shown to significantly increase the mean arterial pressure and pulse pressure index, which can be used as an indicator of kidney blood flow (Ter Beest et al. 2012).

Xylazine has been used for a long period of time, and this has led to an array of literature assessing its effects in nondomestic felids (Rockhill et al. 2011; Lewandowski et al. 2002; Goodrich et al. 2001; Jesús et al. 2014). Some species-specific concerns have been reported, including increased sensitivity and significant respiratory depression in Sumatran tigers (Armstrong 1996).

In felids, xylazine has largely been superseded in zoological medicine by the newer alpha-2 agonists medetomidine and dexmedetomidine. Medetomidine is available in concentrations up to 40 mg/mL, allowing small volumes to be used. The use of 40 mg/mL medetomidine can easily lead to significant over or underdosing, and the author recommends the use of 10 mg/mL solution for large felids. Medetomidine is a racemic mixture of two stereoisomers, dextromedetomidine and levo-medetomidine (Sinclair 2003). Dextro-medetomidine is the active isomer, which makes up 100% of dexmedetomidine. Thus, 1 mg of dexmedetomidine has an equivalent amount of active isomer as 2 mg of medetomidine. Dexmedetomidine is commonly used in small animal medicine and is currently only available as 0.1 or 0.5 mg/mL. For this reason, medetomidine continues to be the most widely used alpha-2 agonist in large felids, with dexmedetomidine being more suited to smaller animals.

Vomiting during induction is a common side effect of alpha-2 agonists (Armstrong 1996; Curro et al. 2004). In the author's experience, pretreatment with oral antiemetics (maropitant) has minimal effect on the incidence of vomiting. The use of injectable maropitant is associated with significant behavioral reactions to administration and should be avoided in cases where follow-up injections or treatments may be needed. Transient apnea during induction may also be seen, particularly with medetomidine, which may manifest as bradypnea during the anesthetic event. Careful monitoring of respiratory rate, depth, and oxygen saturation (SpO_2) parameters is warranted. Stimulation of the nasal philtrum with a needle or finger pinch, or administration of doxapram, can be effective at stimulating respiration.

Antagonism of the alpha-2 agonists is commonly performed using yohimbine with xylazine, or atipamezole with either medetomidine or dexmedetomidine. The use of these antagonists promotes a rapid recovery, but has been shown to promote precipitous declines in blood pressure (Cushing 2020). In addition, the early use of atipamezole may protect against the development of hyperkalemia (see the section on complications for more detail).

Benzodiazepines

In addition to being used as an adjunct sedative in multidrug protocols, benzodiazepines are commonly utilized as premedication agents in large felids. The use of repeated oral diazepam is associated with hepatic failure in domestic cats and a grave prognosis (Hughes et al. 1996; Park 2012; Carvalhana et al. 2017). This has not been reported in nondomestic felids, although benzodiazepines are most commonly used as a single dose prior to immobilization and multiple doses have not been fully investigated. Diazepam also exhibits variable absorption when administered intramuscularly and has been shown to cause pain during injection. For these reasons, midazolam has become the more commonly used benzodiazepine, and the injectable formulation can be administered orally. It has been shown to cause anterograde amnesia in humans (Hirshman et al. 2001), and if this property applies to nondomestic felids, then it could be an advantage when used in cats requiring multiple anesthetic events. Although the sedative effects of benzodiazepines are relatively weak, they are commonly employed to reduce the dose required of alpha-2 agonists, supplement muscle relaxation, and help prevent seizures (Clark-Price et al. 2015). One study in captive tigers showed seizure activity in 25% of cats immobilized with an alpha-2 agonist and ketamine versus zero when midazolam was added to the combination (Clark-Price et al. 2015).

Flumazenil is a benzodiazepine antagonist that can be used to reduce recovery times. In the author's experience, this is rarely required and if antagonism of the benzodiazepine would leave only ketamine as the "active" anesthetic drug, then this is not recommended.

Other Drugs and Combinations

Butorphanol-azaperone-medetomidine fixed-dose combination (known as BAM) is gaining popularity in zoo and wildlife practice. The drug is pre-mixed, resulting in reported dosages in millilitres per kilogram of BAM rather than a traditional milligram per kilogram basis. Reports in cheetah (0.01 ± 0.001 mL/kg) and African lion (0.005–0.008 mL/kg) showed rapid induction (4–10 minutes), no adverse effects, and a rapid recovery with naltrexone and atipamezole (9 minutes) (Semjonov et al. 2017, 2019). The author has not used this combination in large felids to date.

Local Anesthesia

Reports of specific local anesthesia blocks in nondomestic felids are scant, and nerve pathways are assumed to follow a similar course to domestic animals. A brachial plexus block is described in cheetah, which showed prolonged effects on the limb and an isoflurane sparing effect during anesthesia (Kimeli et al. 2014). Lumbosacral epidurals (0.06–0.12 mg/kg morphine [McCain et al. 2009] or 0.1 mg/kg morphine with 1.6 mg/kg ropivacine [Gareth et al. 2013]) have been used in tigers undergoing abdominal surgery and fracture repairs, respectively. The approach is similar to that of a domestic dog. A transverse abdominis plane block using bupivacaine for exploratory laparotomy has also been described in a lynx, which possibly provided up to 10 hours of analgesia (Carrie et al. 2010).

Long-acting Tranquilization

Long-acting tranquilization can be helpful in the management of captive nondomestic felids. Transient or long-term stressors, such as relocation, construction, and the presence or absence of conspecifics, can all lead to potentially harmful behavioral changes such as pacing or self-trauma. In cheetahs, the use of perphenazine enanthate (3 mg/kg) showed satisfactory tranquilization and significantly reduced activity for 6 days after administration. Normal behavior resumed after 14 days. The addition of zuclopenthixol acetate (0.6 mg/kg), either alone or in conjunction with perphenazine, produced a decrease in activity, but also adverse effects including anorexia, ataxia, extra pyramidal reactions, akathisia, and third-eyelid prolapse. The use of zuclopenthixol is therefore not recommended in cheetahs (Christine et al. 2001).

The author has used clomipramine (60 mg once daily, to 20 mg every 48 hours) in tigers and alprazolam in leopards and tigers to aid in self-mutilation or pacing behaviors, with some success.

Maintenance of Anesthesia

In the field, anesthesia is usually maintained with injectable anesthetics. Depth can be assessed with regular monitoring of heart rate, respiratory rate, and, at lighter anesthetic planes, recovery of palpebral reflexes, ear twitches, or conscious movement. Being mindful of time under injectable anesthesia is useful. Using previously described sedation protocols (e.g., butorphanol-medetomdine-midazolam) provides approximately 45 minutes of working sedation time. The half-life of ketamine allows for up to an hour of effect before being metabolized, leaving only sedative drugs active (alpha-2 agonists and benzodiazepines most commonly). At this point, unexpected arousal may occur. Additional injections of ketamine (1 mg/kg IV) or propofol (0.5 mg/kg IV) can provide a rapid return to an adequate depth of anesthesia.

Inhalant anesthesia with isoflurane or sevoflurane is commonly employed for longer procedures. This can be delivered via facemask or orotracheal tube. Depth can be monitored with physical signs and, when available, end-tidal volatile anesthetic concentrations titrated accordingly.

Monitoring

Standard monitoring techniques should be employed during anesthesia of nondomestic felids (Fig. 39.3). Electrocardiogram, capnometry, rectal temperature, and pulse oximetry should be routinely monitored and values do not differ significantly from other mammalian species. Body temperature can fluctuate depending on the capture conditions and clinicians should be prepared to manage hypo- or hyperthermia. Careful planning of procedures with respect to the weather, time of day, and availability of shelter can help reduce the occurrence of these issues. In the author's experience, hypothermia can be a significant contributor to extended recovery times.

Indirect blood pressure monitoring can be performed using cuffs on the forelimb or tail base. When compared to direct blood pressure readings, forelimb cuff placement in subadult lions provided accurate readings for systolic (SAP) and diastolic arterial pressure (DAP), but overestimated



Figure 39.3 Monitoring equipment on anesthetized lions.

mean arterial pressure (MAP). Placement on the tail accurately reflected SAP, but underestimated MAP and DAP (Howard et al. 2006).

In cheetah, Doppler sphygmomanometry (DS) and oscillometry (OM) were applied at the tail base, and both showed a linear relationship to direct readings. Results varied depending on the SAP, but DS showed poorer precision than OM (Sadler et al. 2013). Another study in cheetah showed that high-definition oscillometry at the coccygeal artery overestimated direct pressures from the femoral artery and underestimated those from the dorsal pedal artery (Sant Cassia et al. 2015).

A comparison of oscillometric tail base and forelimb measurements with direct blood pressure readings in tigers suggests that an appropriately sized cuff at the tail base seems to agree reasonably with systolic, diastolic, and mean invasive pressures. Most indirect readings were within 10 mm (C. Smith, pers. comm.). Monitoring trends of noninvasive blood pressure rather than absolute values of these parameters during anesthesia offers the most value, as most are not validated for use in nondomestic felids.

Investigations into newer monitoring tools are ongoing, including the use of the plethysmographic variability index (PVI) to estimate blood pressure state (Smith et al. 2018). This study showed that a PVI was significantly correlated to MAP, and that a PVI reading of >18 was associated with increased odds of hypotension. However, this was performed in mechanically ventilated tigers, which likely has effects on PVI values. An ongoing study in spontaneously respiring tigers has shown limited correlation (A. Cushing, pers. comm.).

Unique Tips for Successful Intubation

Intubation of larger cats is facilitated by the following positioning techniques. With the patient in lateral recumbency, the neck is dorsally flexed and jaw held open by two personnel, with the tongue withdrawn from the oral cavity. The person performing the intubation is placed perpendicular to the cat (see Fig. 39.4) This allows good visualization of the larynx with a laryngoscope and long blade. Local anesthetic agents (e.g., lidocaine) on the arytenoids are rarely required, but may be applied topically if needed. The use of lubrication and an appropriately sized endotracheal tube will facilitate placement. Multiple or aggressive unsuccessful attempts can lead to localized swelling of the cartilages, and should be avoided. In the author's practice, we have seen a number of cats, particularly tigers, with asymmetrical movement of the arytenoids and, in some cases, an almost complete laryngeal paralysis of the right side. It would be prudent to visualize the laryngeal cartilage movements prior to intubation. Animals exhibiting characteristics such as this or other



Figure 39.4 Recommended positioning for ease of intubation of large felids.

airway abnormalities may exhibit respiratory complications in the recovery period.

Complications

Many of the common side effects of anesthetic protocols are documented for nondomestic felids, including alterations in blood pressure, body temperature, or cardiorespiratory depression.

One major complication, occasionally associated with immobilizing large felids (Reilly et al. 2014; Romano et al. 2018; Seal et al. 1987), is the development of hyperkalemia, defined as having a serum potassium concentration of >5.5 mEq/L (Schaer 1999). Although the exact mechanism for this occurrence is not fully understood, the most commonly proposed mechanism is the activation of alpha-2 adrenoreceptors on pancreatic beta cells. This is thought to inhibit insulin release, leading to hyperglycemia and hyperkalemia (McEntire et al. 2020). Time under anesthesia is a significant predictor of K^+ concentration, and administration of atipamezole can mitigate the elevation in K^+ concentration (McEntire et al. 2020). In the author's experience, partial or full antagonism of the alpha-2 adrenoreceptor antagonist should only be performed with a concurrent isoflurane concentration of 2.5–3%, particularly after the initial hour, when ketamine metabolism is largely complete (Hanna et al. 1988). Administration of dextrose, bicarbonate, and regular insulin has been used in the author's practice in attempts to treat hyperkalemia.

Clearly, unexpected arousal in a large felid under anesthesia is a concern for personnel. In the author's experience, successful stimulation of an ear twitch and some return of jaw tone are common early signs, and monitoring of these are recommended, alongside heart and respiratory rate. The author likes to keep 100 mg of ketamine in a syringe during procedures for rapid administration if required.

Prolonged recovery has been seen in the author's practice, often due to the development of hypothermia. Monitoring temperature and providing means to maintain body temperature during anesthesia, as well as the provision of a straw bed or heated area for recovery, will all mitigate this. Occasionally, the author has used additional doses of alpha-2 antagonists or flumazenil to hasten a long recovery. On two occasions in the author's practice, the use of regular insulin at 0.05 units/kg to treat hyperkalemia has led to significant hypoglycemia and a recovery time of 24 hours, despite treatment with intravenous dextrose. The mechanism for this is unknown. In one case, serum insulin levels were measured during the recovery phase and found to be within the normal range.

Analgesia

Provision of analgesia is considered essential for painful procedures or management of chronic, painful disease processes such as osteoarthritis (Christine et al. 2000). There is a lack of pharmacokinetic studies in nondomestic felids, and the clinical determination of efficacy of analgesics makes pharmacodynamic studies difficult to perform. The combination of these factors can make analgesic choices challenging.

Use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been scantily reported in large felids and primarily details the use of meloxicam (Douglas et al. 2006; James et al. 2012). Care should be taken with the use of NSAIDs, particularly in older cats, because of potential kidney damage, particularly renal papillary necrosis due to ischemic injury (Newkirk et al. 2010; Lee et al. 2018). Ideally, doses should be reduced in comparison to domestic animals, with regular monitoring of renal parameters in cats on long-term treatment, particularly urine protein:creatinine (KuKanich et al. 2020).

Opioids and their derivatives provide an alternative group of analgesic compounds. Tramadol, buprenorphine, and butorphanol have all been used in nondomestic felids at similar dosages to those reported in domestic cats (Ronald 2002). During surgical procedures the author recommends the use of meloxicam at 0.1 mg/kg, often in conjunction with buprenorphine. The administration of buprenorphine at 0.01 mg/kg during surgery appears to prolong recovery times, which is avoided if buprenorphine is administered just prior to extubation.

Simbadol™ is a concentrated buprenorphine formulation that is used for 24 hours of analgesia in domestic cats at 0.24 mg/kg prior to surgery. We have used this in animals unwilling to eat, where the risk or presence of renal disease made the use of NSAIDs a concern. Response appears to be mixed, although a single case of presumed opioid excitement was seen in a female African lion, with significant excitatory behaviors noted at a dose of 0.1 mg/kg.

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Table 39.2 Immobilization protocols for non-domestic felids.

Species	Immobilization Protocol (IM unless otherwise stated)	Antagonists	Additional Points	Reference
Panthera leo	K (1.9–5.7 mg/kg) + MED (0.048–0.058 mg/kg)	Atipamezole (0.19–0.23 mg/kg)	Vomiting (3/5) Additional sedation required (1/5)	Tomizawa et al. (1997)
	K (2.2–2.6mg/kg) + X (1.1–1.3 mg/kg)	Y (0.1 or 0.15 mg/kg)	Asiatic lions	Sontakke et al. (2009)
	MID (0.1–0.2 mg/kg) + MED (20–30 μg/kg), followed by K (2–3 mg/kg)	Atipamezole (0.1–0.15 mg/kg)	None reported	Author experience
	T-Z (3.8 mg/kg)	–	Rapid induction, good muscle relaxation, freedom from convulsions	Bush et al. (1978)
	BUT (0.18 mg/kg) + AZ (0.07 mg/kg) + MED (0.07 mg/kg)	NAL + ATI	Rapid induction and recovery	Semjonov et al. (2017)
	BUT (0.31 mg/kg) + MED (0.052 mg/kg) + MID (0.21 mg/kg)	NAL (0.68 mg/kg) + ATI (0.26 mg/kg) + FLU (0.003 mg/kg)	Rapid induction and recovery, mild-moderate hypoxemia	Wenger et al. (2010)
Panthera tigris	MID (0.1 mg/kg) + MED (0.02 mg/kg), followed by K (2 mg/kg)	NAL + ATI		Author experience
	K (10.8 mg/kg) + X (0.81 mg/kg)		Wild, snared Amur tigers	Goodrich et al. (2001)
	K (6.6 mg/kg) + X (0.66 mg/kg)	0.04–0.13 mg/kg Y	Seizures commonly seen, wild Siberian tigers	Quigley et al. (2001)
	K (4 mg/kg) + MED (0.025 mg/kg), ISO for maintenance via orotracheal tube		Bengal tiger cubs, one of two animals required BUT and PRO Profound bradycardia and hypotension	Gareth et al. (2013)
	K (1.66 mg/kg) + MED (0.025 mg/kg)	ATI	Supplemental K needed in 6/17	
	X (0.5 mg/kg) + MID (1 mg/kg), followed by K (10 mg/kg)	Y (0.11 mg/kg)	MMK shorter induction and recovery	Curro et al. (2004)
	MED (0.05 mg/kg) + MID (1 mg/kg), followed by K (2.5 mg/kg)	ATI (0.23 mg/kg)	XMK animals less commonly saw effects before K administration Hyperthermia in XMK	
	DEX (0.025 mg/kg) + K (3 mg/kg)	ATI (0.25 mg/kg)	Seizures observed in 25% of DK animals	Clark-Price et al. (2015)
	DEX (0.0125 mg/kg) + MID (0.1 mg/kg) + K (3 mg/kg)	ATI (0.125 mg/kg)		

Table 39.2 (Continued)

Species	Immobilization Protocol (IM unless otherwise stated)	Antagonists	Additional Points	Reference
Cheetah (*Acinonyx jubatus*)	BUT (0.29 mg/kg) + AZ (0.12 mg/kg) + MED (0.12 mg/kg)	NAL + ATI	Low SpO_2	Semjonov et al. (2019)
	BUT (0.2 mg/kg) + MED (0.035 mg/kg) + MID (0.15 mg/kg)		Unexpected arousal Hypertension Rapid induction and recovery	Lafortune et al. (2004)
	BUT (0.22 mg/kg) + DEX (0.016 mg/kg) + MID (0.18 mg/kg)		Supplementation required (5/20) IPPV required (12/20) Unexpected arousal (3/20)	Woc Colburn et al. (2017)
	T-Z (50 mg/mL), K (80 mg/mL), X (20 mg/mL) 0.023 mL/kg	Y (0.1–0.2 mg/kg)	Reconstituted one 5-mL bottle of T-Z with 400 mg of K and 100 mg of X	Lewandowski et al. (2002)
	T-Z (4.2 mg/kg)	Sarmazenil (0.1 mg/kg) or flumazenil (0.01 mg/kg)	Significantly faster recovery with antagonists versus without, no difference between antagonists	Walzer & Huber (2002)
	K (2 mg/kg) + MID (0.1 mg/kg) + MED (0.02 mg/kg)		Compared to K (2 mg/kg) + MED (0.05 mg/kg), kidney blood flow and MAP significantly higher	Stagegaard et al. (2017)
Snow leopard	MED (0.02 mg/kg) + T-Z (2.2 mg/kg)	Atipamezole (0.1 mg/kg)		Johansson et al. (2013)
	K (2.5–3 mg/kg) + MED (0.06–0.08 mg/kg)	ATI (0.12–0.24 mg/kg)	Hyperglycemia developed, 45-minute duration without antagonist	Harry (1989)
	MED (0.02 mg/kg) + MID (0.15 mg/kg) + BUT (0.2 mg/kg)	Atipamezole	Approx 50% required ketamine supplementation	Author experience
Jaguar	K (3–4 mg/kg) + DEX (23–30 μg/kg)		Significant hyperkalemia observed	Romano et al. (2018)
	K (4.4 mg/kg) + MED (0.04 mg/kg)	ATI (0.1 mg/kg)		Armando et al. (2004)
Ocelot	K (14.7 mg/kg) + X (1.1 mg/kg)		Wild animals	Females required larger K doses (Beltrán & Tewes 1995)
Leopard	K (2.2–2.6 mg/kg) + X (1.1–1.3 mg/kg)	Y (0.1 or 0.15 mg/kg)		Sontakke et al. (2009)
Bobcat	K (13.3 mg/kg) + X (1.2 mg/kg)		Wild animals	Beltrán & Tewes (1995)

ATI, atipamezole; AZ, azaperone; BUT, butorphanol; DEX, dexmedetomidine; DK, dexmedetomidine-ketamine; FLU, flumazenil; IM, intramuscular; IPPV, intermittent positive pressure ventilation; ISO, isoflurane; K, ketamine; MAP, mean arterial pressure; MED, medetomidine; MID, midazolam; MMK, midazolam-medetomidine-ketamine; NAL, naltrexone; PRO, propofol; SpO_2, oxygen saturation; T-Z, tiletamine-zolazepam; X, xylazine; XMK, xylazine-medetomidine-ketamine; Y, yohimbine

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40

Pinnipeds (Seals and Sea Lions)

James E. Bailey and Shawn Johnson

Introduction

Pinnipeds are a diverse group of aquatic, carnivorous marine mammals that have evolved physically and physiologically to survive and thrive in varied marine environments, often at extremes of temperature, water depth, pressure, and in limited daylight or darkness. They have streamlined, torpedo-shaped bodies and limbs modified into flippers (pinniped meaning "feather" or "wing"-footed). The oldest definitive pinniped fossil, found in North Africa, dates back as far as 19 million years, and represents an intermediate stage in the evolution of pinnipeds (Berta et al. 2018). The living representatives of the order Pinnipedia include the families Otariidae, the eared seals (fur seals and sea lions), Phocidae, the earless or "true" seals, and Odobenidae, the tusked seals (walruses, covered in Chapter 41). Tip-of-the-nose to tip-of-the-tail pinnipeds can range from 1200 to 6000 cm and can weigh from 37 to 3700 kg. Most clinical experience is with the California sea lion (*Zalophus californianus*) and harbor seals (*Phoca vitulina*), as they are most common species maintained in managed populations. Fortunately, the pinnipeds most commonly maintained in captivity are not at conservation risk (Corkeron 2009), and most pinnipeds in captivity were not captured from the wild (captive breeding programs). Increases in the longevity of these species, due, in part, to advancements in medical and surgical interventions employed to maintain the well-being of this mature and closed population, have resulted a growing amount of clinical experience with these species. Many other otariid and phocid species have been successfully managed in zoos and aquaria as part of conservation efforts. These include grey seals, harp seals, Hawaiian monk seals, spotted seals, ringed seals, Northern elephant seals, South American sea lions, Stellar sea lions, Australian sea lions, long-nosed fur seals, South American fur seals, northern fur seals, and South African fur seals. Anesthetic expertise is lacking for the many other species that, no doubt, will require conservation measures involving anesthesia in the future. As the longevity of these species advances, and geriatric disease processes are identified, the need and use of advanced surgical procedures increases, in turn leading to increasing need for sedation and general anesthesia of pinnipeds. Here, the prior chapters on phocids (Lynch & Bodley 2007) and otariids (Haulena 2007) have been combined and updated to cover concepts as they relate to the anesthesia of these species.

Breathing, Sleep, and Ventilation

As the 1956 Nobel laureate in medicine, Dr. Dickenson Richards, once said, "Breathing is truly a strange phenomenon of life, caught midway between the conscious and the unconscious, and peculiarly sensitive to both" (Richards 1953). Much anesthesia text has been dedicated to drug combinations and cocktails rather than understanding the consequence of those choices. Of particular importance to pinniped species is an understanding of the influence of our drug choices on breathing and proper ventilatory support.

Breathing

In all marine mammals, successfully managing breathing is crucial for successful diving and survival. The rhythm for breathing is generated by a complex neural network in the brainstem involving both excitatory and inhibitory circuits that are further described in the cetacean anesthesia chapter of this text (Chapter 43). Opioids, commonly used for anesthesia, are potent depressants of respiration (Weil et al. 1975) and significantly alter the response to both hypercapnia and hypoxemia (Pattinson 2008). Pinniped species are reported to be sensitive to opioid-induced

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respiratory depression, with phocids appearing more sensitive than otariids. It has also long been known that inhalation anesthetics depress the response of mammals to carbon dioxide in a dose-dependent fashion (Fourcade et al. 1971; Hickey & Severinghaus 1981). We now know Phox2B transcription factor expressing neurons of the retrotrapezoid nucleus located in the ventrolateral brainstem is sensitive to changes in carbon dioxide and pH levels, and Phox2B is critical to the triggering of breathing (Dubreuil et al. 2009; Coghlan et al. 2018). It has been theorized that Phox2B varies by species and anesthetic drugs appear to change the Phox2B protein structure and localization, thus affecting the protein's ability to trigger breathing in response to rising blood carbon dioxide levels. This depression of the response to carbon dioxide appears clinically to vary between species following the trend: hominid ≅ canid < equid < otariid < phocid ≅ delphinid (Colitz & Bailey 2019). The shift in the response to carbon dioxide is such that moderately anesthetized otariids will not spontaneously ventilate until the arterial partial pressure of carbon dioxide ($PaCO_2$) has climbed to 60–80 mmHg. In addition, the anesthetic or "narcotic" effect of carbon dioxide is well established in terrestrial mammals (Eisele et al. 1967; Brosnan et al. 2007). The phocid shift in response to $PaCO_2$ while under anesthesia may allow $PaCO_2$ levels to rise to the point carbon dioxide causes a degree of narcosis ($PaCO_2$ > 90–95). As such, phocids will be unlikely to spontaneously ventilate even at light planes of inhalation anesthesia without stimulation.

Sleep

The normal conscious breathing pattern of otariids and phocids involves exhalation followed immediately by inhalation and a breath hold or apneustic interval; an apneustic breathing pattern. Species differences in time spent in water over when hauled out on land has led biologists and veterinarians to wonder how some species can sleep and breath in the water. In addition, the superficial appearance of sleep and anesthesia has led investigators to compare drug-induced unconsciousness with that of sleep, despite significant differences between the two states. As discussed in greater detail in Chapter 43, unihemispheric slow-wave sleep is sleep where one half of the brain is at rest while the other half remains vigilant. This contrasts with most mammalian sleep, where both eyes are shut and both halves of the brain show unconsciousness. Unihemispheric sleep, first identified in birds and well described in cetaceans, is evident in a variant form in pinnipeds sleeping in their aquatic environment. Respiration during sleep, both in the water and on land, has been examined in a number of pinniped species, such as the grey seal (Ridgway et al. 1975), walrus (Lyamin et al. 2012; Pryaslova et al. 2009), northern fur seal (Mukhametov et al. 1985; Lapierre et al. 2007b; Lyamin et al. 2008b), southern sea lion (Lyamin et al. 2002), northern elephant seal (Kendall-Bar et al. 2023), and Caspian seal (Mukhametov 1984). Pinnipeds demonstrate a slower respiratory frequency than terrestrial mammals of similar size, and a lower respiratory frequency when in water than when hauled out on land (Mortola & Limoges 2006).

Significant differences appear in the organization of sleep between otariids and phocids, and it has been theorized these differences relate to the their respective ecological niches or range of living conditions (Lyamin & Chetyrbok 1992), with respiratory pauses increasing significantly during sleep of some phocids (ringed seal) (Matishov et al. 2012). The first variant of sleep—and the predominant pattern for pinniped sleep studied on land—is bilaterally symmetrical slow-wave sleep and rapid eye movement (REM) sleep (Mukhametov et al. 1985; Lyamin et al. 2008b), similar to that seen in terrestrial mammals. The second pattern is characterized by interhemispheric electroencephalogram asymmetry during slow-wave sleep and a very small amount of REM sleep. This pattern is recorded when fur seals sleep in water (Lyamin et al. 2008a) and is somewhat similar to cetacean unihemispheric slow-wave sleep (Serafetinides et al. 1972; Mukhametov et al. 1977; Mukhametov 1984; Oleksenko et al. 1992; Ridgway 2002).

Ventilation

Unfortunately, there is scant information published on the respiratory mechanics of pinnipeds undergoing anesthesia. The elastic properties of the excised lungs of pinnipeds have been examined and static inflation and deflation, and pressure–volume curves measured. Inflation curves of excised sea lion lungs were found to be similar to those measured in the dog (Fahlman et al. 2011; Denison 1972; Ponganis 2011). Further review of marine mammal ventilation is covered in Chapter 43. In brief, manual hand ventilation, or controlled mechanical ventilation is the mode of ventilation most often employed for pinnipeds (Table 40.1). The apneustic plateau ventilation mode used in early dolphin ventilation (Nagel et al. 1964; Ridgway 1965) was designed in an attempt to mimic conscious dolphin breathing patterns and proved superior to controlled mechanical ventilation, but it still allowed for development of atelectasis (Ridgway & McCormick 1971). New modes of ventilation are becoming available to not only mimic the normal breathing pattern of pinnipeds, but also improve mechanical ventilation of the anesthetized pinniped. Airway pressure release ventilation (APRV) was

Table 40.1 Current recommended values for controlled mechanical ventilation of pinnipeds.

Parameter	Equine Foal	Equine Adult	Phocid	Otariid
Respiratory rate (breaths/minute)	8–15	4–10	6–10	6–10
Tidal volume (mL/kg)	10–16	12–16	15–20	15–20
Inspiratory time (seconds)	1–1.5	2–3	2.5–3	2.5–3
Peak inspiratory pressure (cmH_2O)	20–30	20–30	20–30	20–30

When ventilating pinnipeds with conventional controlled mechanical ventilation, we recommend targeting respiratory rates from 6 to 10 breaths per minute with an inspiratory time of 2.5–3 seconds (or an inspiratory to expiratory ratio of 1 to 1). Pinniped tidal volumes are larger than those of terrestrial animals (Mortola & Seguin 2009) and during anesthetic ventilation we target 15–20 mL/kg, not to exceed a peak inspiratory pressure (PIP or P_{peak}) of 20–30 cmH_2O. PIP (P_{peak}) is the highest proximal airway pressure reached during inspiration. These ventilation parameters are adjusted for each individual subject to account for respiratory compliance and targeted End-tidal carbon dioxide concenration values. Worsening of respiratory mechanics is associated with an increase in PIP. Changes in compliance from pulmonary disease may require higher PIP. Adapted from (Hubbell 1991).

developed to improve ventilation of patients with low thoracic compliance. Apneustic anesthesia ventilation (AAV) was designed to normalize the pulmonary physiology of "mammals" while under anesthesia. Although both APRV and AAV mechanically mimic the breathing patterns of sleeping and conscious pinnipeds, the true objective of mechanical ventilation of anesthetized marine mammals is to provide physiologically appropriate ventilation that supports cardiopulmonary function. These modes of ventilation are expanded on in Chapter 43 and testing of AAV in marine mammals is active, producing promising results in both pinnipeds and cetaceans (Bailey & Ridgeway 2020; McCormick & Ridgway 2018; Le-Bert et al. 2020; Bukoski et al. 2022). This novel mode of ventilation also allows for the use of lower inspired oxygen concentrations, which may reduce absorption atelectasis (Le-Bert et al. 2023).

To summarize, pinnipeds are capable of both bihemispheric sleep and variants of unihemispheric sleep, but sleep and anesthetic induced unconsciousness are markedly different from one another. Anesthetic agents depress respiration such that even subanesthetic dosages in pinniped species may cause significant respiratory depression or apnea as inhalation anesthetics depress the response to carbon dioxide in a dose-dependent fashion. This depression of the response to carbon dioxide appears to vary with species and is seemingly more severe in phocids than otariids. New modes of ventilation that mimic the natural breathing pattern of pinnipeds are becoming available and may have benefit over historical methods.

Permissive or Intentional Hypercapnia

Lung protective strategies and permissive hypercapnia are discussed in the cetacean chapter (Chapter 43). To summarize, permissive hypercapnia involves accepting variable levels of hypercapnia in avoidance of potentially negative effects produced by mechanical ventilation. Allowing a degree of intentional or permissive hypercapnia will also tend to lead to increases in cardiac output and promote downloading of oxygen to tissues if held to a reasonable level. If intentional or permissive hypercapnia is used, the $PaCO_2$ should be maintained below 80 mmHg, the pH above 7.2, and the PaO_2 well above 80 mmHg. A blood gas analyzer should be considered mandatory for prompt, accurate decision making when implementing such protocols. Many marine mammal specialists insist on a degree of hypercapnia as they see the benefit of improved cardiac output and earlier return to spontaneous ventilation in otariids. The authors apply both mild intentional hypercapnia and eucapnia, situationally dependent. However, caution is advised when using eucapnia since hypotension is common in anesthetized pinnipeds. Individuals accustomed to permissive hypercapnia who begin to achieve eucapnia as a choice or out of necessity in managing hypoxemic subjects will need to be prepared to manage hypotension. Eucapnia is normal and common, but the anesthetist converting from routine clinical use of permissive hypercapnia to eucapnia must understand the physiologic change and respond accordingly. Although one may rationalize a degree of benefit of elevated $PaCO_2$, recent work has suggested that high levels of carbon dioxide are not beneficial to pinnipeds and indicate a need for enhanced monitoring and support, particularly in recovery (Ponganis et al. 2017).

Dive Reflex

Discussing the dive reflex or dive response in pinnipeds handled for sedation and anesthesia generally involves concerns for breath-holding and circulatory adjustments, specifically apnea, bradycardia, and regional vasoconstriction. It is well known from pinniped dive studies that subjects demonstrate a profound "dive reflex" when strapped to a board and forced to dive (Irving et al. 1941). It is also known that the same animals, when allowed to dive voluntarily, do not demonstrate the same degree of reflex bradycardia as when forced into a dive (Thompson & Fedak 1993; Kooyman & Ponganis 1998; Davis et al. 1983). As such, the normal dive response of pinnipeds appears to be more

graded and under conscious control when compared to the lack of control of a forced dive (not knowing when the dive will end). It should also be noted that in none of these instances of dive responses did the subjects have a dive reflex leading to their death. There is no evidence to suggest an animal will die directly from the dive reflex, although they will die if not allowed to surface and breath. Furthermore, there is no evidence that the dive reflex remains intact during pharmacologically induced unconsciousness of pinnipeds. On the contrary, there is evidence that anesthesia depresses or eliminates the dive reflex (Whayne et al. 1971; Elsner et al. 1966). In addition, there is clinical evidence that heart rates of marine mammals stabilize under general anesthesia when proper physiologic support is provided. However, some reflexes (e.g., the laryngeal and other vagally-mediated reflexes) may be present at light anesthetic planes. They are most evident at induction and recovery, and vary with the anesthetic drugs used. These reflexes, or inadequate respiratory support of the anesthetized pinniped, may well be confused with a "dive reflex". Insufficient ventilation will ultimately cause severe hypoxemia leading to myocardial hypoxemia and terminal bradycardia, but is not mediated by a reflex. As such, a patent airway and adequate ventilation are of primary concern in the anesthetized pinniped.

Although a proper dive response may not be triggered during general anesthesia, the anesthetist should be aware of another related trigemino-cardiac reflex, the oculocardiac reflex, which can still be triggered during eye surgery. This reflex is a well-known, albeit rare, cause of cardiac arrest during eye surgery of mammals. It can be observed during traction on the extra-ocular muscle and is exaggerated in the presence of hypoventilation, hypoxemia, and acidosis. It might be prevented by administration of parasympatholytic drugs or a retrobulbar local anesthetic block (Gutiérrez et al. 2016). The laryngeal/pharyngeal reflexes can lead to bradycardia as well. It is well established that general anesthetics modify the laryngeal reflex, but at light planes of anesthesia, activation of laryngeal vagal reflexes can occur during manipulation of the airway. Adequate anesthesia prior to attempting intubation, topical local anesthetic sprays, and parasympatholytic drugs prevent this reflex.

The goal of the natural dive response is to direct oxygen stores (oxygen delivery) to vital organs and reduce oxygen consumption to extend foraging time. General anesthesia appears to blunt or eliminate this dive response. Although activation of the dive reflex is often blamed for the negative outcomes of pinniped anesthetic events, it is more likely the problems are from anesthetic-induced apnea as well as the lack of a dive response that directs blood flow to vital organs. Without a dive response, blood readily flows to the periphery, leading to heat loss and hypothermia. Heart rate and regional circulation are no longer in synchrony with cardiac output, and both blood pressure and perfusion pressure fall. Oxygenated red blood cells stored in the now engorged spleen (Ponganis et al. 2011) remain out of circulation and unavailable to contribute to oxygen delivery. Indeed, an intact dive response might well enhance the probability of more positive outcomes of anesthetized pinnipeds. The anesthesiologist will likely need to intervene with inotropic and pressor agents to manage the loss of this elegant circulatory control.

Preanesthetic Preparation, Sedation, and Anesthetic Induction

A voluntary preanesthetic health assessment can provide a general overview of the animal's current health status prior to anesthesia in managed populations where medical behaviors can be cultivated. Where possible this should include complete blood count, serum chemistry panel, and physical examination. Further information can be garnered from urinalysis, radiographs, ultrasound, and echocardiography where appropriate. Unfortunately, changes in physiology and vision from illness and disease, as well as pain, can lead to loss of useful medical behaviors. Preoperative analgesia may be necessary, and trainers must be vigilant to maintain necessary medical behaviors. Given a growing number of surgical procedures are often performed on geriatric patients in managed populations, the preanesthetic health assessment is truly necessary to identify other potential underlying disease states. In situations where the subject is noncompliant, limiting the preanesthetic health to visual inspection from a distance or interview of the managing trainers and veterinarians, the risk is increased and the anesthetist must be prepared with a variety of medical supportive measures. Collection and evaluation of blood for analysis (complete blood count, biochemical/electrolyte panel) should be a priority once the animal is induced.

The choices of anesthetic and perianesthetic drugs applied to pinnipeds has been rather limited (Tables 40.2 and 40.3), but has been reviewed many times over the years, with a focus primarily on immobilization cocktails and field applications of anesthetic drugs (Haulena & Heath 2001; Brunson 2015; Haulena 2007; Gulland et al. 2018). Successful anesthetic induction has ranged from heavy mechanical restraint by lasso of free-living juvenile Stellar sea lions followed by dowel and board squeeze/entrapment and mask induction with inhalation anesthetic alone (McAllister 2001; Mellish et al. 2006; Lian et al. 2018) to solely chemical restraint by various potent

Table 40.2 Anesthetic drug dosages in otariids.

Species	N	Drug(s)	Dosage	Route	Comments	Reference
Arctocephalus australis South American fur seal	32	Tiletamine/ zolazepam	1.43 mg/kg	IM dart	Partial reversal with flumazenil	Karesh et al. (1997)
Arctocephalus australis South American fur seal	4	Tiletamine/ zolazepam, ketamine	1.43 mg/kg 0.81 mg/kg	IM dart IM	Supplemental ketamine given due to insufficient sedation	Karesh et al. (1997)
Arctocephalus australis South American fur seal	8	Tiletamine/ zolazepam, ketamine	1.15 mg/kg 0.27 mg/kg	IM dart	All administered together, partial reversal with flumazenil	Karesh et al. (1997)
Arctocephalus australis Peruvian fur seal	37	Medetomidine/ midazolam/ butorphanol	0.061 mg/kg 0.36 mg/kg 0.36 mg/kg	IM dart	Supplementation with isoflurane in 28 animals	Adkesson et al. (2019)
Arctocephalus australis Peruvian fur seal	6	Alfaxalone	2.5 mg/kg	IM	Deep sedation	Adkesson et al. (2013)
Arctocephalus forsteri New Zealand fur seal	5	Isoflurane	1.2–4.0%	IH		Gales & Mattlin (1998)
Arctocephalus forsteri New Zealand fur seal	22	Midazolam	0.3–0.7 mg/kg	IM dart	Light sedation and increased wariness on recapture	McKenzie et al. (2013)
Arctocephalus forsteri New Zealand fur seal	120	Tiletamine/ zolazepam	0.9–2.4 mg/kg	IM dart	87% of darted animals were successfully captured	McKenzie et al. (2013)
Arctocephalus forsteri	2	Alfaxalone/ midazolam/ pethidine	0.5–1 mg/kg 0.25 mg/kg 2.0 mg/kg		Achieved immobilization	Madden et al. (2023)
Arctocephalus gazella Antarctic fur seal	172	Tiletamine/ zolazepam	1.2–1.7 mg/kg	IM dart	Respiratory depression	Boyd et al. (1990)
Arctocephalus gazella Antarctic fur seal	30	Ketamine	6.9 ± 0.1 mg/kg	IM dart	Muscle tremors	Boyd et al. (1990)
Arctocephalus gazella Antarctic fur seal	23	Ketamine/ diazepam	6.3 ± 0.1 mg/kg/ 6.3 μg/kg	IM dart IM dart	Muscle tremors	Boyd et al. (1990)
Arctocephalus gazella Antarctic fur seal	14	Ketamine/ xylazine	3.8–10.8 mg/kg 0.7–2.0 mg/kg	IM IM	Poor sedation with ketamine ≤5.6 mg/kg	Bester (1988)
Arctocephalus gazella Antarctic fur seal	45	Ketamine/ xylazine	7.3 ± 0.3 mg/kg 0.6 ± 0.02 mg/kg	IM dart IM dart		Boyd et al. (1990)
Arctocephalus gazella Antarctic fur seal	7	Ketamine/ xylazine	5.6–7.8 mg/kg 0.5–1.3 mg/kg	IM dart		Ferreira & Bester (1999)
Arctocephalus phillipi Juan Fernández fur seal	12	Ketamine/ diazepam	2.16–6.76 mg/kg 0.04–0.28 mg/kg	IM	Variable plane of anesthesia	Sepúlveda et al. (1994)
Arctocephalus phillipi Juan Fernández fur seal	10	Ketamine/ diazepam	2.16–6.76 mg/kg 0.04–0.28 mg/kg	IV	Deeper immobilization compared to IM	Sepúlveda et al. (1994)

(*Continued*)

Table 40.2 (Continued)

Species	N	Drug(s)	Dosage	Route	Comments	Reference
Arctocephalus pusillus pusillus South African fur seal	27	Ketamine	4.3–7.8 mg/kg	IM dart	Variable anesthesia	David et al. (1988)
Arctocephalus pusillus pusillus South African fur seal	7	Ketamine/ xylazine	4.2–5.2 mg/kg 0.6–0.9 mg/kg	IM dart IM dart	Xylazine dosage estimated	David et al. (1988)
Arctocephalus pusillus pusillus South African fur seal	5	Carfentanil/ xylazine	6–18 μg/kg NA	IM dart IM dart	20% of animals given combination with carfentanil died	David et al. (1988)
Arctocephalus pusillus pusillus South African fur seal	15	Xylazine/ azaperone	0.57–2.0 mg/kg 0.57–2.0 mg/kg	IM dart IM dart	Sufficient for branding, short immobilization time	David et al. (1988)
Arctocephalus pusillus pusillus Cape fur seal		Medetomidine/ midazolam/ butorphanol	0.03 mg/kg 0.2 mg/kg 0.2 mg/kg	IM dart	Suitable sedation for disentanglement	Gardner et al. (2021)
Arctocephalus tropicalis Subantarctic fur seal	58	Ketamine	1.9–2.8 mg/kg	IM	Sufficient for tooth extraction, some tremors noted	Dabin et al. (2002)
Arctocephalus tropicalis Subantarctic fur seal	32	Ketamine/ xylazine	3.1–11.4 mg/kg 0.3–1.7 mg/kg	IM dart	Variable anesthesia	Ferreira & Bester (1999)
Arctocephalus tropicalis Subantarctic fur seal	49	Tiletamine/ zolazepam	0.7–1.9 mg/kg	IM	Prolonged recovery, apnea requiring ventilation	Dabin et al. (2002)
Callorhinus ursinus *Northern fur seal*	5	Tiletamine/ zolazepam/ medetomidine	0.77–1.14 mg/kg 0.03–0.04 mg/kg	IM	Reversal with atipamezole and flumazenil	Sterling et al. (2014)
Eumetopias jubatus Steller sea lion	29	Tiletamine/ zolazepam	1.8–8.1 mg/kg	IM dart	Best results with 1.8–2.5 mg/kg	Loughlin & Spraker (1989)
Eumetopias jubatus Steller sea lion	51	Tiletamine/ zolazepam, isoflurane	1.6–3.3 mg/kg	IM dart IM dart IH		Heath et al. (1996)
Eumetopias jubatus Steller sea lion	12	Medetomidine/ midazolam/ butorphanol	0.04–0.06 mg/kg 0.2–0.22 mg/kg 0.13–0.15 mg/kg	IM dart	Successful immobilization, float and with spontaneous respirations	Haulena (2014)
Eumetopias jubatus	602	Isoflurane	NA	IH	Aged 2–45 months old	Lian et al. (2018)
Steller sea lion	19	Sevoflurane	NA	IH	Weight range: 20–232 kg	
Otaria byronia South American sea lion	13	Tiletamine/ zolazepam	2.75 mg/kg	IM		Karesh et al. (1997)
Otaria byronia South American sea lion	7	Medetomidine/ midazolam/ butorphanol	0.057 mg/kg 0.31 mg/kg 0.31 mg/kg	IM dart	Sedate enough to handle	Adkesson et al. (2012)
Phocarctos hookeri New Zealand sea lion	29	Isoflurane	0.8–4.0%	IH		Gales & Mattlin (1998)
Phocarctos hookeri New Zealand sea lion	6	Tiletamine/ zolazepam Isoflurane	1.6–2.0 mg/kg 2–3%	IM dart IH	Adult males up to 330 kg	Geschke & Chilvers (2009)

Table 40.2 (Continued)

Species	N	Drug(s)	Dosage	Route	Comments	Reference
Neophoca cinerea Australian sea lion	2	Alfaxalone/ midazolam/ pethidine	0.5–1 mg/kg 0.25 mg/kg 2.0 mg/kg		Achieved immobilization	Madden et al. (2023)
Zalophus californianus California sea lion	4	Detomidine/ ketamine/ isoflurane	40–55 µg/kg 2.0–4.3 mg/kg 1–5% in oxygen	IM IM IH		Heard & Beusse (1993)
Zalophus californianus California sea lions	60	Tiletamine/ zolazepam	1.7 mg/kg	IM	Apnea	Gage et al. (1993)
Zalophus californianus California sea lion	115	Isoflurane	0.75–3%	IH		Heath et al. (1997)
Zalophus californianus California sea lion	35	Medetomidine/ ketamine	140 µg/kg 2.5 mg/kg	IM IM	Variable anesthesia, reversal with atipamezole	Haulena et al. (2000)
Zalophus californianus California sea lion	16	Medetomidine/ ketamine, isoflurane	140 µg/kg 2.5 mg/kg 1–5%	IM IM IH	Reversal with atipamezole	Haulena et al. (2000)
Zalophus californianus California sea lion	17	Medetomidine, tiletamine/ zolazepam	70 µg/kg 1 mg/kg	IM IM	Reliable anesthesia, reversal with atipamezole, ataxia and disorientation during recovery in some animals	Haulena & Gulland (2001)
Zalophus californianus California sea lion	22	Medetomidine/ tiletamine/ zolazepam, isoflurane	70 µg/kg 1 mg/kg 1–5%	IM IM IH	Reliable anesthesia, reversal with atipamezole, ataxia and disorientation during recovery in some animals	Haulena & Gulland (2001)
Zalophus californianus California sea lion	2	Medetomidine/ midazolam/ butorphanol, isoflurane	10–13 µg/kg 0.2–0.26 mg/kg 0.2–0.4 mg/kg 0.5–2.0%	IM IM IM IH	Two animals anesthetized 13 times, reversal with atipamezole, flumazenil, naltrexone	Spelman (2004)
Zalophus californianus California sea lion	29	Medetomidine	70 µg/kg	IM	Good sedation for electroencephalography	Dennison et al. (2008)
Zalophus californianus California sea lion	12	Medetomidine/ butorphanol	70 µg/kg 0.2 mg/kg	IM IM	Butorphanol resulted in decreased quality of encephalographs due to muscle jerks	Dennison et al. (2008)
Zalophus californianus California sea lion	3	Medetomidine/ midazolam/ butorphanol	30 µg/kg 0.15 mg/kg 0.1 mg/kg	IM IM IM	Adult males up to 280 kg	Melin et al. (2013)
Zalophus californianus California sea lion	15	Medetomidine/ midazolam/ butorphanol	0.017–0.056 mg/kg 0.11–0.37 mg/kg 0.11–0.37 mg/kg	IM dart IM dart IM dart	Remote immobilization for disentanglement	Frankfurter et al. (2016)
Zalophus californianus California sea lion	9	Alfaxalone/ midazolam	1.07–2.02 mg/kg 0.2–0.3 mg/kg	IM IM	Deep plane of sedation	Nevitt et al. (2015)
Zalophus californianus California sea lion	2	Alfaxalone/ midazolam/ pethidine	0.5–1 mg/kg 0.25 mg/kg 2.0 mg/kg		Achieved immobilization	Madden et al. (2023)

IH, Inhaled; IM, intramuscular; NA, not applicable.

Table 40.3 Anesthetics used in phocids.

Species	N	Agent	Dosage	Route	Comments	Reference
Cystophora cristata Hooded seal	7	Tiletamine/ zolazepam	0.5–0.7 mg/kg	IM	Pups immobilized for tagging	Folkow et al. (2010)
Erignathus barbatus Bearded seal	3 7	Diazepam Midazolam	0.11–0.19 mg/kg 0.14–0.18 mg/kg	IV IM, IV	Safe and adequate sedation for sampling and tagging, repeat dosing performed	Johnson et al. (2017)
Halichoerus grypus Grey seal	271	Ketamine/ diazepam	6 mg/kg 0.3 mg/kg	IM		Baker et al. (1988)
Halichoerus grypus Grey seal	44	Tiletamine/ zolazepam	1 mg/kg	IM	Some animals became apneic, requiring ventilation. Tremors noted.	Baker et al. (1990)
	7	Tiletamine/ zolazepam	0.5 mg/kg	IM	Additional doses given to maintain sedation; palpebral reflex maintained	Lawson et al. (1996)
	30	Tiletamine/ zolazepam	0.93–1.67 mg/kg	IM	Minor tremor, vocalisation and mild dyspnoea in some	Langton et al. (2017)
		Medetomidine	50–100 μg/kg	IM	Effects dependent on dose rate.	Barnett (1998)
	4	Midazolam/ medetomidine	0.32 mg/kg 0.021 mg/kg	IM	Delivered by dart – moderate sedation, allowed for capture	Sharp et al. (2017)
	3	Midazolam/ pethidine/ propofol/ isoflurane/ sevoflurane	0.2–0.3 mg/kg 2 mg/kg 1.25–2.0 mg/kg	IM IM IV IH IH	Anesthesia for surgical procedures	Huuskonen et al. (2011)
	2	Alfaxalone	2.0 mg/kg 0.5 mg/kg	IM IV	Used as total intravenous anesthesia after intubation	Gómez Fernández et al. (2022)
Histriophoca fasciata Ribbon seal	45	Diazepam Midazolam	0.8–0.2 mg/kg 0.1–0.2 mg/kg	IV IV	Safe and adequate sedation for sampling and tagging	Johnson et al. (2017)
Hydrurga leptonyx Leopard seal	3	Ketamine, xylazine	2.2–5.9 mg/kg 0.2–0.5 mg/kg	IM IM	Muscle tremors, apnea, bradycardia, 2 mortalities	Mitchell & Burton (1991)
	1	Tiletamine/ zolazepam	2 mg/kg	IM	Apnea, bradycardia, death	Mitchell & Burton (1991)
	34	Xylazine	0.8–2.8 mg/kg	IM	Variable plane of anesthesia with lower dose, high doses cause vomiting/aspiration	Mitchell & Burton (1991)
	16	Midazolam, pethidine	0.18–0.27 mg/kg 1.0–1.5 mg/kg	IM IM	Unpredictable immobilization, poor airway maintenance.	Higgins et al. (2002)
	19	Tiletamine/ zolazepam	0.5–1.5 mg/kg	IM	1.2–1.4mg/kg IM gave most reliable response.	Higgins et al. (2002)
	13	Midazolam/ butorphanol	0.16–0.38 mg/kg 0.05–0.17 mg/kg	IM IM	Midazolam repeat doses given	Pussini & Goebel (2015)
Leptonychotes weddellii Weddell seal	5	Ketamine, halothane	0.15–0.25 mg/kg 1–4%	IM IH		Hurford et al. (1996)
	30	Tiletamine/ zolazepam	0.3–1.1 mg/kg	IM	Plane of anesthesia varied with dosage, mortalities	Phelan & Green (1992)
	106	Tiletamine/ zolazepam	0.6–0.86 mg/kg	IM, IV	IM resulted in mortality while IV was very reliable.	Wheatley et al. (2006)
	7	Midazolam, isoflurane	0.3–0.5 mg/kg 1.9–5%	IM IH	Dose rate for midazolam based on estimated body mass only	Bodley et al. (2005)

Table 40.3 (Continued)

Species	N	Agent	Dosage	Route	Comments	Reference
	30	Ketamine, midazolam	1.6–2.4 mg/kg 0.08–0.12 mg/kg	IM IM	Induction dose administered IM and additional doses given IV if required.	Mellish et al. (2010)
	11	Ketamine, diazepam	2.0 mg/kg 0.01 mg/kg	IM	mild sedation	Harcourt et al. (2010)
	18	Midazolam, butorphanol	0.2–0.3 mg/kg 0.1–0.2 mg/kg		safe and effective sedation	Whoriskey et al. (2022)
Lobodon carcinophagus Crabeater seal	17	Ketamine, diazepam	2.9–7.7 mg/kg	IM		Shaughnessy (1991)
	31	Midazolam, pethidine	0.15–0.4 mg/kg 1–3 mg/kg	IM	Unpredictable sedation	Tahmindjis et al. (2003)
	35	Midazolam, isoflurane	0.26–0.85 mg/kg 1–5%	IM IH	Purpose-built gas anesthetic machine for field use.	Gales et al. (2005)
Mirounga angustirostris Northern elephant seal	66	Tiletamine/ zolazepam, diazepam, ketamine	1.0 mg/kg 1.0–4.0 mg 0.25–1 mg/kg	IM IV IV	IV doses given as needed to maintain sedation	Champagne et al. (2012)
Mirounga leonine Southern elephant seal	15	Ketamine, diazepam	2.3–3.9 mg/kg 0.02–0.35 mg/kg	IM IM	Apnea, poor muscle relaxation	Woods et al. (1994a)
	37	Ketamine, diazepam	4.4–8.6 mg/kg 0.04–0.13 mg/kg	IM	Apnea	Slip & Woods (1996)
	55	Ketamine, xylazine	2.1–11.4 mg/kg 0.2–0.5 mg/kg	IM	Prolonged apnea	Mitchell & Burton (1991)
	15	Ketamine, xylazine	2.1–3.1 mg/kg 0.2–0.5 mg/kg	IM IM	Apnea, tremors	Woods et al. (1994a)
	25	Ketamine, xylazine	2.5–3.4 mg/kg 0.5–0.6 mg/kg	IM IM	Apnea, responsive to doxapram (2mg/kg)	Woods et al. (1996a)
	2	Medetomidine	13–27 µg/kg	IM	Vomiting, hyperthermia, bradycardia	Woods et al. (1996b)
	10	Medetomidine, ketamine	12–27 µg/kg 1.4–2.2 mg/kg	IM IM	Hyperthermia, variable plane of anesthesia, poor reversibility, bradycardia	Woods et al. (1996b)
	13	Midazolam, pethidine	0.02–0.07 mg/kg 1.2–6.7 mg/kg	IM IM	Deeper sedation with higher doses of pethidine (2.7–6.7mg/kg), faster recovery after naloxone or naltrexone	Woods et al. (1994b)
	10	Midazolam, pethidine, thiopentone	0.02–0.07 mg/kg 2.7–6.7 mg/kg 2.2–5.9 mg/kg	IM IM IV	Good immobilization allowing intubation of 5 min duration after thiopentone	Woods et al. (1994b)
	597	Tiletamine/ zolazepam	0.38–0.54 mg/kg	IV	Mean duration of immobilization 15.48 min. Immobilized such that stomach lavage and blood sampling were possible.	McMahon et al. (2000)
	77 47	Tiletamine/ zolazepam, ketamine	0.36–1.5 mg/kg 0.28–2.60 mg/kg	IM IM	Doses of ketamine useful when initial level of sedation or duration of immobilization was unsatisfactory.	Carlini et al. (2009)

(*Continued*)

Table 40.3 (Continued)

Species	N	Agent	Dosage	Route	Comments	Reference
Phoca groenlandica Harp seal	14	Midazolam, isoflurane	0.1–0.2 mg/kg 4%	IM IH		Pang et al. (2006)
Phoca vitulina Harbor seal	9	Propofol	2–6 mg/kg	IV	Optimum short-acting anesthesia at 5mg/kg. Apnea.	Gulland et al. (1999)
	12	Propofol, isoflurane	3–5 mg/kg 2–5%	IV IH	Easily intubated, apnea	Gulland et al. (1999)
	18	Diazepam	0.32 mg/kg	IV	bradycardia	Lapierre et al. (2007b)
	80	Midazolam	0.06–0.25 mg/kg	IM IV	Safe and adequate sedation for sampling and tagging, Repeat dosing	Johnson et al. (2017)
Pusa hispida Ringed seal	4	Midazolam, butorphanol, propofol Isoflurane	0.2–0.5 mg/kg 0.27–0.7 mg/kg 2–3 mg/kg	IM IM IV IH	Induction protocol for procedure	Hermann-Sorensen et al. (2021)
Phoca largha Spotted seal	14 6	Diazepam Midazolam	0.09–0.2 mg/kg 0.19–0.2 mg/kg	IV IV	Safe and adequate sedation for sampling and tagging, Repeat dosing	Johnson et al. (2017)

IH, Inhale; IM, intramuscular; IV, intravenous.

and efficacious combinations of anesthetic agents delivered by dart, to remarkable behavior control by training for mask induction with inhalation anesthetic agent alone under trainer command. Induction of anesthesia of pinnipeds requires a balance of behavioral restraint, mechanical restraint, and chemical restraint (Fig. 40.1). The term "balanced anesthesia" has traditionally meant the use of a combination of drugs, with each drug delivered in an amount sufficient to produce the desired effect while keeping undesirable effects to a minimum. A balanced approach to pinniped anesthesia includes far more considerations than just the anesthetic drugs.

The rationale for the anesthetic protocol begins with an assessment of behaviors. Desensitization training and voluntary medical behaviors contribute in no small part to more positive outcomes in managed populations, eliminating the need for aggressive restraint methods or potent cocktails with severe physiologic consequences. Quality trainers and animal handlers are truly necessary for safe anesthesia, and they must be given both the opportunity and time required for training. Without strong medical behaviors there is greater reliance on mechanical and chemical restraint. Without training, mechanical devices can become dangerous and can lead to injury. Without behavior or mechanical control, the chemical restraint must become more aggressive. One of the most commonly applied drug combinations for chemical restraint pinnipeds has been variations in the combination of midazolam, butorphanol, and medetomidine (Spelman 2004), proven effective in field immobilization of young, healthy otariids for short procedures. Unfortunately, this somewhat overused combination has a high incidence of negative outcomes in some managed populations. The necessary use of variations of this drug combination on rescued, untrained, free-living otariids of variable disease condition and severity is associated with the nearly 4% fatality rate (Stringer et al. 2012). In addition, a historically high negative outcome rate is reported in ophthalmologic cases receiving medetomidine or dexmedetomidine, leading not only to the development of unanticipated ciliary body hemorrhage, with or without postoperative hyphemia, but also death. In a series of 13 consecutive, lengthy ophthalmologic procedures on geriatric California sea lions after immobilization with a combination of midazolam, butorphanol, and dexmedetomidine, one subject vomited, one had an irregular heart rate and another arrhythmias, two had prolonged recoveries, and three died during anesthesia or within 72 hours of failed recovery (Colitz & Bailey 2019). For these reasons, the alpha-2 agonists are considered a poor choice in geriatric pinnipeds undergoing lengthy procedures, despite reversibility, and would be ill-advised in phocids (Li 2023). This is not to say the alpha-2 agonists are not effective or on occasion necessary, but the anesthetist must recall Maslow's axiom that "it is tempting, if the only tool you have is a hammer, to treat everything as if it were a nail" (Maslow 1966). The anesthetist

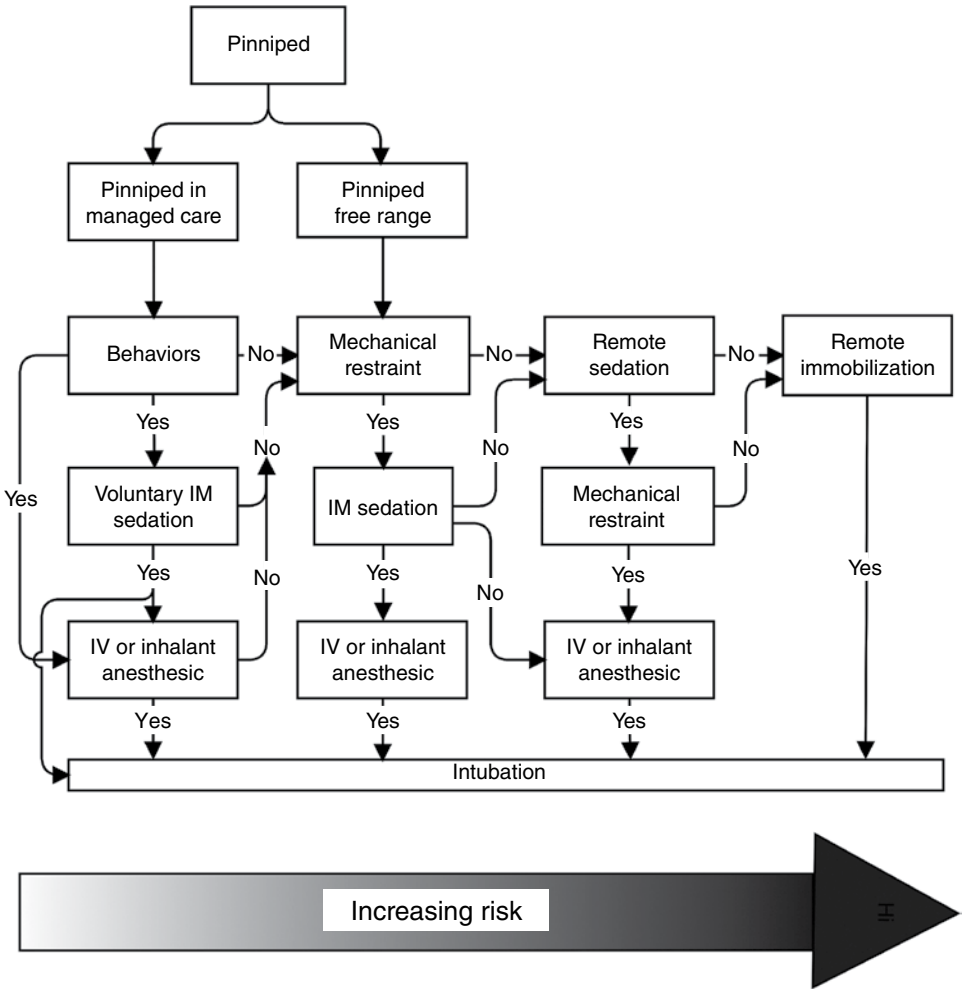


Figure 40.1 Anesthesia in pinnipeds requires a balance of behaviors, mechanical restraint, and chemical restraint. Behaviors are useful responses taught to pinnipeds by qualified trainers. Although free-living pinnipeds may have natural behaviors, we can take advantage of for capture, behavioral control is poor. Mechanical restraint is the physical control of the subject by devices such as nets, slings, husbandry boxes, or squeeze cage. Chemical restraint is the application of pharmacologic agents (drugs) to bring the subject to a manageable state by producing tranquilization, sedation, neuroleptanalgesia, immobilization, or anesthesia as described in the text. Immobilization cocktails should be considered higher risk. Risk increases with lack of proximity to the subject as we move from behavioral control to chemical immobilization delivered by remote means. IM, intramuscular; IV, intravenous. Reproduced with permission (Bailey 2023).

must understand and consider all options available before making drug choices and understand the potential consequences. It is easy to dart an animal with potent, efficacious anesthetic agents, but the physiologic consequences for this convenience are significant. That being said, more judicious use of alpha-2 adrenergic agonists may yet prove beneficial.

Behaviors are useful responses taught to pinnipeds by qualified trainers. Examples of useful medical behaviors are holding on target for injections by hand, tolerance of mechanical restraint in a squeeze cage, or acceptance of an anesthetic mask for inhalation anesthetic delivery. Such behaviors can even be sufficiently robust to allow free-standing application of anesthetic drug delivery without physical restraint. Mechanical restraint is the physical control of the subject by devices such as nets, slings, husbandry boxes, or squeeze cages to improve control and safety for humans involved in necessary medical care. Desensitization work (behaviors) to make the subject comfortable and accepting of mechanical restraint is invaluable in enhancing the safety of such devices. Chemical restraint is the application of pharmacologic agents (drugs) to bring the subject to a manageable state.

Tranquilization is the use of pharmacologic agents to promote peace of mind for the subject, such as the anxiolytic effect of the benzodiazepines when delivered alone. In

subjects with appropriate training, the anxiolytic effect of midazolam alone may be sufficient to move to anesthetic induction by intravenous (IV) injection or inhalation anesthetic by mask under behavioral control. Sedation is the use of pharmacologic agents to produce a drowsy state of consciousness where the subject can still respond to some commands, although this may interfere with some trained behaviors, particularly when opioids are used. Neuroleptanalgesia is produced by combination of a tranquilizer with an analgesic drug (opioid) producing quiescence, altered awareness, and analgesia, potentially to the point of unconsciousness. Immobilization involves the use of injectable pharmacologic agents to create an altered state of consciousness, outwardly indistinguishable from general anesthesia. However, general anesthesia is a pharmacologic state where there is analgesia, amnesia, areflexia, muscle relaxation, and unconsciousness, which may not all be present in routine immobilization techniques applied to pinnipeds. For patient safety, immobilization should be treated with the same supportive efforts as needed for general anesthesia.

With chemical restraint, *ut est rerum omnium magister usus*, or experience is the best teacher (Julius Caesar, *Commentarii de bello civili*). Anesthesia methods applied to free-living subjects are highly variable and often depend on the experience of the personnel, as well as the historical success of the method applied. For example, though less commonly used in managed species today, the combination of tiletamine and zolazepam (Telazol or Zoletil) is still the preferred immobilization method for free-living elephant seals. However, most free-living subjects are only anesthetized to facilitate study of the species and its interaction with the environment for the betterment of not only the subject species, but also the ecosystem and related species. As such, most free-living subjects will also be young, healthy individuals and may better tolerate the physiologic challenges of a broader range of necessary mechanical and chemical restraint methods. On the contrary, rescued free-living subjects are often debilitated or otherwise unhealthy and are at greater risk of negative outcomes in the face of the immobilization methods necessary for the safety of human caretakers (Stringer et al. 2012). The authors recognize the broad range of sedation and anesthesia methods applied to the wide variety of pinnipeds species over the past many decades (Tables 40.2 and 40.3). We offer only to share our experience and provide some general, repeatable methods in the hope of improved outcomes for all the species under our care, including the growing geriatric population developing from the quality medical care provided to our managed populations.

A relatively few pharmacologic agents have gained acceptance for use in managed populations of pinnipeds. Benzodiazepines (diazepam 0.05–0.3 mg/kg PO, IM, IV; midazolam 0.05–0.3 mg/kg IM, IV) are commonly used, often in combination with opioids (butorphanol 0.1–0.4 mg/kg IM; meperidine 0.1–2.0 mg/kg IM) to produce sedation or neuroleptanalgesia. Immobilization can be achieved with the addition of medetomidine (0.01–0.03 mg/kg IM) or dexmedetomidine (0.002–0.01 mg/kg IM) to this sedative combination. Concentrated versions of midazolam, butorphanol, and medetomidine assist with remote delivery by dart or pole syringe. Alternatively, alfaxalone (0.5–2.0 mg/kg IM, IV) has been introduced for immobilization where large volume or multiple intramuscular (IM) injections are feasible (Adkesson et al. 2013). An experimental, concentrated alfaxalone formulation, RD0387, allowing for reduced volumes, combined with midazolam and meperidine or butorphanol, has recently been used successfully for immobilization of large otariids in lieu of medetomidine (Madden et al. 2023). Other parenteral anesthetic agents have been used for immobilization or induction of general anesthesia. The cyclohexamines ketamine (1–10 mg/kg IM, IV), tiletamine (in Telazol or Zoletil, 1–2 mg/kg IM, IV) have been applied, but are not reversable so are now less favored. However, as an NMDA glutamate receptor antagonist, ketamine provides an alternative method of pain management, contributing to a balanced anesthetic and analgesic approach. Ketamine also infrequently interrupts spontaneous breathing at clinically relevant dosages. Although not reversible, ketamine is worthy of consideration where immobilization is necessary and is used in various free-living species. The phenolic compound propofol (1–6 mg/kg IV), injected directly in the extradural vein, producing rapid induction and control of airway, is routinely used for induction of anesthesia of phocids and odobenids in preference to mask induction with inhalation anesthetics.

Both the inhalation anesthetics isoflurane and sevoflurane have been used successfully in pinnipeds and are low-solubility agents, with most of the drug being eliminated by exhalation. For mask induction, isoflurane has a greater pungency and slower onset, such that sevoflurane has become preferred. The amount of these inhalation anesthetic agents needed to cause 50% of animals to show no gross purposeful response to noxious stimuli (minimum anesthetic concentration [MAC] or effective dose 50% [ED_{50}]) has not yet been determined for pinnipeds, making comparison of equipotent concentrations to other species imprecise. However, the effect of inhalation anesthetic agents is well preserved over the wide variety of mammalian species tested, so the amount of inhalation anesthetic for pinnipeds will likely differ little from that required for other mammalian species.

The MAC can be estimated at 1.3% isoflurane and 2.3% sevoflurane. It requires 1.2 to 1.5 times the MAC to ensure the majority of subjects do not respond to a surgical stimulus when inhalation anesthetic is used as the sole anesthetic drug. Addition of other drugs and hypothermia contribute to significant reductions in the required inhalation anesthetic for surgery. Based on cases over the past decade applying similar preanesthetic sedative drug dosages, one will find the end-expired sevoflurane will likely need to be maintained no lower than 1.8–2.0% to ensure no gross purposeful movement to surgical stimulus of pinnipeds under general anesthesia.

Phocid Anesthesia in Brief

Benzodiazepines are very effective in tranquilizing phocids. In wild captures, diazepam (0.25 mg/kg IV) preceding mechanical restraint with a simple hoop-net prior to mask induction with inhalation anesthetic is not uncommon. In managed populations, subjects have been trained to accept an injection of midazolam and an inhalation anesthetic mask without mechanical restraint. Free-living phocids remain somewhat excitable and tend to inhale gas anesthetics by mask, where those in managed populations will tend to breath-hold and delay induction or become apneic from anesthetic exposure before being sufficiently relaxed for smooth intubation. More often a phocid will receive a neuroleptanalgesia combination (e.g., midazolam 0.2 mg/kg IM and butorphanol 0.2 mg/kg IM) followed by mechanical restraint and extradural venipuncture for delivery of a parenteral anesthetic agent (propofol 2 mg/kg IV) allowing prompt intubation under direct laryngoscopy for maintenance of inhalation anesthetic (sevoflurane 1.8–2.0% end-tidal concentration). In field settings where inhalation anesthesia is not available, heavy sedation can be maintained for longer procedures with multiple smaller doses of midazolam, butorphanol, and ketamine IV, alone or in combination. The partial agonist opioids (butorphanol) are often sufficient for purposes of control without undue respiratory depression, but full agonist opioids (meperidine) have been used for greater sedation of larger phocid species where there is inadequate behavioral control. Regular desensitization work, making the subject comfortable and accepting mechanical restraint in a blood collection box or husbandry "dog house" for routine extradural venipuncture as part of health assessments, makes anesthetic management of phocids much smoother and less stressful for the subject. Larger pinnipeds species, such as grey seals, have also been trained to accept mechanical restraint in squeeze cages.

Otariid Anesthesia in Brief

Training robust medical behaviors is crucial to reducing anesthesia risk in otariids. Behaviors such as free-standing anesthetic induction by mask have been trained even in extremely large otariid species, with or without the anxiolytic effects of benzodiazepines. Benzodiazepines are anxiolytic, but further sedation with opioids is generally needed for most otariid subjects, even when properly trained for mechanical restraint. A scissor-style squeeze cage is commonly used for mechanical restraint in managed populations (Ridgway & Simpson 1969) and has been used for some free-living capture and long-term holding programs (Skinner et al. 2015). Subjects are trained to accept temporary restraint by squeezing, allowing for injection of sedative agents. The drugs must be delivered accurately intramuscularly or uptake will be poor. The sedative combination (midazolam 0.2 mg/kg IM and butorphanol 0.2 mg/kg IM or meperidine 2.0 mg/kg) is allowed time for uptake and full effect (20–25 minutes). Sedation is followed with mechanical restraint by squeezing to allow mask induction with inhalation anesthetic. The mechanical restraint significantly enhances control and human safety, but is not without risk. Inadequately trained or sedated subjects may attempt to bite at the bars and resist mask induction. Subjects that bite these metal bars have been known to break teeth and fracture jaws. Even subjects that know to tolerate a squeeze cage can become intolerant when ill. Only properly designed squeeze cages with padded bars should be used for this method of restraint. Boat bumpers and rolled towels can be used to center the head in the cage for mask induction and act as safe bite "toy". Additional padding can be used above the head to prevent biting of bars. It is preferred that the anesthetic mask is malleable to move between cage bars if necessary, mold to the face of the subject, and tolerate biting without injury to the subject or causing equipment failure. A modified traffic cone has proven ideal for this purpose (Heath et al. 1997). The combination of midazolam 0.2 mg/kg IM and meperidine 2.0 mg/kg IM may prove neuroleptanalgesic in some species, such as southern sea lions, and nearly allow intubation. Higher dosages of midazolam (0.2–0.5 mg/kg IM) have been used with an opioid to produce a neuroleptanalgesic state and allow for awake intubation. A squeeze cage is not always available or may be of inadequate size for larger subjects, making mechanical restraint impractical. Large custom walrus restraint nets (Wally-nets) can be effective for large sea lions and fur seals. Improvised squeeze cages have been created, but efficacy and response are often variable. Where mechanical restraint is not possible, a greater reliance is placed on pharmacologic agents. A combination of concentrated midazolam (0.2 mg/kg IM),

butorphanol (0.2 mg/kg IM), and medetomidine (0.010 mg/kg IM) is commonly used, but problematic in producing bradycardia, vasoconstriction, and reduction in cardiac output, complicating vascular access, and challenging debilitated and geriatric patients physiologically. The medetomidine and vatinoxan combination (Zenalpha®) has recently been used in otariids, but clear benefit is not yet evident. Alternatively, concentrated midazolam (0.2 mg/kg IM), butorphanol (0.2 mg/kg IM), and alfaxalone (1.0 mg/kg IM) is currently under review with promising results (Madden et al. 2023). Delivery of the efficacious immobilization combinations, and those described in the tables, can be delivered by pole-syringe or dart where necessary. Accurate intramuscular delivery is problematic with these methods, but there is generally adequate uptake for effect even when delivered imprecisely. However, caution is advised in redosing after apparent failed darting, as overdosing from delayed uptake is possible.

Odobenid Anesthesia in Brief

Walrus subjects in managed populations can be very well trained such that delivery of the anxiolytic agent midazolam (0.2 mg/kg IM) or even direct extradural venous needle placement for delivery of propofol (2–4 mg/kg IV) can be performed under behavioral control. However, most will need additional sedation and analgesia from an opioid (butorphanol 0.2 mg/kg IM or meperidine 2.0 mg/kg IM), particularly when behaviors are off due to illness and discomfort. Difficult patients can be injected remotely by pole syringe or dart, but it is imperative the drug is accurately delivered intramuscularly or uptake will be poor. Repeat dosing from failed delivery can lead to cumulative drug uptake and overdose, with sudden onset and severe respiratory depression. Dosing of midazolam and meperidine can be sufficient to be considered neuroleptic and awake intubation has been possible in some young patients with supplemental dosage of the combination. Low-dose alfaxalone has been used to bridge control where this neurolept combination has failed, but further evaluation is needed before recommending this drug. However, most subjects will be adequately sedated and follow limited commands on midazolam (0.2 mg/kg IM) and meperidine (2.0 mg/kg IM) or butorphanol (0.2 mg/kg IM), when delivered with precision. Extradural needles and saphenous venous catheters have been placed under sedation for induction of anesthesia with propofol (0.5–4.0 mg/kg IV). With intubation performed blindly after rapid sequence induction with propofol, the anesthetist must be well prepared for intubation of these large now apneic subjects.

Pinniped Vascular Access

Vascular access is feasible in pinnipeds, similar to terrestrial species, with ultrasound facilitating visualization in the majority of locations (Fig. 40.2). Venipuncture of the

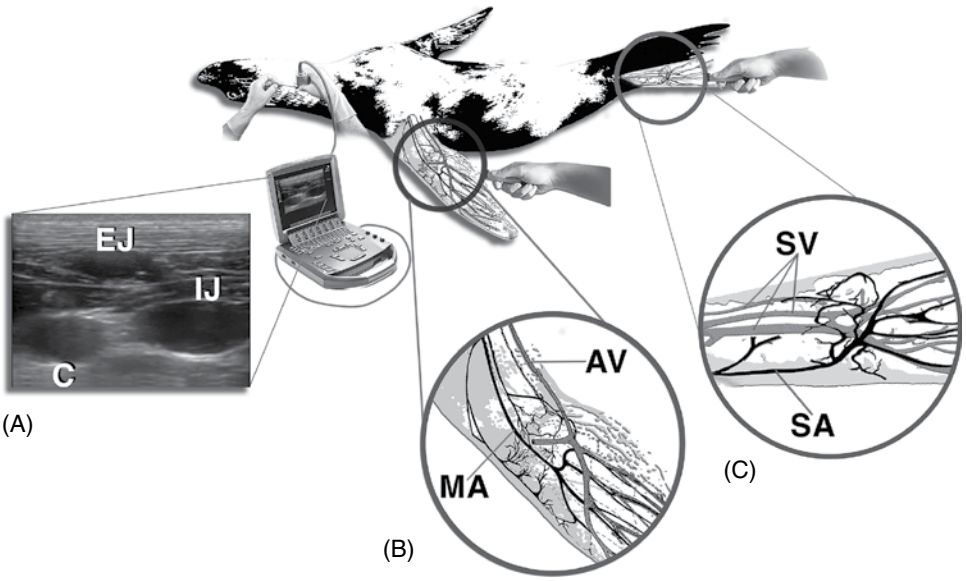


Figure 40.2 Pinniped jugular (A), pectoral flipper (B), and pelvic flipper (C) vasculature. Section A shows a transverse ultrasound image of the external jugular vein (EJ), internal jugular vein (IJ), and carotid artery (C). Section B shows the median artery (MA) and antebrachial vein (AV). Section C shows the saphenous artery (SA) and plantar branches of the saphenous vein (SV) (adapted from St-Pierre 1974 and Erxleben 1777 in St-Pierre 1974). Reproduced with permission (Bailey 2023).

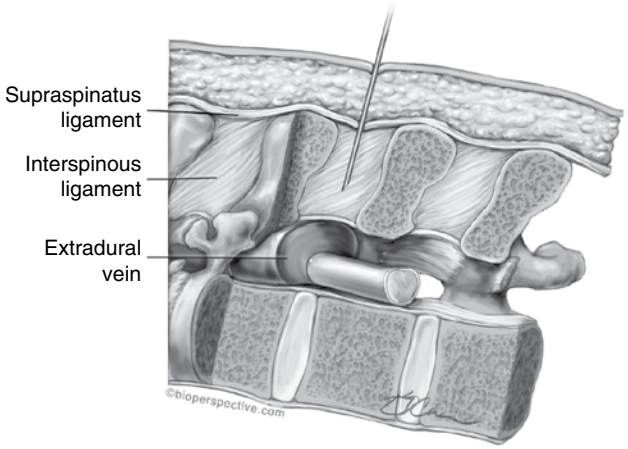


Figure 40.3 The phocid extradural intravertebral vein (Harrison & Tomlinson 1956) is a large, flat vein situated on the dorsal aspect inside the spinal canal, dorsal to the spinal cord and external to the dura mater, between the dura and the periosteum lining the vertebral canal. The vein extends for the entire length of the spinal canal, communicating caudad with the pelvic venous plexus and craniad with the dural sinuses. It is often incorrectly referenced in the literature as epidural vertebral vein, vertebral venous sinus, etc.

extradural intravertebral vein of phocids (Fig. 40.3), placed in a manner like epidural needles, can be maintained or be converted to a small-diameter cannula using available epidural catheter kits. Although small in diameter, thus limiting fluid volume delivery, such extradural venous catheters have been aseptically maintained up a week postoperatively for drug delivery. Venous access of the jugular vein, although visible on smaller subjects, is facilitated by ultrasound, and is more commonly performed in otariids than phocids and odobenids. Longer peripherally inserted central catheters may be more easily maintained in the jugular vein of larger subjects. Cannulation of the pectoral flipper antibrachial vein (also referred to as the brachial or superficial palmar vein) (Renner & Bailey 2013) and occasionally the cephalic vein can be performed without ultrasound. However, ultrasound is a useful tool to facilitate access to these as well as the pelvic flipper medial saphenous vein and plantar digital veins, particularly in phocids and odobenids. Doppler flow probes and ultrasound can facilitate identification and cannulation of the median and saphenous arteries, but the location is also digitally palpable. Standard over-the-needle catheters can be used to cannulate both arteries and veins to reduce cost, but modern micro-introducer kits using a modified Seldinger method (Seldinger 1953) simplify and expedite cannulation. Anecdotally, it is clear from the well-initiated marine mammal anesthetist that alpha-2 adrenergic agonists severely complicate even ultrasound-guided venous cannulation of pinnipeds due to vasoconstriction.

Pinniped Intubation

The adequately anesthetized pinniped is probably the least difficult marine mammal species to intubate since the larynx can be visualized in many subjects and is relatively immobile. Cuffed endotracheal tubes of 8–24 mm internal diameter are suitable for the range of species. After induction of anesthesia, the patient is positioned in sternal recumbency. An assistant holds the top and bottom jaw open with appropriate rope or similar material and extends the neck to create a linear oral–pharyngeal–laryngeal axis. It is important to avoid twisting the head on the body axis since this will distort the normal anatomy of the pharynx and larynx, and hinder recognition of landmarks. This is particularly true in larger pinnipeds, where the larynx can be observed to fall horizontally. The anesthetist uses the tip of the endotracheal tube to move the soft palate off the epiglottis, which is then depressed with the endotracheal tube or an elongated laryngoscope blade and the tube is slid between the arytenoid cartilages. If a laryngoscope is used, the tip of the blade is best placed into the space between the base of the tongue and the epiglottis. The tip is gently forced downward, stretching the hypoepiglottic ligament, thus dropping the epiglottis and exposing the glottic opening (Fig. 40.4). It is best to resist the compulsion to rake the epiglottis with the laryngoscope blade or lever the blade against the teeth as trauma leading to hemorrhage and edema of the epiglottis or dental damage can occur. Placement of the endotracheal tube in the airway is then timed with inspiration as the arytenoid cartilages abduct, easing intubation. The endotracheal tube should be checked for length to assure it is not passed beyond the thoracic inlet because the trachea bifurcates at the thoracic inlet into the two mainstem bronchi. The tube is then secured in position with gauze or other material to the rostrum or maxilla.

Larger pinnipeds have excessive pharyngeal tissue and an overlong soft palate, making visualization difficult for direct laryngoscopy. These larger subjects may even obstruct their airway when in sternal recumbency under profound sedation, and ventilation must be monitored continually after sedation. They can be intubated blindly by palpation in a manner similar to the domestic large animal species, although it may be at considerably greater risk to the individual intubating. An appropriate level of anesthesia, with or without protective gear such as bite blocks, is necessary to ensure safety of the anesthetist during intubation by manual palpation. However, the method is simple and more reliable when visualization is difficult. With the animal in sternal recumbency, the mouth is held open using ropes and the hand protecting the endotracheal tube cuff is inserted until the epiglottis can be felt (Fig. 40.4).

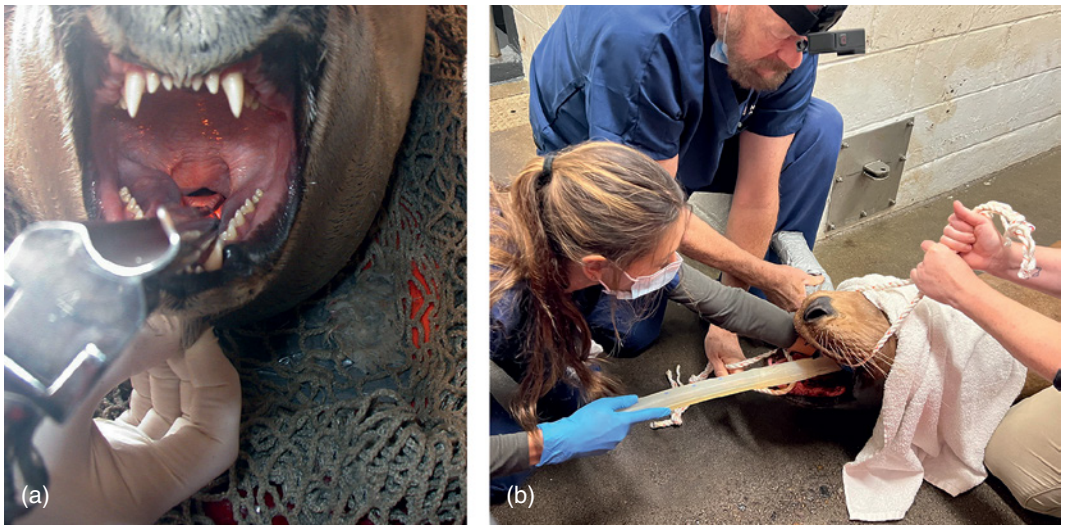


Figure 40.4 Intubation. (a) Intubation by direct laryngoscopy in a 37-kg phocid versus (b) intubation by manual palpation of a 370-kg otariid.

The soft palate is elevated manually, the epiglottis depressed, the opening of the larynx identified, and the endotracheal tube is guided into the trachea by hand. The anesthetist may find both their hand and the endotracheal tube in the airway of larger subjects when too small an endotracheal tube is chosen. In lieu of this palpation method, bite blocks and fiberoptic intubation scopes can be used to improve human safety and visualization, but may complicate the logistics of the process, particularly in field conditions. Caution is advised when using immobilization cocktails, as they are sufficiently depressive that large subjects will partially or fully obstruct their airway, particularly in sternal recumbency. Immobilization cocktails may appear to involve minimal exertion and subjects may appear to ventilate, flaring their nostrils and attempting to move their diaphragm and chest, but may be obstructed. Ventilation, with evidence of airflow, must be monitored from the time of first handling to after full recovery.

Vigilance Monitoring and Support

Monitoring is often noninvasive (ECG, pulse oximetry, capnography, temperature, and inspired/expired gases) (Fig. 40.5). However, invasive blood pressure monitoring has become a standard of care for otariids, with some greater difficulty in small phocids (Bailey 2013). Doppler flow probes and ultrasound facilitate cannulation of the median artery of the pectoral flipper or saphenous artery of the pelvic flippers of pinnipeds. Hypotension cannot be detected if it is not measured. The purpose of monitoring blood pressure is to obtain an objective measure of systemic circulation. Significant hypotension may be defined as a mean arterial blood pressure of <60 mmHg. Where anesthesia is the sole cause of hypotension, the appropriate response would involve reducing the level of anesthesia



Figure 40.5 Patient monitoring, such as a portable ECG, is essential to a successful field anesthesia procedure, as seen here in an immobilized Weddell seal (NMFS Permit #23273). Hooding can be beneficial to limit external stimulus during sedation and immobilization versus during general anesthesia.

where possible, balancing the anesthetic technique with less cardio-depressive drugs (e.g., opioids), volume loading where appropriate, inotropes such as dobutamine (0.2–2.0 μg/kg/min IV, lower than terrestrial mammals) or ephedrine (0.05–0.1 mg/kg IV) (Trumbull et al. 2021), and possibly vasopressors such as phenylephrine (0.1–0.5 μg/kg/min IV) or norepinephrine (0.01–0.05 μg/kg/min IV). Noninvasive methods of estimating blood pressure have yet to be validated. The use of oscillometric cuffs on the pectoral and occasionally pelvic flippers of phocids have been used to follow trends in blood pressure where invasive blood pressure measurement is not possible.

Blood gas, and electrolyte and lactate analysis should be considered mandatory for lengthy anesthetic procedures or procedures on compromised or geriatric pinnipeds. Arterial blood gases are preferred over venous data in assessing the efficacy of ventilation, but venous data is still useful. Early analysis can detect changes in lactate and potassium related to excessive anaerobic metabolism or exertional rhabdomyolysis, regardless of how the induction process was perceived by the anesthesia team. Aggressive immobilization cocktails may appear to involve minimal exertion, but these highly physiologically challenging drug combinations may lead to inadequate cardiac output and tissue perfusion. Rhabdomyolysis (Chapter 4) is a graded disease where one subject may experience mere muscle pain, while similar individual under the same conditions may experience severe myopathy, dump myoglobin from muscle into the bloodstream, and shower the kidney with this protein, causing renal failure. Blood gas data interpretation has been reviewed (Bailey & Pablo 1998) and such information can inform regarding the adequacy of ventilation. Late-onset myopathic conditions from inadequate padding, perfusion, or other causes can be detected by continuing such monitoring through recovery (Bailey et al. 2012). Vitamin E/selenium combinations have been used in the prevention and treatment of pinniped myopathic conditions at 0.06 mg/kg of selenium IM.

Cushioning with thick (4–8-inch) medium-density, open-cell foam padding similar to that used for large terrestrial mammals is necessary to prevent both myopathy and neuropathy from developing during longer procedures (Bednarski 1991). Waterproof closed-cell foam provides little if any cushioning and should be reserved for short procedures on the floor. The insulating effect of foam padding also prevents conductive heat loss. During anesthesia, body heat is lost through radiation, conduction, convection, and evaporation. Conductive and convective heat loss can be minimized by various methods of insulation, including the padding and blanket covers. Evaporative heat loss is more difficult to control, such as losses to the breathing of anesthetic circuit dry gases. However, dry-docking the patient prior to surgery or towel drying after induction is helpful in limiting surface evaporative cooling. Warming of replacement fluids generally has a relative minimal effect on patient warming, but delivery of cold fluids is of no benefit. Several types of patient-warming devices are available. The most effective systems are likely the warm circulating air-blanket systems, but circulating warm water blankets are often used in conjunction. The need for warming will depend on the working environment, but most patients in a routine surgical environment will arrive normothermic and quickly become hypothermic after induction of anesthesia if the presurgical environment is temperature controlled to the comfort of the surgeon, and if the presurgical process does not lead to exertion of the patient. Lack of presurgical environmental control, excitement, and exertion in the anesthetic process, and certain drugs can lead to hyperthermia at induction. It is important to remember that the dosage of inhalant anesthetic gas necessary to maintain anesthesia is increased by hyperthermia and reduced by hypothermia, and recovery is prolonged by hypothermia. Hypothermia also causes reduced cardiac contractility. Most patients do not benefit from hypothermia, and it should be prevented.

Neuromuscular blockade is often needed for ophthalmologic procedures of pinnipeds to properly centralize and immobilize the eye for surgery. Atracurium, which undergoes simple Hofmann degradation (elimination), has been successfully used by the authors for neuromuscular blockade in phocids, otariids, and odobenids. Even though it is easily eliminated from pinnipeds, any residual muscle weakness caused by atracurium can be antagonized by delivery of edrophonium. Delivery of edrophonium should be done slowly, while still monitoring to detect and avoid bradycardia that has been observed occasionally in pinnipeds. The need for edrophonium may be assessed in part by the use of nerve stimulators, but the method is imprecise for firm judge of any residual paralysis. With edrophonium recently going out of production, neostigmine may be used with caution as a replacement. Neostigmine has greater muscarinic effects leading to extreme bradycardia, requiring preemptive treatment with atropine. New true reversal agents, like sugammadex in combination with rocuronium, have been used in several pinniped species by the authors and may well replace the use of atracurium in pinnipeds in the future.

Anesthetic vigilance monitoring and support do not end just because the anesthetic vaporizer has been turned off. The respiratory depressive effects of anesthetic drugs are profound in pinnipeds and ventilatory support (mechanical ventilator, manual resuscitator bag, or oxygen demand valve) will be necessary well into recovery. Inhalation anesthetic agents are eliminated nearly entirely though

exhalation, so slowing respirations in recovery to produce a degree of permissive hypercapnia can delay elimination of inhalation anesthetic, although isoflurane and sevoflurane do washout rapidly. Monitoring the end-expired anesthetic concentration while supporting ventilation in recovery can be informative of the point where the inhalation anesthetic agent will have minimal effect on awareness (approximate MAC awake isoflurane <0.4%, sevoflurane <0.8%). After achieving this gas anesthetic level, other drugs may be reversed to expedite recovery without undue dysphoria from inhalation anesthetic remaining.

Anesthetic Recovery

Pharmacokinetics is the study of the relationship between time and the serum concentration of a drug (and drug metabolites) and involves absorption, distribution, and elimination of the drug. Pharmacodynamics is a measurement of what a drug does in the body (therapeutic, toxic, and pharmacologic). Neither the pharmacokinetics nor pharmacodynamics are well defined for most drugs used in pinniped anesthesia. Limited pharmacokinetic data on opioids (Nutter et al. 1998; Molter et al. 2015) and nonsteroidal anti-inflammatory drugs (Trumbull 2023; Simeone et al. 2014) in marine mammals suggest the half-life of many useful anesthetic and perianesthetic drugs will have surprisingly long duration of action when compared to terrestrial species. For this reason, it is preferrable to use anesthetic drugs that can be eliminated easily without metabolism (inhalation anesthetics) or are reversable. As anesthetic drugs appear to have slower elimination than observed in terrestrial species, it is common to reverse the benzodiazepines, opioids, and alpha-2 agonists (at least temporarily) to speed recovery and the return of effective spontaneous ventilation in pinnipeds.

The benzodiazepines can be reversed with flumazenil. Full reversal requires 1 part flumazenil for every 13 parts of midazolam or every 26 parts diazepam, milligram for milligram (Pawson 2008). The functional half-life of flumazenil can be estimated from terrestrial animal models as at least 1 hour. Although irrelevant at these practical clinical dosages, some studies suggest flumazenil may have intrinsic benzodiazepine partial agonist or inverse agonist activity in certain animal models. For this reason, repeat dosing of flumazenil should not be considered limitless, but repeated dosages are not uncommon and may be necessary. Since delivery intravenously may lead to abrupt recovery with associated excitement and large volumes are often needed, half the dose of flumazenil is delivered intramuscularly and half intravenously approximately 5 minutes later to promote smoother, yet timely recovery. The response is then evaluated before any redosing.

Opioids can be reversed with naloxone or naltrexone. Full reversal can be achieved with naloxone (0.01 mg/kg) or naltrexone (0.05–0.1 mg/kg), but 100 mg of naloxone for every 1 mg of opioid is often referenced for reversal of ultra-potent opioids used in some capture methods. The half-life of naloxone is variable in terrestrial species but can be approximated at 20–30 minutes, where naltrexone can be anticipated to have a much longer species dependent half-life of 7–8 hours and a slow terminal elimination-phase half-life of around 24 hours. Naloxone can be used to probe the level of opioid-induced depression postoperatively by using lower dosages to partially reverse the opioid effect or allow for the opioid effect to return after the short duration of action of a full dose of naloxone. Where invasive surgery has been performed, it is preferred to only use naloxone for a partial or temporary reversal of opioid effect to facilitate recovery and return spontaneous respiratory control, without long-term interference with postoperative pain management. Where analgesia is not necessary, or the subject is perceived to have excessive opioid-induced respiratory depression, naltrexone can be used to provide sustained reversal of the opioid effect. Since intravenous delivery may lead to abrupt recovery and excitement, half the dose of naloxone or naltrexone is delivered intramuscularly and half intravenously approximately 5 minutes later to promote smoother, yet timely recovery. If flumazenil is also necessary, it is delivered as the first reversal agent of the combination, and the response is evaluated before any redosing of either reversal agent. Alternatively, all reversal agents are given IM and recovery is more gradual, but generally smooth.

Medetomidine and dexmedetomidine are reversed with atipamezole. When concentrated medetomidine is used it is important to recognize that reversal is dependent on a ratio of milligrams of reversal drug to milligrams of alpha-2 agonist, and not the volume. Atipamezole is delivered at 5 times the milligram dose of medetomidine and 10 times the milligram dose of dexmedetomidine for full reversal. Atipamezole is delivered intramuscularly to avoid overly rapid onset of reversal and potential hypotension. When alpha-2 agonists are deemed necessary for induction of anesthesia, but the effects of the alpha-2 are considered undesirable for the specific patient, the authors will often deliver atipamezole after achieving an appropriate end expired gas anesthetic level, and preferably after gaining vascular access for necessary support. However, it has become common practice to reverse alpha-2 agonists immediately after inhalation anesthetic is introduced early in the procedure to counter the vasoconstriction caused by the alpha-2 agonist to better enable vascular access. We only advise caution to this approach as the subject will likely become hypotensive after reversal and support will

likely be necessary. When reversal is a part of recovery, excitement during recovery must also be avoided as catecholamine-induced vascular beta-receptor stimulation in the face of alpha-receptor blockade by atipamezole can cause unopposed vasodilation and potential cardiovascular collapse from excessively abrupt and profound vasodilation, particularly in cardiovascular compromised patients.

The endotracheal tube should be maintained as long as possible within the safety guidelines for the species involved. Protective contract restrictions for large pinnipeds can influence this decision-making process in favor of human safety. Subjects will routinely attempt to extubate prematurely or cough and inadvertently extubate as they regain reflex control of the airway. Given the severe respiratory depressive effect of anesthetic agents in pinnipeds, it is possible for them to extubate prematurely and become apneic. This is particularly true of phocids, and reintubation may not be possible without additional anesthetic agent being delivered. For this reason, it is advisable to have available a spare endotracheal tube one size smaller than used for the procedure as well both drugs and tools for reintubation until extubation is successful. Phenylephrine 0.5–1.0% nasal spray can be used to reduce nasal edema that can develop from recumbency and endotracheal tube ties around the muzzle. Respiratory stimulants such as the nonspecific central nervous stimulant doxapram (1 mg/kg IM, IV) are generally unnecessary, but worthy of mention as a tool for managing respiratory depression when there is a lack of control of airway and consciousness. Unfortunately, this only increases cerebral oxygen consumption in the face of inadequate ventilation and may do more harm than good in most instances. Best practice is to keep the endotracheal tube in place as long as possible.

Assigning someone to provide oversight of all activities related to the procedure — an incident commander — ensures personnel, policies and procedures are optimized to improve the emergency response. Cardiopulmonary resuscitation procedures, medications, and methods should be discussed and lead personnel should be identified in advance for such emergencies. Quality training staff should be informed and readily available to facilitate any potential emergency response. Assigning an individual to focus solely on the management of the anesthetized patient is critical to preventing anesthesia-related problems. Given the potential for anesthesia-related problems such as high carbon dioxide levels, apnea, hypoxemia, bradycardia, thermoregulatory problems, and prolonged recoveries, it is important to assign an individual to focus solely on the management of the anesthetic event who has a thorough understanding of intubation, mechanical ventilation, vascular access, and drug delivery methods for species undergoing the procedure. Understanding the potential complications of anesthesia, appropriate vigilance monitoring, and being prepared to manage complications improves the overall outcome of anesthetic procedures in pinnipeds.

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41

Walrus

Michael T. Walsh, James E. Bailey, and David B. Brunson

Natural History, Physiology, and Anatomy

There is one species of walrus with two accepted subspecies of walruses: the Atlantic walrus, *Odobenus rosmarus rosmarus*, and the Pacific walrus, *O. rosmarus divergens*. The walrus is the second largest pinniped at only half the size of the southern elephant seal. Fay (1982) reviewed the biology and ecology of the Pacific walrus, and the reader is referred to his book for additional background information. Initial animals in managed care at modern facilities in the United States originated from the Artic as a result of being orphaned, often from indigenous hunting. Births in this managed population are still limited and as of 2022 there were only 14 walruses in US facilities.

Atlantic subspecies males can measure more than 300 cm and weigh 1200 kg. Females can measure 250 cm and weigh 750 kg. At birth, pups range in length and weight, approximating 140 cm long and 50 kg. The Pacific walrus is slightly larger, with males being up to 360 cm long and weighing up to 1600 kg; specimens of Pacific walrus males maintained at Marineland of the Pacific reached 1900 kg but were considered obese. Pacific walrus females are up to 260 cm long and weigh approximately 1250 kg. Young Pacific walrus pups measure 140 cm and weigh approximately 60 kg (Garlich-Miller & Stewart 1999). Walruses have enlarged upper canine teeth commonly referred to as tusks. The bases of the tusks are like other teeth, with a large area of germinal tissue responsible for tusk growth.

Walruses can sleep on land and in water, with the majority of sleep occurring on land (Pryaslova et al. 2009, Lyamin et al. 2012). The concept of sleep, breathing, thermoregulation, and vigilance while in the aquatic environment is discussed in greater detail in Chapters 40 and 42. Respiration during sleep, both in the water and on land, has been examined in walruses, (Pryaslova et al. 2009), demonstrating a slower respiratory frequency when in water and when compared with terrestrial mammals of similar size.

The dive reflex has been extensively studied and is present in all air-breathing vertebrates but was first studied in pelagic pinnipeds. It is composed of a series of physiologic changes that take place during diving that include the onset of bradycardia, a parasympathetic response that results in a reduction of cardiac output with a potential drop in arterial blood pressure (Irving et al. 1942). There is confusion in the application of physiologic changes in a normal awake dive reflex with the stages of heavy sedation or general anesthesia. The clinical signs during chemical immobilization can appear similar to this classic physiological reflex: apnea, bradycardia, and regional vasoconstriction. Even so, many still use activation of the "dive reflex" as an explanation for negative outcomes in marine mammal anesthesia. It is more probable that during drug- or disease-induced physiologic changes, it is instead the lack of this elegant reflex control and the lack of ability to direct blood flow to vital organs that may precipitate negative consequences, not a "dive reflex". This reinforces the need for greater vigilance monitoring during anesthetic procedures in walruses.

Anatomic considerations for the clinician and anesthesiologist include relatively small nostrils that close during submersion, narrow nasal passages, and nasal turbinates arranged such that the nasal passages lack a large meatus. The oral cavity is narrow, characterized by a high arched hard palate, and is more accessible for hand-guided intubation in larger subjects. The walrus tongue is large and thick, lacking thin edges for standard veterinary pulse oximetry probes. Hand-guided intubation of smaller walruses is difficult to impossible and long lighted laryngoscope blades, or preferably an intubation scope, are mandatory for timely intubation. Walruses have a unique pharyngeal pouch, more common in males and wild walrus, that can be inflated to provide buoyancy while resting on the ocean surface (Fay 1960). It may also present a potential challenge for airway management in

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captive-raised walruses. During tracheal intubation, the pharynx lateral to the laryngeal cartilage may be confused with the laryngeal opening and misguide the individual performing intubation.

There is a potential for trauma to handlers, and while quite trainable, protected contact may be used in some facilities, especially during breeding season. Behavioral training has become essential for health and welfare management because of the size of walruses, and veterinarians should be part of a desensitization program for voluntary health behaviors such as general examinations, oral examinations, eye treatment, ultrasound, and blood sampling. There have been a small number of publications regarding anesthesia techniques of wild and facility walrus with application variations in environments, drugs, and mortality levels (Haulena & Heath 2001; Haulena & Schmitt 2018). The commonality of methods between walrus and other pinnipeds is reinforced in the pinniped chapter (Chapter 40), which is recommended to the reader to complete the understanding of their use. This chapter is not meant to be a review of all anesthetic approaches as much as illustrating techniques that are potentially safer for the patient as we improve applications to reduce the anesthesia death rate to match more closely that of more commonly anesthetized domestic patients.

Behavioral Training for Medical Management and Anesthesia

Early anesthesia management of walruses did not include behavioral training. Training for potential anesthetic procedures should be part of standard health management. The inclusion of walruses in managed care has resulted in the application of positive reinforcement training techniques that can make elective procedures such as biopsy and blood samples possible without physical restraint or sedation. Additional behavioral training promotes voluntary safe injection for sedation and anesthesia with less stress on both handlers and the animal. Walruses have also been trained to accept a facemask for gas induction, peripheral venous and extradural intravertebral venous cannulation for intravenous (IV) anesthetic induction drugs, and for smaller animals to enter and tolerate a squeeze cage for mechanical restraint assistance. Full contact for walrus has been used but protective contact with spaced bars for induction should be considered for larger tusked animals depending on the age, temperament, and policies in facilities. Skilled trainers and animal handlers are necessary to support safe anesthesia, and they must be given both the opportunity and time required for training where possible or where there is a lead time for elective procedures. Veterinarians should always participate in injection or blood sampling training so they are not a novel addition on the day of the procedure and the walrus is comfortable with them during the induction.

Physical Restraint

Physical restraint of untrained wild adult walruses is generally impractical. This results in the use of drugs that have rapid onset and higher potential for negative outcomes. For facilities housing walruses, cargo nets have been used for nontrained young animals, but effectiveness decreases in animals with more than 300 kg of body weight and require experienced personnel to avoid human injury and extended stress on the animal. Smaller juveniles have been trained to enter larger squeeze cages voluntarily, but those systems are limited in usefulness and availability for larger animals. Darting may become necessary if the animal is not trained for voluntary intramuscular (IM) injections or intravertebral IV access but is not the preferred approach.

Pharmacological Considerations

Whether immobilizing a walrus in captivity or in the wild, the attendant problems are similar. Clinicians should be prepared for all management components of the anesthetized walrus, including resuscitation. Table 41.1 reviews a number of anesthetic techniques used with wild walrus for reference by the reader. The listing of these techniques is not an endorsement by the authors and researchers and facility clinicians are advised to consult with experienced personnel and to compare the procedural requirements and the relative success rates of those mentioned.

Drugs are usually administered via IM injection by hand, or in some cases by jab stick or dart from a greater distance in wild environments. Darting may result in drugs not reaching the intended muscles accurately and volumes are limited by drug concentrations and dart size. Dart volumes are necessarily small, which often restricts drug combinations to concentrated versions of alpha-2 agonists, benzodiazepines, and opioids, with or without dissociative class drugs. It has been postulated that very concentrated drugs may also have altered or variable uptake by tissue, but this needs further study. Recently, the steroid anesthetic agent alfaxalone has been used in combination with sedative drugs. Numerous drug groups and combinations have been used with different levels of success, safety, and mortality. The reversibility of alpha-2 agonists, benzodiazepines, and opioids has made them the preferred drugs for sedation and immobilization, but reversibility should not be mistaken to mean the drugs have equal levels of safety. Early mortalities may have also been associated

Table 41.1 Anesthetic protocols used with wild and facility walrus. Note that some techniques vary in their effects on survival rate and are mentioned for comparison and not endorsed for application to facility walrus. It is recommended that experienced personnel be contacted before their application.

Species	Drug Combination	Reversal	Comments	Reference
Wild walrus techniques				
Odobenus rosmarus	Phencyclidine hydrochloride 0.2–0.3 mg/kg ($n = 8$) Acepromazine hydrochloride 0–15 mg/kg ($n = 8$) Ketamine hydrochloride ($n = 1$)	N/A	Two mortalities Ketamine volume exceeded dart capability	DeMaster et al. (1981)
Rosmarus rosmarus	Etorphine 4.0–15.5 mg	Diprenorphine 15–19 mg/10 mg of etorphine	Severe respiratory depression, mortality 15–20%	Griffiths et al. (1993)
Rosmarus rosmarus	Etorphine 7.8 mg all sizes ($n = 40$)	Naltrexone 250 mg IV or IM	Oxygen supplementation intubation $n = 27$	Ølberg et al. (2017)
Rosmarus rosmarus	Teletamine/zolazepam 1.4–2.2 mg/kg		1 of 3 died	Griffiths et al. (1993)
Rosmarus rosmarus	Carfentanil 2.7–3.0 mg/kg IM		Apnea muscle rigidity Workshop	Lanthier & Stewart (2002)
Rosmarus rosmarus	Telazol 3.3 mg/kg IM Medetomidine 17 mg/kg	Atipamizole 9.5–19 mg/kg IM/IV	Workshop No muscle anomalies	Lanthier & Stewart (2002)
	Ketamine 2.5–4.0 mg/kg Medetomidine 11–18 mg/kg	Atipamizole	Workshop	Lanthier & Stewart (2002)
Rosmarus rosmarus	Carfentanil 2.7–3.0 mg/kg IM	Naltrexone 150 mg/mg	Apnea, muscle spasms	Lanthier et al. (1999)
Rosmarus divergens	Carfentanil citrate 2.7–3 mg/kg IM Medetomidine 30 mg	Naltrexone hydrochloride atipamizole	Apnea	Mulcahy et al. (2003)
Rosmarus divergens	Carfentanil, isoflurane	Naltrexone hydrochloride 150–350 mg		Tuomi et al. (2002)
Facility Walrus Anesthesia Techniques				
Rosmarus divergens	Midazolam 0.1–0.2 mg/kg IM Butorphanol 0.1–0.2 mg/kg IM Propofol 0.3–0.9 mg/kg IV Sevoflurane 0.5–2.0%	Flumazenil Naltrexone	1 of 6 required sevoflurane masking, 3 did not require propofol	Schmitt (unpubl. data); Haulena & Schmitt (2018)
Rosmarus divergens, rosmarus rosmarus	Midazolam 0.1–0.2 mg/kg Meperidine 2–3mg/kg Propofol to effect Isoflurane	Flumazenil Naltrexone	Uneventful recovery	Kaartinen et al. (2018)
Rosmarus divergens	Midazolam 0.03–0.05 mg/kg IM Meperidine 3 mg/kg IM Thiamylal sodium to effect IV Isoflurane 1–2%	Naloxone, naltrexone	Initial approach to decrease barbiturate use	Walsh et al. (1988)
Authors recommendations for facility walruses	Midazolam 0.1 mg/kg IM Meperidine 2.0 mg/kg IM Propofol 1–2 mg/kg IV Sevoflurane	Flumazenil Naloxone Naltrexone		

(*Continued*)

Table 41.1 (Continued)

Species	Drug Combination	Reversal	Comments	Reference
NSAID use end of procedure or post procedure	Carprofen ($n = 4$) 2 mg/kg Meloxicam ($n = 3$) 0.1 mg/kg		Consider appetite and hydration status and monitor renal parameters	Kaartinen et al. (2018)
	Flunixin meglumine 0.25 mg/kg IM		Should have information of renal status, not recommended as first choice	Walsh (pers. comm.)
	Galliprant 1.5–2 mg/kg SID			Schmitt (pers. comm.)

IM, intramuscular; IV, intravenous; N/A, not applicable; SID, once daily.

with inadequate ventilation, monitoring levels, and fewer options available for response to cardiorespiratory complications.

Barbiturates

In the 1980s, with less clinical experience in anesthesia of walruses and fewer drug options, ultrashort-acting barbiturates (e.g., thiamylal sodium) were initially one of the drugs of choice with controlled access to walruses. As physical restraint with nets was used with the goal of immediate IV induction, it was often administered without preanesthetic sedatives. General anesthesia was successfully induced in walruses with dosages of 3.3–4.8 mg/kg, with half of the calculated dose administered initially and the additional drug given to effect as needed (Walsh et al. 1990). Apnea was a common problem, and monitoring and support were not emphasized. Barbiturate inclusion was gradually and intentionally reduced and replaced with the addition of benzodiazepines and opioids.

Benzodiazepines

Diazepam as a preanesthetic in walruses was not commonly used although as a class the benzodiazepines were generally considered safe. The sedative effects of midazolam and diazepam can be overridden in an excited patient so it is combined with other compounds such as meperidine and later butorphanol. First attempts with each drug type were tried using lower doses until confidence in their safety was established.

Opioids

Meperidine (Pethidine)

Based on early anesthesia development of marine mammals in numerous institutions, meperidine was shown to be an effective sedative in a variety of species (Joseph & Cornell 1988). Meperidine was administered by hand injection to 10 walruses at a dosage of 0.23 and 0.45 mg/kg in the first facility. Sedation/restraint was moderate without apparent detrimental effects. If used as an analgesic, meperidine was associated with obvious sedation (Cornell 1978, Cornell and Antrim 1987). As a result of clinical experience over time (Walsh et al. 1988), a higher dose of meperidine (2.2 mg/kg) was eventually reached as part of a two-drug preanesthetic protocol by the authors.

Butorphanol Tartrate

This synthetic opioid with mixed agonist–antagonist properties is used as an alternative drug to meperidine in some facility sedation protocols. In wild walruses, opioid analgesics have been used for capture and immobilization (DeMaster et al. 1981; Gales 1989; Griffiths et al. 1993; Lynch et al. 1999). Of the opioid analgesics, meperidine and butorphanol have been used with benzodiazepines or alpha-2 agonists (Griffiths et al. 2014), but anecdotally there have been occasional mortalities associated with alpha-2 use. Assessment of the analgesic effects of opioids has been limited to the responses observed during immobilization. Facility walruses have been sedated with 0.1–0.2 mg/kg butorphanal, usually in combination with midazolam (Haulena & Schmitt 2018).

Potent Opioids With or Without Alpha-2 agonists: Wild Walruses

The use of ultrapotent opioid analgesics for immobilization of walruses has proven to be less than ideal and is limited to wild individuals. Complications in wild walruses include apnea, muscle spasms, rigidity, and death. Adult male Atlantic walruses on a land haul out were effectively immobilized with carfentanil with an IM dose of 2.7–3.0 mg. Muscle spasms were associated with the onset of immobilization. All of the animals had extended periods of apnea, but tracheal intubation was not possible due to muscle rigidity (Lanthier & Stewart 2002; Lanthier et al. 1999). The estimated effective dosage range was 4–5 mg/kg.

Many factors make accurate drug dosing difficult in field situations: the body weight can only be estimated prior to drug administration, and dart placement and vascularity of the injection site affect the ultimate success of remote drug delivery. Pacific walruses injected with similar carfentanil dosages were not adequately immobilized despite the presence of apnea and muscle spasms.

A field study was performed to test combinations of the alpha-2 agonist medetomidine with the opioid carfentanil in adult Pacific walruses. Medetomidine was selected because of the presence of an effective antagonist (atipamezole) and the availability of a concentrated formulation that minimized dart size and injection volume. The addition of medetomidine with carfentanil would likely decrease the opioid dose and improve muscle relaxation (Mulcahy et al. 2003). A medetomidine dose of 30 mg was combined with carfentanil doses that varied from 0.06 to 3.0 mg per animal. At the 0.06-mg carfentanil dose, immobilization was inadequate, while a dose of 3.0 mg caused severe respiratory and circulatory depression that was judged to be life-threatening. Carfentanil doses of 0.15 and 0.3 mg with 30 mg of medetomidine enabled approach and handling, but apnea occurred and immediate reversal of both drugs was administered. Due to the low numbers of animals, it was not possible to further evaluate this combination. It should be noted that the addition of medetomidine did markedly decrease the carfentanil needed for immobilization, although respiratory depression was still severe. Dexmedetomidine is simply a chiral-separated form of medetomidine. The dosage can be estimated as half of the total racemic medetomidine dose due to the elimination of the "left-handed" enantiomer, levomedetomidine. However, in clinical use this may appear an underestimate. Thus, it would be appropriate to use half of the medetomidine milligram dosage if using dexmedetomidine, but one might choose to adjust that dosage 10% higher. Atipamezole is an effective and recommended reversal agent for dexmedetomidine. However, regardless of reversal, mortalities have been associated with alpha-2 agonist use in facility walruses.

In another study, 17 walruses were immobilized with carfentanil alone with immediate reversal with naltrexone. Carfentanil (2.4–2.7 mg total dose) was administered via dart to the muscular area of the rump. Sedation occurred in 7–21 minutes. Muscle twitching of the muzzle was noted with full-body tremors lasting a few seconds, leading to muscle rigidity and immobilization (Tuomi et al. 2002). Naltrexone at 175–350 mg total dose was administered into the muscular area of the lip as soon as the walrus was safe to approach. Reversal occurred between 10 and 20 minutes after administration. One animal had a rapid reversal in approximately 5 minutes following injection. An additional dose of naltrexone (175–350 mg) was administered to each animal at the completion of the desired work time to ensure complete reversal of the carfentanil. Use of gas anesthesia provided additional anesthesia when needed (Tuomi et al. 2002).

Field immobilizations with etorphine HCl have had similar effects. Dosages between 4.0 and 15.5 mg per adult male based on estimated body weight were used in field immobilizations of Pacific walruses, with or without reversal with either diprenorphine or naloxone. A dose of 7 mg per adult male was used for the standard dose. Overall mortality rates varied but were in the range of 15–20% (Griffiths et al. 1993; Hills 1992). With this level of mortality, the authors do not recommend this approach for managed walruses as other options or balanced approaches, including behavioral compliance or mechanical restraint methods, can be considered in more controlled environments.

Because of the rapid onset of severe respiratory depression associated with potent opioid administration in walruses, an opioid antagonist should be available. Naltrexone is recommended because the antagonism will last beyond the expected effects of opioid antagonist. A naltrexone dose of 0.1 mg/kg of the estimated body weight has been used in field immobilization situations, with complete reversal occurring in less than 5 minutes. Naloxone, lasting only 20–30 minutes, can be used for reversal where return of the opioid effect is desired while under proper observation. If the immobilization technique includes the use of an alpha-2 agonist such as medetomidine, atipamezole should be administered if full immediate recovery is desired. A 5:1 ratio of atipamezole to medetomidine and a 10:1 ratio of atipamezole to dexmedetomidine is recommended for complete reversal.

Dissociative Anesthetics (Arylcyclohexylamines)

Tiletamine and ketamine have been used to immobilize free-ranging walruses. The principal problem associated with dissociative chemical restraint is the long duration of effect and the lack of a reversal agent. Since walruses are often immobilized near water, it is imperative that conditions prevent the partially anesthetized animal from entering the water. Tiletamine and zolazepam (Telazol® or Zolatil®) at a dose of 1.4–2.2 mg/kg IM have been studied for chemical restraint of walruses. Induction time ranged from 14 to 29 minutes, and the duration of immobilization lasted from as short as 75 minutes to as long as 220 minutes. The induction and recoveries were reported to be smooth. Apnea was not reported, although one of the three animals died during recovery (Griffiths et al. 1993) and other deaths have been reported (Hills 1987).

Atlantic walruses have also been immobilized with a combination of Telazol and medetomidine. A total dose of

Telazol and 100 mg of medetomidine (approximately 3.3 mg/kg Telazol and 17 mg/kg medetomidine) was administered by dart to two animals. The respiratory rate varied between 10 and 12 breaths per minute throughout the procedure. Despite oxygen supplementation via a nasal cannula, pulse oximetry showed low oxygen saturation (37–79%) (Lanthier & Stewart 2002). Atipamezole was used to antagonize medetomidine. Three additional walruses (one male and two females) were injected with a total dose of 2 g of ketamine and 90 mg of medetomidine (approximately 2.5–4.0 mg/kg of ketamine and 0.11–0.18 mg/kg of medetomidine). In each case, the respiration rate appeared to be normal (rate and depth). Immobilization occurred in 15 minutes. None of the walrus showed muscle spasms. Procedure length varied between 16 and 40 minutes. Atipamezole was injected intravenously and intramuscularly 50/50 as the antagonist (approximately 9.5–19.0 mg/kg). Recoveries were smooth and rapid (6–23 minutes) (Lanthier & Stewart 2002). However, these drugs are rarely used to manage animals in a controlled environment, and atipamezole would not be delivered intravenously.

Propofol

Where the combination of behaviors and sedation are adequate to allow IV delivery of drug in the extradural intravertebral vein, propofol can be delivered to produce unconsciousness and facilitate endotracheal intubation. Propofol provides some degree of muscle relaxation through central motor effects, making intubation easier in comparison to the dissociative agents. Although apnea is likely and intentional with this approach, intubation is easier when performing manual intubation by palpation. This has replaced the aforementioned barbiturates.

Volatile Anesthetics

Isoflurane has been used to maintain general anesthesia in walruses. However, because of the low solubility of sevoflurane, both uptake and elimination will be faster and may reduce the time to achieving surgical anesthetic levels and recovery when compared to isoflurane. In addition, sevoflurane is less pungent (less irritating) than isoflurane, making mask induction under behavioral control or with mild sedation more feasible. Oxygen flow rates and vaporizer settings should be determined by monitoring the response to the anesthesia and surgery, but can be enhanced by inhalation anesthetic monitoring. Initial vaporizer settings will likely be maximal if the circuit is not primed in advance and mask induction is necessary. However, vaporizer settings should be reduced in anticipation of equilibration of the animal with the anesthetic machine and the response to procedure-related stimulation. With preanesthetic drugs such as midazolam and meperidine, and induction agents such as propofol, the vaporizer settings may be raised less aggressively and adjusted as needed. Monitoring the end-expired anesthetic concentration can better guide anesthetic maintenance and assist in determining the timing of administration of reversal agents in recovery.

Preanesthetic Considerations

For improved welfare, emphasis has been placed on training for medical behaviors to increase cooperation with anesthesia and on the environmental design of walrus habitats to improve safety during anesthetic events. Field techniques in wild environments may require rapid induction to achieve control, utilizing drugs that have a higher risk factor compared to those applied in a controlled environment. Reasons for general anesthesia of managed walrus have included tusk removal surgery, foreign body ingestion, dehiscence of the surgical incision sites, abdominal hernia, and ophthalmology procedures. A preanesthetic blood sample for elective procedures, including full complete blood count and chemistries, is recommended. Alternatively, blood gas and chemistry data are acquired immediately after intubation and intermittently as needed. Here we offer only a general protocol and pick list (inventory items; Fig. 41.1) to prepare support staff for the necessary tasking and required supplies prior to a walrus anesthetic event.

An event management plan should include one veterinarian assigned as the procedure manager who oversees the plan, including organizing personnel, coordinating assignments, and collaborating with the surgeon and anesthesiologist. They in turn work with other veterinarians and technicians who assist in management of the environment, transport, surgery, anesthesia, and recovery. If the walrus requires transport under anesthesia to a secondary site, the induction area, transport vehicles, and recovery site must possess all equipment and materials for any possible complications, including resuscitation. Induction and recovery locations should be evaluated for potential environmental threats when animals are uncoordinated and may incur head or tusk injury from hard concrete surfaces, water troughs, or grating. Personnel should be prepared to remove an animal's head from room corners when sedated and unable to breathe. Closed cell foam pads can be used under the walrus to prevent heat loss to the concrete floor or provide some cushioning in the event of any uncoordinated efforts to stand. Padding throughout the anesthesia event will also decrease neurologic and muscle injury from the animals' body weight. With induction and recovery in a transport cage,

Walrus Anesthesia Picklist

Animal name: _____
Date / time: _____
Location: _____



Anesthesia machine

☐ Oxygen: ☐ Two large (7000 L) oxygen tanks ☐ Oxygen regulators appropriate to tank(s)
☐ Multiple smaller (600-1700 L) tanks if transport ☐ Oxygen hoses length fits location (> 5 meters)

☐ Breathing Circuit: ☐ Size appropriate ☐ small animal ☐ large animal ☐ Vaporizer: ☐ sevoflurane (preferred) ☐ isoflurane
☐ Ventilator (15 L bellows, adjustable) ☐ Appropriate size induction mask or traffic cone
☐ Demand valve (160 LPM) with 5 meter hose ☐ Waste anesthetic scavenging vacuum/passive

Airway management

☐ Intubation: ☐ Appropriate size endotracheal tubes (ET tubes): ☐ 18 ☐ 20 ☐ 22 ☐ 26 ☐ 30 mm ID with tested cuff
☐ Soft ropes or straps to open mouth ☐ Roll gauze for securing endotracheal tube
☐ Long blade laryngoscope or bronchoscope ☐ Oral suction and/or swabs

Vigilance Montitoring

☐ Monitor: ☐ ECG: ☐ Lead II ☐ Base-Apex ☐ other ☐ Expire gases: ☐ ETCO2 ☐ ETSevo or ETIso
☐ SpO2 sensor: ☐ transmittance ☐ reflectance ☐ Blood pressure: ☐ invasive ☐ non-Invasive
☐ Temp: ☐ rectal ☐ esophageal ☐ Stethescope: ☐ standard ☐ esophageal

☐ Blood Gas: ☐ Measured values: ☐ pH ☐ PO2 ☐ PCO2 ☐ Na+ ☐ K+ ☐ Cl- ☐ lactate
☐ Calculated values: ☐ BE ☐ HCO3
☐ Other: ☐ Albumin ☐ TP ☐ Phosphorus

Behavioral training

☐ Hand inject ☐ Position in procedure area ☐ Venous access ☐ Mask ☐ Squeeze cage ☐ Walrus net

Mechanical Restraint

☐ Squeeze cage (small walrus) ☐ Walrus net ☐ If no behaviors darting may be necessary

Support Equipment

☐ Warming ☐ Warm water circulating blanket ☐ IV Infusion: ☐ Intravenous fluid infusion pump
☐ Warm air blanket ☐ Syringe pump
☐ Temp checked water bottles (< 104 F or 40 C) ☐ Pressure bag for fluids ("slam" bags)
⊘ No electric heating pads or blankets! ☐ Darting equipment if no behavioral training

Positioning & Padding

☐ Position: ☐ Sternal recumbency ☐ Padding: Minimum: ☐ Closed-cell foam 5 cm thick
☐ Lateral recumbency: ☐ Right ☐ Left ☐ 3 meters by 3 meters
☐ Dorsal recumbency Ideal: ☐ Open-cell foam 10-20 cm thick

Catheterization

☐ Standard over-the-needle ☐ Ultrasound guided catheterization
☐ 5 cm ☐ 20 g ☐ 18 g ☐ 5-10 mHz linear probe ☐ micro-introducer - 4F or 5F - 10 cm
☐ 15 cm ☐ 14 g ☐ 12 g ☐ sterile ultrasound gel ☐ PICC catheter kit - 4F to 8F - 20 to 60 cm

Drugs

☐ All medications calculated in advance, prepared and printed for distribution

☐ Anesthetic:	☐ Midazolam	☐ Reversal:	☐ Flumazenil	☐ Ancillary:	☐ Dextrose
	☐ Meperidine		☐ Naloxone		☐ Sodium bicarbonate
	☐ Butorphanol		☐ Naltrexone		☐ Methylprednisolone
	☐ Propofol		☐ Neostigmine		☐ Dexamethazone
	☐ Sevoflurane		☐ Sugammadex		☐ Diphenhydramine
	☐ Isoflurane		☐ Atipamezole		☐ Lidocaine
	☐ Alfaxalone	☐ Emergency:	☐ Atropine		☐ Furosemide
☐ Intra-op:	☐ Ephedrine		☐ Epinephrine		☐ Doxapram
	☐ Dobutamine		☐ Vasopressin		☐ Calcium gluconate
	☐ Atracurium		☐ Colloid (low molecular wt.)		☐ Vitamine E/selenium
	☐ Rocuronium		☐ Hypertonic saline		☐ Maropitant

☐ 24-hour post anesthesia watch recommended - first 3-4 hours most critical **Signature:** _____

Figure 41.1 Preoperative walrus anesthesia picklist.

the interior can be padded with foam to decrease potential trauma, in particular after ophthalmic surgery. Recovered animals are removed from padded areas to avoid any ingestion of these materials. The induction environmental temperature should be controlled or adjustable to avoid hyperthermia or intraprocedural hypothermia.

Walrus procedures often take place in holding areas or other nonhospital locations. As such, the equipment and supplies of the hospital must be brought to the procedure location. A checklist of items (Fig. 41.1) can assist in assuring all necessary items are staged for use at the procedure location. A common error is not ensuring adequate oxygen supplies are available for this field location, particularly when used to support ventilation with a gas-powered mechanical ventilator. Unfortunately, gas-powered ventilators consume the drive gas, usually oxygen, at a very high rate. It can be difficult to calculate the exact oxygen supply needs for gas-powered ventilators in field situations, but experience can be a guide. We do know that the total compressed oxygen use will be directly proportional to tidal volume and inversely proportional to compliance (Szpisjak et al. 2008). When we need higher peak inspiratory pressures and higher tidal volumes, such as in the ventilation of larger pinnipeds, drive gas will be consumed more quickly. However, most of the large animal anesthesia machines will use less compressed gas because the air injector venturi entrains room air as part of the drive gas volume. The traditional medical demand valves use only the drive gas (oxygen) and consume more oxygen than a mechanical ventilator. Alternative venturi-based demand valves, such as the Megavertebrate Demand Ventilator, will consume far less compressed gas, but deliver lower inspire oxygen concentrations. At typical adult walrus ventilator settings of a respiratory rate of 6–8 breaths per minute, tidal volumes of 10–15 L, peak inspiratory pressures of 30 cmH_2O (at standard temperature and pressure), and an oxygen flow to the breathing circuit at 5 L/min, the compressed oxygen use could be estimated at a minimum of 20 L/min for a typical large animal anesthesia machine and 60 L/min for a high-flow demand valve. A large US standard H-cylinder of oxygen holding approximately 7000 L could last from 3 to 5 hours for a large animal anesthesia machine but not even 2 hours when using a traditional demand valve. The authors' clinical experience supports these estimations.

Anesthesia

A general protocol involves medical behavioral training to allow IM injection by hand and extradural venous needle cannulation by hand. The caudal epaxial muscles of walruses are large and provide a good target area for remote drug injection in wild animals. The front limbs can also be used for small-volume IM drug administration. Like seals and sea lions, walruses have relatively small pelvic limbs and muscles, but the lateral muscles of the tibial/fibula can be palpated and the drugs accurately injected in this location. If behavioral training is limited or behaviors change due to illness, remote delivery by pole syringe or dart may be necessary. In such cases, long needles (>2 inches) and accurate targeting will be necessary to ensure effective uptake using the lumbar epaxial muscles as the preferred site. Some walruses may need only the anxiolytic effect of midazolam 0.1–0.2 mg/kg IM to allow extradural venous needle placement under behavioral control. Other subjects will need the neurolepanalgestic combination of midazolam 0.1–0.2 mg/kg IM with either butorphanol 0.2 mg/kg IM (mild sedation) or meperidine (pethidine) 2.0 mg/kg IM (more profound sedation) prior to extradural venous needle placement. The full effect of the neurolepanalgestic combination will require a full 20–25 minutes. Due to a potential bradycardia during such sedation, some recommend atropine (0.04 mg/kg IM, subcutaneous, or IV) should be included in the immobilization technique (Klein et al. 2002), but more often it is added only if there are concerns noted during the procedure. In addition, the authors have recently used low-dose alfaxalone (<0.5 mg/kg IM) to bridge control, producing more profound sedation without excessive respiratory depression, but further evaluation is needed before recommending this drug.

Local Anesthesia

Because of the large size and physical power of walruses, most procedures are performed with the animal immobilized with drugs or general anesthetics. If the animal is well trained and will allow handling while awake, minor surgical procedures can be performed using local anesthetics. The thick skin and heavy layer of insulating fat present mechanical challenges for effective regional nerve blocks. However, infiltration of the skin can be performed to provide effective local anesthesia. Both lidocaine HCl and bupivicaine HCl are effective for blocking pain.

Intubation

Manual palpation and placement of the endotracheal (ET) tube (18–24 mm internal diameter cuffed) involves three individuals helping hold open the mouth with straps (one on each side for maxilla and one person below for mandible; Fig. 41.2). Because of the small size of the oral cavity and large bore ET tube, it may be necessary to use a blunted small diameter stylet for initial intubation. The



Figure 41.2 Manual intubation of a walrus. Atraumatic rope or gauze is placed at the base of each tusk to open the oral cavity for maximum space between the tongue and hard palate, and between the tusks.

stylet must be at least twice as long as the ET tube to maintain the position while the ET tube is then fed over the stylet and into the trachea. Turning the ET the 90° may be helpful to match the distal slope of the tube to the anatomy of the glottis to facilitate placement. Blind intubation without verification with an endoscope or bronchoscope is not recommended because of the difficulty in correct placement and the potential for the ET tube to enter the esophagus or pharyngeal pouch. Walrus have been successfully intubated under heavy sedation using a bronchoscope to guide intubation. The head is held up and forward, creating a linear oro-pharyngeal–laryngeal axis for best access to the airway. Anesthesia is then maintained with sevoflurane (~1.8–2.0% end-expired concentration). The walrus is positioned for surgeon/internist needs, but preferably in sternal recumbency. Procedures such as tusk removal may involve lateral and laparotomy dorsal recumbency. The authors caution that the heart is not held tightly to the sternum and may fall back on the vena cava, affecting venous return in dorsal recumbency.

Vascular Access

Intravenous access for delivery of the induction anesthetic agent propofol can be accomplished by spinal needle venipuncture of the extradural intravertebral vein (EIV) or venous catheterization of a plantar branch of the saphenous vein (Fig. 41.3c) or digital veins of the pelvic flipper. Placement of a catheter into the dorsal EIV has been described (Stetter et al. 1997). The extradural IV access can be used for fluid administration, emergency drugs, and IV anesthetic administration for limited periods of time. The spinal cord terminates in the thorax vertebrae-like phocids with branches of the cauda equina present in the lumbar vertebra. Dorsal spinous processes of the lumbar vertebrate can often be palpated to determine the intervertebral space. If a spinal catheter kit is being used for IV access, a Tuohy needle is recommended to assist in directing the catheter cranially into the vein. The needle will be placed on the midline approximately 3–5 cm behind a line transecting the midline from the cranial aspects of each ileum. In adult walruses, a 16- or 17-gauge up to a 25-cm long needle in large adults may be necessary to access the EIV. The needle is advanced into the animal at a perpendicular angle to the skin. A syringe can be placed on the needle and gentle aspiration may be used to determine entrance into the vein. The authors recommend placement of a catheter in the EIV if alternative venous access is not acquired. Propofol IV 1–4 mg/kg is then delivered "to effect" sufficient to allow orotracheal intubation. Venous access is necessary for support, but also for drug delivery and a catheter is preferred over needle placement alone. Arterial access is feasible in the median artery or in a plantar branch of the saphenous artery for direct arterial blood pressure and blood gas analysis. Blood pressure estimation can be attempted with noninvasive blood pressure cuffs with variable success. Often experiencing hypotension, blood pressure is supported by reductions in inhalation anesthetic where possible, volume loading with crystalloid fluids and inotropic agents (ephedrine 0.05–0.1 mg/kg IV and/or dobutamine 0.2–2.0 μg/kg/min IV). Alternative vascular access from the flippers has been described in phocid seals but not walruses, but the authors have placed catheters in digital veins, plantar branches of the saphenous vein and artery of the pelvic flipper, as well as the antebrachial vein and medial artery of the pectoral flipper (Figs 41.3a,b), most often ultrasound-guided (see also Chapter 40). In the event of an emergency where vascular access has not been established and subjects are not yet intubated, injections can be made into the base of the tongue. Sublingual injections have the advantage over other IM injections in that there is more rapid absorption due to the high blood flow to this tissue. When intubated, diluted emergency drugs can be administered by flushing the drugs into the lungs via the ET tube. A long semirigid piece of plastic tubing can be passed through the ET tube and the medications deposited in the distal airway. Dilution of the drugs or flushing the tubing with saline is recommended to ensure that the entire drug dosage has been administered. Antagonists for immobilization drugs may also be given by

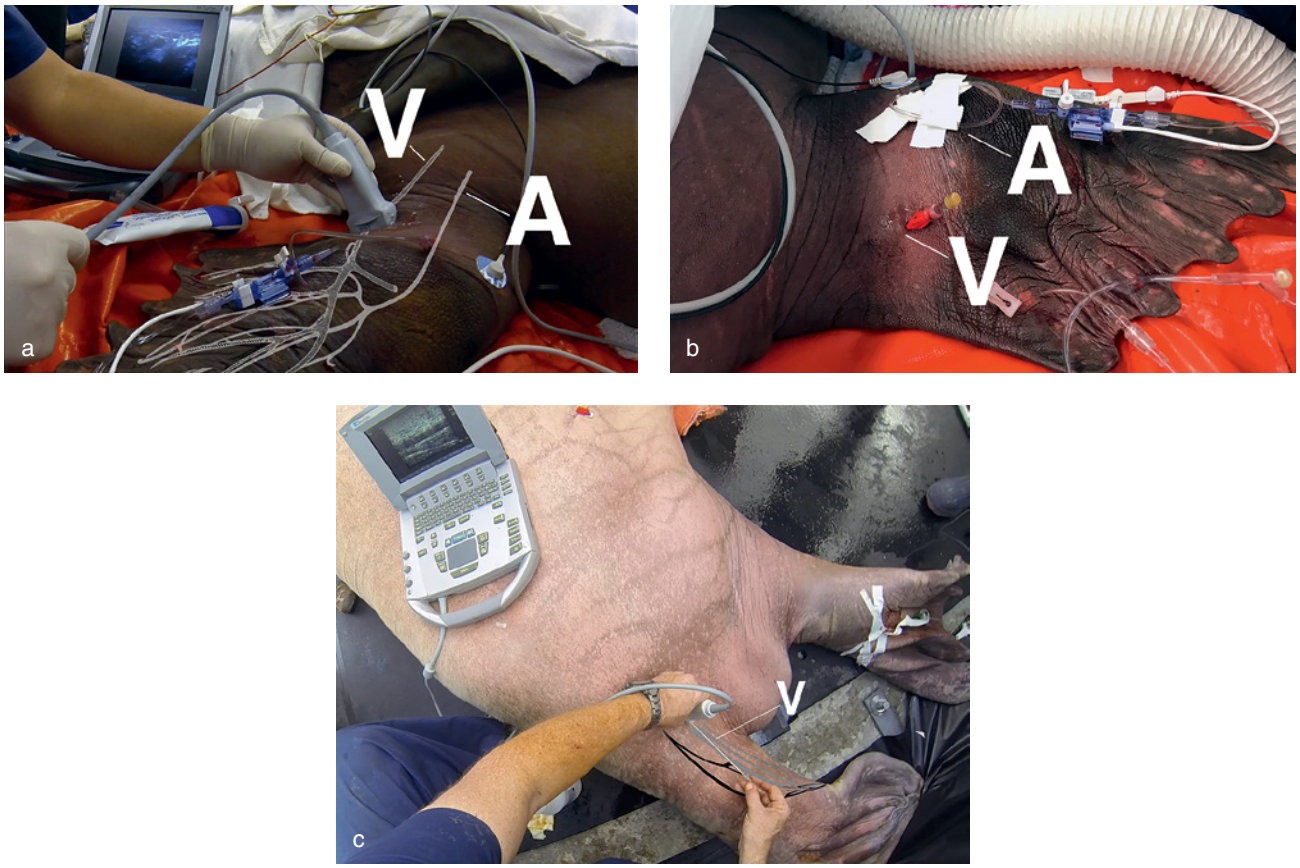


Figure 41.3 (a) Palmar vascular overlay on the left pectoral flipper with the location of the antebrachial vein (V) located with ultrasound and the median artery (A). (b) Venous catheter (V) placed caudally (red) and arterial catheter (A) cranially. (c) Plantar vascular overlay on the right pelvic flipper of an adult male walrus showing location of plantar branches of the saphenous vein (gray) and artery (black). Ultrasound-guided venous catheter (V) placement of a 25-cm, over-the-needle, 14-gauge catheter in the plantar branch of the saphenous vein is demonstrated.

these routes when necessary. However, establishing vascular access in the EIV at a minimum would be preferrable.

Ventilation

In an adult walrus, conventional controlled mechanical ventilation is supported mechanically with 6–8 breaths per minute at 30 cmH_2O peak inspiratory pressure and a 2–3-second inspiratory time, adjusted to the desired capnography and blood gas data. Hand ventilation using a reservoir bag is feasible in this large species, but human beings in lengthy procedures do fatigue and deliver inconsistent ventilation, leading to significant variations in hemodynamic and arterial blood gas parameters (Chauhan et al. 2023) so it is not advised. Alternatively, compressed air can be used to drive gas-powered ventilators, even in field situations. The authors have used SCUBA tanks with modified gauges to provide compressed gas at the proper pressure and flow to drive a large animal ventilator. Where portable SCUBA tank refilling bumps are available, this allows for an endless supply of ventilator drive gas in the field and the oxygen supply can be conserved for use only in the breathing circuit. Where inhalation anesthetics are not required, demand valves or the Megavertebrate Demand Ventilator can be used to provide ventilation.

Vigilance, Monitoring, and Support

Improvements in outcome are based on proper preparation for the procedure (Fig. 41.1), knowledge of health parameters prior to anesthesia, and early intervention of patient physiological anomalies during the procedure. Multiparameter monitors should be used to provide ongoing evaluation of cardiac, respiratory, expired gas, direct blood pressure, anesthetic gas levels, and temperature. Vigilance monitoring and support of pinnipeds are described in further detail in Chapter 40.

Respiratory Function

Apnea is a common sequela to anesthetic or immobilization drugs. Ventilatory support is essential when working with these animals. End-tidal gas monitoring is recommended to assess the efficacy of ventilation and to determine the relative anesthetic concentrations in the animal. Spontaneous ventilation is likely to be inadequate and methods for assisting ventilation should be available. In contrast to the conscious animal's ability to breath hold for long time periods, apnea during immobilization and anesthesia are associated with respiratory and metabolic acidosis, arrhythmias, and poor anesthetic delivery. For this reason, controlled ventilation coupled with expired gas monitoring is important for immobilization or anesthesia. It is essential to monitor the ventilation rate during all phases of handling, and an individual should be assigned to monitor and verbalize the respiratory rate from prior to sedation through recovery. Adequacy of ventilation is best determined by measurement of blood gas values, but indirect measures such as end-tidal carbon dioxide ($EtCO_2$) are also useful. $EtCO_2$ can be monitored with battery-operated side-stream style monitors from a catheter placed into the animal's airway or penetrating an ET tube in the intubated animal. Blood gases can be measured on blood samples taken from any vessel, including the extradural intravertebral vein, but arterial blood gas data is more desirable.

Monitoring the Cardiovascular System

Heart rate during the onset of immobilization and anesthesia is usually between 80 and 100 beats per minute (bpm). As anesthesia deepens, the heart rate slows to around 60 bpm. Heart rate can be determined by observation of the movement of the animal's chest wall between respirations. Once at the animal's side, auscultation of the heart with a stethoscope or use of an electrocardiograph to determine the rate and rhythm of the heart is essential to detect early changes in cardiac function. The use of a pulse oximeter has proven difficult because of the lack of places to position the sensing probes. A reflectance style pulse oximeter probe placed against the oral mucosa or rectal wall has worked intermittently. A flat or pencil-type small-animal 8–9 MHz Doppler flow probe has been used on the cornea as a quick check of pulsatile blood flow after induction. These indirect measures provide limited information, but improvements in invasive monitoring techniques, such as direct arterial blood pressure, may result in better management and outcomes. Direct arterial blood pressure monitoring with ultrasound-guided catheter placement has become more applicable with increased experience. Micro-introducer kits using echogenic tipped needles and stiffened dilators have improved ease of arterial cannulation (see also Fig. 41.1).

Body Temperature

Although walruses are thought to have adequate blubber to keep warm in severe cold environments, they do become hypothermic under anesthesia. Maintenance of normal body temperature can be challenging as large walrus location temperatures are variable. Facility design for walruses should include an area where the animals can be anesthetized in a temperature-regulated environment. Typically, close cell foam is used to cushion animals slightly and interfere with direct concrete contact. Temperature probes are often part of a multiparameter patient monitor, and probes may be inserted rectally or esophageal. Mylar space blankets can be used to decrease radiant heat loss with care taken to cover flippers and body on early warning of body temperature loss. Circulating warm air and warm water systems have been used, but will have limited coverage. With flippers a major site of heat loss, focusing these systems on the flippers may be effective.

Recovery, Postprocedure Observation Schedule, and Duties

At the conclusion of the surgical procedure the walrus may be transported to the recovery area or recovered on site, in a recovery cage, or even in the squeeze cage if small. The anesthetic gas, if not already discontinued, is stopped, although expired gas level detection may continue. The walrus may be maintained on the anesthesia ventilator or removed from the anesthesia machine with ventilation support from a demand valve to ensure proper ventilation and anesthetic gas washout while waiting for improvement in consciousness and reversal. Some practitioners have switched to medical-grade room air with the demand valve if oxygen levels are within normal range, or have purposefully limited ventilation to induce a degree of permissive hypercapnia in hopes of earlier spontaneous ventilation. Walrus that do not follow expected recovery times may still have sedative drug activity on board, requiring reversal to improve recovery time. The theory of the timed loss of sedative activity is based on assumptions of the half-life of drugs from other species, but these timelines may be underestimated. Behavioral response to stimulus is often used, although reactions to discomfort are not initially indicative of true recovery.

Monitoring and ventilation continue through recovery. Ventilation in recovery can be supported by a demand valve as an alternative. When the end-expired concentration of sevoflurane is below MAC awake (~0.6–0.8 % sevoflurane)



Figure 41.4 Recovery of young walrus. The endotracheal tube gauze ties are left 0.6–1 m long to facilitate a secure attachment for control and removal during the final phase of recovery when the animal may be ready to extubate.

the midazolam and meperidine (pethidine) are reversed, thus minimizing inhalation anesthetic-induced dysphoria. Full reversal of the midazolam will depend on the total dosage of midazolam delivered, requiring 1 part flumazenil for every 13 parts midazolam. The meperidine (pethidine) can be fully or partially reverse with naloxone 0.01 mg/kg or less, and may require repeat dosages. Alternatively, long-acting naltrexone 0.05–0.1 mg/kg can be given if opioid analgesia is unwarranted. Typically, one half of the flumazenil and naloxone dosage is delivered intramuscularly after reaching MACawake and the remaining half of the reversal agents is given intravenously after about 5 minutes (allowing some IM uptake before the IV dosing, leading to less excitement in recovery). Repeat dosing may be necessary so adequate amounts of reversal agents should be on hand. The ET tube will be maintained as long as possible. As such, long-roll gauze is used to tie the ET tube in and is retained for recovery (Fig. 41.4). A bite block (PVC tube) can be used to protect the ET tube when necessary.

Postoperative Mangement

Postoperative pain management can be addressed after the animal is fully awake, as indicated by a stable upright position and near-alert attitude. Other possible causes for slow recovery include hypothermia, so supplemental heat and protection from cold contact surfaces should be available. The ET tube gauze ties are left 0.6–1 m long to facilitate a secure attachment for control and removal during the final phase of recovery when the animal may finally work to pull away (Fig. 41.4). Initial coughing while lateral is not enough reason to decide to pull the ET tube, but the walrus will usually sit up with eyes open prior to removal. The walrus may again drift toward sleep if extubated early so it may be necessary to rouse them again to eventually move within the environment. After the anesthesiologist and veterinarians are confident the animal is stable and there is no indication of the potential for narcotization, experienced personnel should be left in place for a minimum number of hours and potentially overnight if there is any concern. A medical contact list, nutritional instructions, and orders for observation are left on site. It is often prudent to leave any equipment and drugs needed for reintubation or resuscitation nearby until confident the patient is completely alert and stable.

Postoperative Analgesia

Utilization of premedication opioids for immediate postprocedural pain relief may result in a lengthy recovery as the assumed rate of metabolism may be extended in the anesthetized walrus. A smooth but rapid recovery for the walrus is ideal and may be best achieved by full reversal if the animal is not following an expected recovery timeline according to anesthetic gas levels. Nonsteroidal anti-inflammatory drugs (NSAIDs) have included flunixin meglumine, meloxicam, and carprofen (Table 41.1). Newer NSAIDs may have fewer side effects, but this is not tested in this species and the original use of flunixin was due to a lack of alternative options. With a dose of flunixin in cattle and horses (1.1 mg/kg) originally used as a guide, the dose was decreased to 0.25 mg/kg. If the walrus has been ill preprocedure for a period of time, blood analysis suggests dehydration, or the walrus does not return to eating, the dose of flunixin should be decreased to avoid complications and limited in the length of therapy.

Products Mentioned

Megavertebrate Demand Ventilator, In Case of Anesthesia, 5580 La Jolla Blvd, #459, La Jolla, CA 92037,

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Sirenians (Manatees and Dugongs)

Elizabeth C. Nolan, Michael T. Walsh, and James E. Bailey

Introduction

Distributed throughout fresh, brackish, and marine tropical waters of North and South America, Africa, and Australia, three species of manatees (Trichechidae) and one species of dugong (Dugongidae) comprise the family Sirenia (Table 42.1) (Domning & Hayek 1986; Reynolds & Odell 1991). Genetically related to elephants (Probosicidae) and hyrax (Hyracoidea), these hind gut fermenters are the sole obligate herbivores of the marine mammal world although they have been observed to ingest a wide variety of invertebrates (barnacles, bivalves, gastropods, crabs, tunicates) (Courbis & Worthy 2003). Manatees are considered "weakly" social species, establishing no long-term bonds other than mother–calf pairs and forming temporary congregations of individuals during winter months at warm water sites or when breeding (Hartman 1979; Reynolds 1981; Wells et al. 1999; Odell 2003). Calves generally stay with their mothers for 1–2 years and reach sexual maturity between 2 and 5 years of age (United States Fish and Wildlife Service 2001; Odell 2003). In comparison, dugongs take approximately 9–10 years to reach sexual maturity and are often found in large herds with "amorphous" social organization, the only close identifiable social bonds being those between mother and calf (Wells et al. 1999; Odell 2002).

Due to habitat loss or degradation, human interaction problems, and natural disease in their home ranges, sirenians are currently listed under CITES Appendix I and the IUCN Red List as "vulnerable" (Reynolds & Odell 1991; CITES 2019; IUCN 2020). The United States Endangered Species Act categorizes Amazonian manatees and dugongs as endangered, and the West Indian and West African manatee as threatened (United States Fish and Wildlife Service 2020). Mortality associated with human interaction owing to hunting, boat injury, or habitat loss is believed to have had significant impacts on sirenian populations in general (Reynolds & Odell 1991; Odell 2003). Natural causes of mortality such as cold stress and brevetoxicosis also result in widely fluctuating and sometimes unusual mortality events (Unusual Mortality Event – National Marine Fisheries Service) in manatee populations in Florida. Current conservation efforts for sirenians include worldwide public education campaigns, increased research, local and national legal protection, enhancement of warm water sites (Florida), and rescue and rehabilitation programs in some countries.

Medical advancements in the care of rescued sirenians have improved survivability and potential for reintroduction to the wild. The use of sedative agents was first applied in Florida manatees in the late 1980s and general anesthesia first accomplished in 1990 (Walsh et al. 1997). Anesthesia of manatees and dugongs is still an emerging field for many of the species, but much has been learned to effectively sedate, anesthetize, and improve potential therapy for these animals. The information presented in this chapter focuses predominately on the West Indian manatee, but likely has applications across the Sirenia family.

Anatomy and Physiology

Sirenians have a somewhat tubular body shape and a wide dorsoventrally flattened fluke that is paddle-shaped in manatees, but bilobed and similar in shape to that of a dolphin in dugongs. Whereas manatees tend to have more dorsoventrally flattened bodies, dugongs are more laterally compressed, particularly caudally. Sirenian skeletons are composed of dense pachyostotic bone (Fawcett 1942a). They have relatively short but mobile pectoral flippers and lack hindlimbs. Flippers of male manatees are longer in length than those of females, and have more roughened

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Table 42.1 Family Sirenia.

Genus and Species	Common Name	Length[a,b]	Mass[b]	Distribution
Dugong dugon	Dugong	Adults: 2.7 m average, up to 3.3 m Calves: 1–1.3 m	Adults: 250–300 kg average, up to 400 kg Calves: 20–35 kg	Coastal waters of Indo-Pacific
Trichechus senegalensis	West African manatee	Adults: 3–4 m	Adults: <500 kg	Coastal waters, rivers, and lakes of west-central Africa
Trichechus inunguis	Amazonian manatee	Adults: 2.8–3 m Calves: 0.8–1 m	Adults: 450–480 kg Calves: 10–15 kg	Freshwater rivers and lakes of Amazonian basin
Trichechus manatus	West Indian manatee (2 subspecies)			
T. m. manatus	Antillean manatee	Adults: 1.85–2.7 m, up to 3.5 m	Adults: maximum 1000 kg	West Indies, Caribbean, coastal waters and rivers of Mexico, Central America, northeastern South America
T. m. latirostris	Florida manatee	Adults: 2.7–4 m, average 3 m Calves: 1.2–1.4 m	Adults: 400–1775 kg, average 400–600 kg males, maximum 1600 kg females Calves: 18–45 kg, average 30 kg	Coastal waters and rivers of southeastern United States

Sources: Domning & Hayek (1986), Reynolds & Odell (1991), Converse et al. (1994), Nowak (1999), Walsh & Bossart (1999), Odell (2002), and Murphy (2003).
[a] Straight length, snout to tail tip.
[b] Calf length and mass ranges at time of birth.

epithelium medially, which likely aids in holding a female during copulation. Male manatees also tend to weigh less than females and have a leaner body composition.

The skin of manatees is generally thick and tough with sparsely distributed sensory hairs, with the exception of the Amazonian manatee, which has smooth skin (Domning & Hayek 1986; Reynolds & Odell 1991). Nill et al. (1999) found the increased collagen network of the manatee dermis is roughly 2.5 times denser than that of terrestrial mammals. This unique skin density, along with their pachyostotic bones, is a counterbalance to the positive buoyancy effects of the air-filled lungs and intralumenal gas of the gastrointestinal tract (GIT) in these animals (Nill et al. 1999; Kipps et al. 2002).

Unique sirenian facial features include small eyes which close by a sphincter rather than upper and lower eyelids, a flexible upper lip and a sensitive oral disk covered with modified vibrissae for use when foraging, and nostrils with valves that close between breaths. Dentition varies between manatees and dugongs. Manatees horizontally replace their molars throughout life, while dugongs do not. In addition, manatees lack functional incisors and premolars, whereas dugongs have both premolars and small tusk-like maxillary incisors (Reynolds & Odell 1991). In place of incisors, manatees have a dorsal dental pad that articulates with the lower jaw just caudal to a firm gingival ridge overlying the symphysis of the mandible. Due to manatees' relatively small mouth, laterally narrowed oral cavity, thick short tongue, and elongated soft palate, oral visualization of the glottis is not possible even with maximal extension of the jaw angle in an adult manatee.

The manatee trachea is relatively short and bifurcates at the thoracic inlet into two separate pleural cavities or hemithorax. The specialized diaphragm of sirenians has a transverse septum separating the heart from the lungs and other organs, as well as two hemi-diaphragms that horizontally extend the length of the body and divide the pleural spaces from the abdominal cavity (Rommel & Reynolds 2000). Unlike other marine mammals, manatee and dugong respiratory tracts comprise the dorsal third of their body cavity, extending from the shoulders to the pelvis and remaining dorsal to the heart (Fig. 42.1). Manatee lungs are single lobed and attach to the vertebrae, except for the caudal 30% that is free floating (Rommel & Reynolds 2000). This position of the lungs warrants intramuscular (IM) injections be delivered in the gluteal or shoulder muscles to avoid injury to organs under mid-body epaxial musculature. Another consideration with regards to the respiratory system of sirenians is the position of the GIT, which lies ventral to the thorax and can comprise 23% of an animal's weight (Reynolds & Rommel 1996). As hindgut fermenters, manatees have a small, distinct round cecum with two

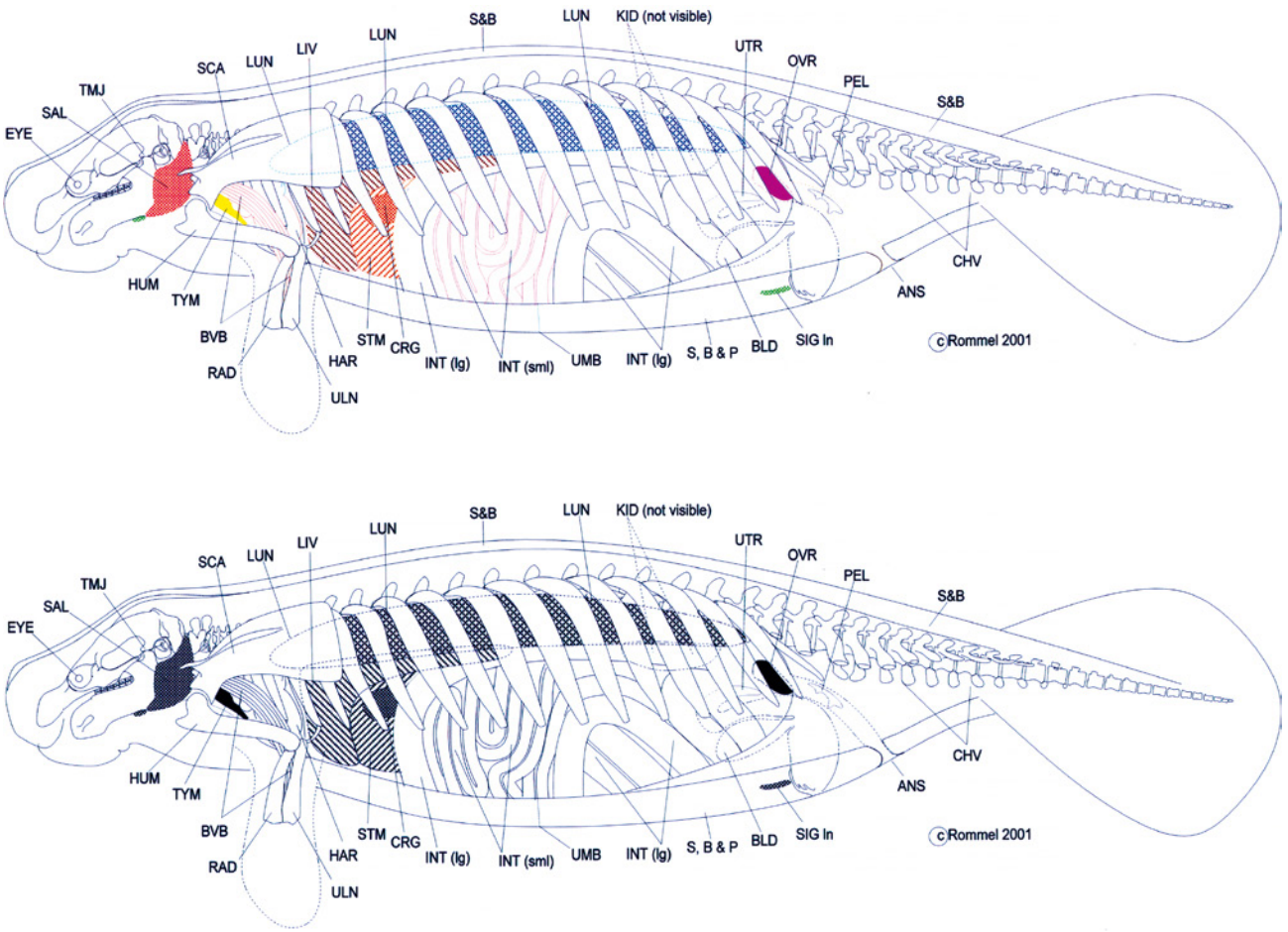


Figure 42.1 Florida manatee (*Trichechus manatus latirostris*) internal organ position. ANS, anus; BLD, urinary bladder; BVB, brachial vascular bundle; CRG, cardiac gland; CHV, chevrons; EYE, eye; HAR, heart; HUM, humerus; INT, intestines; KID, left kidney, not visible from this vantage in the manatee; LIV, liver; LUN, lung; OVR, left ovary; PEL, pelvic vestige; RAD, radius; SAL, salivary gland; S&B, skin and blubber; SCA, scapula; SIG ln, superficial inguinal lymph node; S,B&P, skin, blubber, and panniculus muscle, cut at midline; STM, stomach; TMJ, temporomandibular joint; TYM, thymus gland; ULN, ulna; UMB, umbilical scar; UTR, uterine horn; VAG, vagina. Used with permission, Dr. Sentinel Rommel.

ovoid diverticula and an enlarged colon, which aids with digestion of vegetation. In well-nourished animals, the cecum and large intestine together comprise approximately 10% of the body weight in dugongs and 14% in manatees (Marsh et al. 1977; Reynolds & Rommel 1996). The nutritional status of the animal and the amount of ingesta present in the intestinal tract can influence the respiratory capacity in the awake and sedated animal. When animals are removed from water for anesthetic procedures, pulmonary compression can occur from these internal organs and ventilatory variables must be closely monitored.

Respiratory adaptations for diving in sirenians are similar to those of other marine mammals. The terminal airways of manatees are reinforced with cartilage (Pabst et al. 1999). Inspiration is closely paired with and follows forceful expiration, allowing animals to dive with replenished oxygen stores. Resting in water, sirenians also have long intervals between breaths. In Florida manatees this generally lasts 2–3 minutes, but can extend as long as 24 minutes in "bottom-resting" individuals (Reynolds 1981). Respiratory rates when out of water may vary, with younger animals more likely to breath-hold. These animals may also become hypercapnic and acidemic if they struggle during capture. In studies evaluating the response of Amazonian manatees to hypoxemia and hypercapnia in relation to respiratory drive, carbon dioxide rather than oxygen was concluded to be the "primary controller of ventilation and dive time" (Gallivan 1980). Similar to other marine mammal dive responses, dugongs and manatees develop bradycardia, but it has been characterized as "sluggish and modest" compared to that of cetaceans and pinnipeds (Scholander & Irving 1941; Elsner 1999).

The sirenian heart lies cranioventral to the lungs and anterior to the abdominal organs between the pectoral flippers

and dorsal to the sternum. When an animal is lying on its back out of water, the heart rate can be assessed by evaluating the skin pulse over this area or by using a stethoscope, Doppler (2-MHz fetal or veterinary system), commercially available Bluetooth heart rate monitor, or standard electrocardiography during sedation and anesthesia.

Unlike other marine mammals, West Indian manatee metabolic rates are 25–30% of predicted values and result in their unique warm water thermoregulatory requirements and relative cold intolerance (Irvine 1983; Worthy 2001). Amazonian manatees also have relatively low metabolic rates and limited capacity for thermogenesis (Gallivan et al. 1983). Depending on the season, Florida manatees are found in water ranging from 22ºC (72ºF) to over 32ºC (90ºF). While manatees may reside in water cooler than 21ºC (70ºF) during winter months, they have been observed to shiver at these temperatures and develop skin damage in temperatures ≤16ºC (61ºF). The degree of damage is dependent on the environmental temperature, the length of cold water exposure, and the animal's nutritional state and size. Manatees ≤300 kg are physiologically less adaptable to cold stress than larger manatees; juveniles seem unable to increase their metabolic rates to compensate for cold temperatures ≤16ºC (61ºF) (Worthy 2001). For long-term rehabilitation of manatees, water temperatures are generally maintained ≥24.5ºC (76–80°F), though often raised to 27–29ºC (80–84ºF) for neonates, cold–stressed, or thin individuals. The recommended ambient air temperature for animals removed from the water for procedures is 22–26ºC (72–79ºF) (Bossart 2001). If ambient temperatures drop ≤20ºC (68ºF) time for out-of-water procedures is minimized to reduce skin exposure to cooler air. Water is often used to cool animals maintained out of water in warm ambient temperatures or in direct sunlight. In addition to thermoregulatory impacts, it has been suggested the lower metabolic rate of sirenians has implications for drug metabolism, distribution, and elimination (Murphy 2003).

Capture and Physical Restraint

To minimize injury to an animal or handlers, it is preferred that manatees are removed from the water for medical and surgical procedures. Acquisition of sick or injured wild manatees usually involves setting long seine nets to encircle then "bag" an animal before pulling it onshore or into a boat (Fig. 42.2). When working with nets in bodies of water, particular care is taken to avoid net entanglement of the animal(s) or personnel, which can lead to injury or drowning. Hoop netting has limited success with dugongs, and where regulatory and equipment constraints exist for handling this species, a "rodeo method" of capture in shallow open water has been described (Lanyon et al. 2006), though this technique can result in increased serum creatinine kinase, and higher lactate and CO_2. Given the stress and potential development of fatal capture myopathy, as well as the possibility of injury to animal handlers associated with this method, chase and handling time are held to a minimum (Marsh & Anderson 1983). The authors do not recommend this capture method for manatees although proper post-capture handling and timely return to water did not suggest overt capture myopathy involvement in dugongs (Lanyon et al. 2012).



Figure 42.2 Restraint of a Florida manatee (*Trichechus manatus latirostris*) during rhinoscopic-assisted intubation.

In captive environments, physical restraint is accomplished by corralling the animal using nets, dry-docking with pool water drops, or raising a medical pool floor above the water level, then placing an animal within a stretcher for transport. Medical pool floors are preferred to decrease handing and treatment time. Whether in managed populations or the wild, care is taken during any acquisition, as these animals may actively avoid capture and restraint. The strong thrust of sirenian tails and often large body size (Table 42.1) make injury a possibility for both handlers and animals. Rehabilitation facilities for manatees may have

personnel wear helmets for general safety when handling or moving these animals. It is recommended that only trained personnel participate in the capture and restraint of sirenians.

While manatees spend their entire lives in water, they are capable of being sustained outside of the aquatic environment for a number of hours. Intermittently spraying with water throughout a procedure will help prevent skin desiccation and overheating, though manatee skin is much more resistant to drying than cetaceans. When out of the water for diagnostics or therapeutics, animals are generally placed on closed or open-cell foam to cushion their body mass and reduce pressure on internal organs; open-cell foam is preferred for longer restraints or procedures as closed-cell foam affords only minimal cushioning. Animal position is adjusted with stretchers, boat sling straps (placed around the animal's body), forklifts, cranes, and, in smaller animals, manually. When animals are in sternal recumbency, a sheet of closed-cell foam can be placed over the dorsal aspect of the fluke on which handlers kneel to restrain the tail. Handlers also position themselves on either side of the animal to prevent lateral movement and, in some cases, place closed-cell foam over the animal's back with handlers kneeling on either side of the foam to limit movement. It is not uncommon for manatees to lie quietly in either sternal or dorsal recumbency during transport or nonpainful procedures. Care must be taken around the head and tail areas. Manatees can explosively resist restraint and are capable of touching the tips of their tails to their rostrum and/or rolling quickly. Particularly fractious animals can be secured to restraint boards or administered sedatives if necessary. In cases of thoracic trauma where rib fractures exist, manatees may be sedated with oral diazepam or injectable sedatives to decrease reactions and minimize further damage to the chest during diagnostic or treatment procedures. A plywood board can also be placed in the bottom of the stretcher to avoid displacement of the fractured ribs by the stretcher material compressing the sides of the animal. Handlers should avoid placing body pressure on the fracture sites. In some cases less restraint may be more productive, however some animals seemingly anticipate procedures, such as blood draws and nasogastric tubing, and can react without warning.

Vascular Access

The typical site for health assessment blood sampling in manatees of all ages is the interosseous space between the radius and ulna. "The most characteristic feature of the circulatory system of the manatee is the complete subdivision of the larger arteries, usually near their sources, into great numbers of small arteries which run parallel for considerable distances without any significant diminution in caliber." This is "most highly developed in the vascularization of the pectoral limb" and "resembles rather the arrangement of a broom" (Fawcett 1942b). This brachial vascular bundle of veins and arteries runs in the interosseous space between the radius and ulna (Fawcett 1942b), and can be accessed from the medial or lateral sides of the pectoral flippers (Fig. 42.3). "Cephalic" and "caudal" veins have also been described and diagramed for the pectoral flipper of manatees (White & Francis-Floyd 1990) (Fig. 42.4). This described cephalic vein has been cannulated by a cut-down and standard over-the-needle catheter during anesthesia of one Florida manatee (Bailey et al. 1998).

A caudal tail ventral vertebral arch vascular bundle is also available for venipuncture, particularly in younger animals, where pectoral vessels are small (Fig. 42.5).

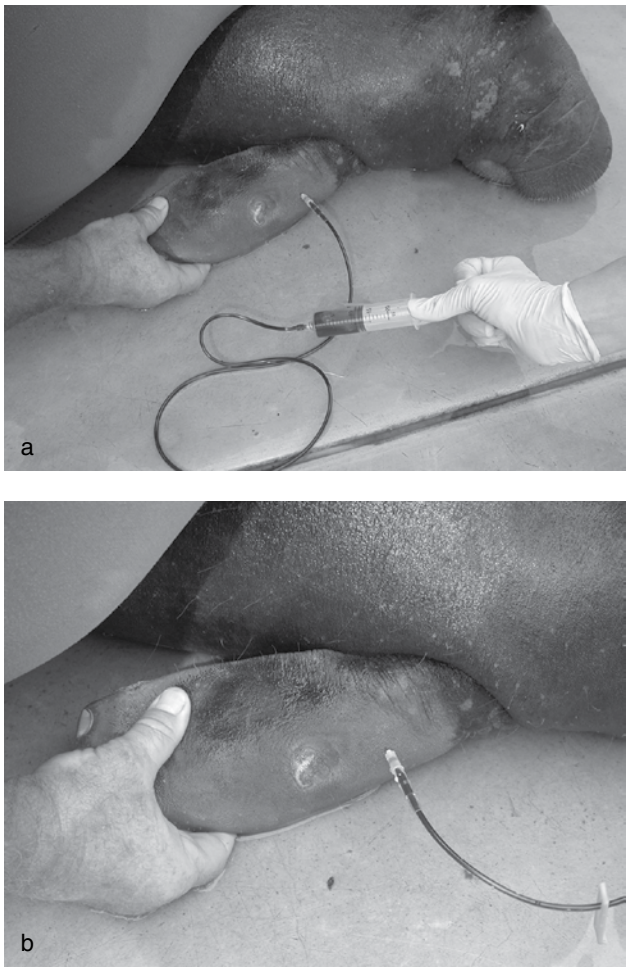


Figure 42.3 Brachial vascular bundle venipuncture site in a Florida manatee calf (*Trichechus manatus latirostris*). Note the lateral approach to the vascular bundle (medial approach not shown).

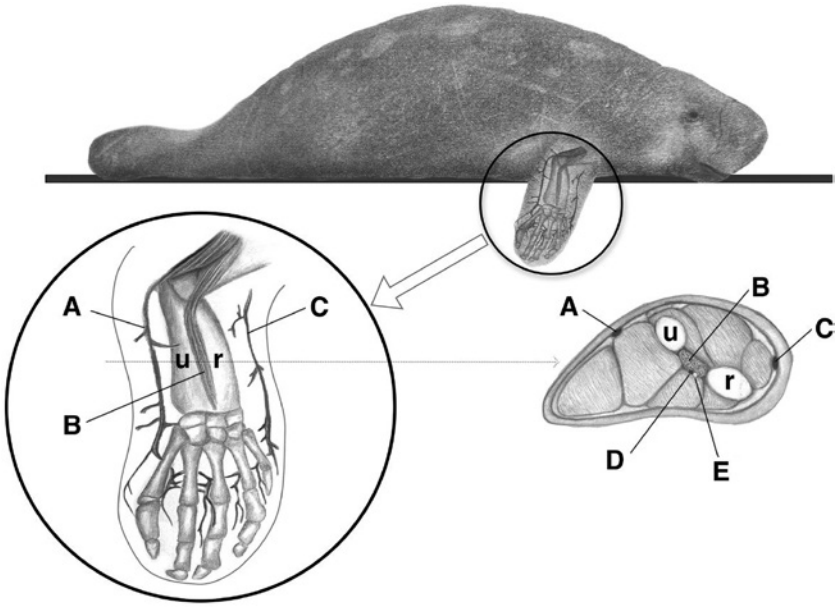


Figure 42.4 Florida manatee (*Trichechus manatus latirostris*) pectoral flipper vasculature position. A, caudal vein; B, brachial vascular bundle; C, cephalic vein; D, median artery; E, median nerve; r, radius; u, ulna. To the right is a cross-section view with the palmar surface facing downward. Adapted from an illustration by B. Rommel.



Figure 42.5 Caudal tail vascular bundle venipuncture site of the Florida manatee calf (*Trichechus manatus latirostris*). Note that caution must be taken using this approach for the safety of the phlebotomist, handlers, and manatee.

This caudal tail site for intravenous (IV) access in unsedated animals is not recommended except for compromised neonates, since forward thrust of the fluke could injure the phlebotomist and needle position can be difficult to maintain with movement.

Spinal or touhy needles may be used to obtain IV access for drug and fluid administration in anesthetized adult manatees in the caudal tail vascular bundle. This site is accessed by either elevating the tail to visualize its ventral aspect or placing the animal in lateral or dorsal recumbency. Tissue glue may be used to secure needles in place. Calves that are easily restrained due to size or illness may occasionally undergo venipuncture awake in the caudal tail site with 20- or 21-gauge, 3.75–5-cm (1.5–2-inch) needles. Cannulation of the brachial vascular bundle is difficult due to needle placement perpendicular to the arteriovenous plexus. It has been accessed with 18-gauge, 5-cm (2-inch) needles in adults and 20-gauge, 3.75-cm (1.5-inch) needles in juveniles (Murphy 2003). Although venipuncture or cannulation of the pectoral flippers can be accomplished either medially or laterally, contact between the body wall and a medially placed needle may displace the cannula. The skin over the lateral aspect of the flipper is subjectively thicker, making needle redirection more challenging. Perivascular leakage of drugs can occur in these sites, potentially resulting in local tissue inflammation or necrosis. To reduce the likelihood of needle displacement, venous access is best attempted after sedative administration, tracheal intubation, and/or final patient positioning for a medical or surgical procedure. During fluid administration, closely monitoring flow rates and observing vascular access sites for swelling are recommended.

In recent years it has become feasible to catheterize palmar digital veins, as well as what we have called the median artery of the manatee pectoral flipper (Fig. 42.4). The artery sits snuggly in the interosseous space between the radius and ulna, slightly palmar on the flipper, under the thick dermis and connective tissue. Doppler flow probes and ultrasound are mandatory to facilitate identification and cannulation of the artery, as it is not palpable. The authors have had success catheterizing the median artery of three adult Florida manatees with ultrasound guidance using linear transducer (10–5 MHz) and 4–5

French micro-introducer catheter kits utilizing a modified Seldinger method (Seldinger 1953), similar to those used for cetacean vascular access. In a transverse ultrasound view across the palmar surface of the flipper, the artery sits slightly superficial to the convergence of the radius and ulna. In addition, palmar digital veins (perhaps branches of the so-called cephalic and caudal veins) have been catheterized by similar methods. To maintain patency of the cannula, 2–5 unit/mL heparinized normal saline is used to regularly flush the catheter. Modern disposable blood pressure transducers with integrated pressurized flush mechanisms can be used to simplify maintenance of the catheter. The transducer is zeroed to the level of the right atrium (physiologic zero) and blood pressures are continuously monitored. Mean arterial blood pressures measured have ranged from 59 to 126 mmHg. After reducing the level of anesthetic, balancing the anesthetic technique with less cardio-depressive drugs (e.g., opioids), and volume loading with fluids through the palmar digital venous catheter, the inotropes dobutamine (0.2–2 μg/kg/min IV) and/or ephedrine (0.05–0.1 mg/kg IV) have been used successfully to manage hypotension (mean <60 mmHg). Further investigations of the vascular anatomy through radiographic angiography as well as blood pressure assessment through repeated measure are recommended for the manatee clinical community.

Preanesthetic Considerations

Similar to other mammals, sirenians are physically examined and their bloodwork evaluated prior to anesthesia to identify any health conditions that would pose risks. Florida manatees present to rescue and rehabilitation programs with a variety of injuries and illnesses secondary to both natural and human causes, as described in previous mortality studies (O'Shea et al. 1985; Ackerman et al. 1995; Walsh & Bossart 1999; United States Fish and Wildlife Service 2001; Bossart et al. 2004). Two of the more commonly seen naturally occurring conditions in Florida manatees are cold stress and brevetoxicosis. Traumatic injuries from crab trap, monofilament line entanglement, or boat strike are also common presentations to rescue and rehabilitation programs. Understanding the extent of illness or injury is critical to assessing the anesthetic risk to a manatee patient.

Prior to anesthesia, sirenians are ideally fasted for 24 hours to reduce the likelihood of regurgitation. However, these species have a slow gut transit time (4–7 days in the Florida and 5–9 days in the Amazonian manatee) so complete emptying of the GIT in 24 hours does not occur (Gallivan & Best 1986; Walsh & Bossart 1999).

Respiratory rates are monitored prior to sedation and through the induction procedure. In sirenians respirations are counted over 5 minutes to determine a rate because they are usually ≤1 breath per minute. If a manatee in the water shows signs of depression or incoordination after sedatives are administered, it is removed prior to the usual 20–25 minutes before handling. In animals with pulmonary compromise, oxygen supplementation with a portable oxygen tank and demand valve is often provided during field or short sedative procedures or prior to administration of general anesthesia.

Sedation, Anesthesia, and Analgesia

Information regarding sedation and anesthesia has been included in a number of book chapters on sirenian health (Walsh & Bossart 1999; Murphy 2003; Walsh & deWit 2014; Davis & Walsh 2018; Haulena & Schmitt 2018). Sedative or analgesic drugs are generally administered IM or IV. Onset of drug effects after IM injection is approximately 15–20 minutes (Bossart 2001), though maximum effect may not occur until 25 minutes in some individuals. For smaller volume IM injections, the shoulder muscles of adult Florida manatees may be accessed with 21-gauge, 5-cm (2-inch) needles with or without attachment to an extension line. When injecting sedatives in the lumbar region, because of the thickness of the skin and subcutaneous blubber, needles are advanced perpendicularly and forcefully to reach the deep layers of the lumbar epaxial musculature. For adult Florida manatees, 18-gauge, 8.75-cm (3.5-inch) spinal needles are used to administer drugs IM in this region, whereas 20- or 21-gauge, 3.75–5-cm (1.5–2-inch) needles are used in calves. The individual administering the drug keeps pressure on the syringe plunger to avoid reflux of sedative agent back into the syringe. Digital pressure is applied to the injection site to avoid drug leakage after removal of the needle. One advantage to administering smaller volume sedatives in the shoulder muscles is minimizing incidence of post-injection abscesses sometimes noted with deeper injections in the lumbar area.

Reported sedative, anesthetic, and analgesic drugs and dosages for Florida manatees are listed in Table 42.2. It has been suggested that the relatively low metabolic rate of sirenians may contribute to their apparent sensitivity to sedative and opioid drugs compared to terrestrial mammals (Murphy 2003), but further work has shown that manatees can be successfully sedated with similar dosages of some drugs. Diazepam and midazolam have been used extensively for both mild and preoperative sedation. Meperidine (pethidine) in conjunction with

Table 42.2 Analgesic, anesthetic, and reversal agents for the Florida manatee (*Trichechus manatus latirostris*).

Drug Combination	Reversal	Comments	Reference
Detomidine 0.005–0.01 mg/kg IM	Yohimbine 2–3 mg/1 mg detomidine IV/IM or atipamezole 1 mg/2 mg detomidine IV	Moderate sedation, beware of narrow therapeutic index, cardiac and blood pressure effects not noted	Murphy (2003)
Detomidine 0.025–0.005 mg/kg, butorphanol 0.005–0.01 mg/kg IV	Yohimbine 2–3 mg/1 mg detomidine IV/IM or atipamezole 1 mg/2 mg detomidine IV, naltrexone 1–2 mg/1 mg butorphanol IV/IM	Excellent analgesia and muscle relaxation, for minor surgical procedures or anesthetic induction, beware of narrow therapeutic index for this combination	Murphy (2003)
Detomidine 0.0085 mg/kg IM, butorphanol 0.0085 mg/kg IM	Atipamezole 5 mg/1 mg detomidine IM, naltrexone 1–2 mg/1 mg butorphanol IV/IM	In combination with butorphanol for heavier sedation, ± intubation	
Diazepam 0.02–0.035 mg/kg IV	Flumazenil 1 mg/10–20 mg diazepam IV	For nonpainful diagnostics	Murphy (2003)
Diazepam 0.066 mg/kg IM	Flumazenil at equal volume diazepam IM	For tranquilization, lasts 60–90 minutes	Bossart (2001)
Diazepam 0.01–0.025 mg/kg IV, butorphanol 0.01–0.025 mg/kg IV	Flumazenil 1 mg/10–20 mg diazepam IV, naltrexone 1–2 mg/1 mg butorphanol IV, IM	For mild-moderate painful procedures, anesthetic induction Give butorphanol 10 minutes prior to diazepam	Murphy (2003)
Isoflurane 0.5–5%		Similar settings as in domestic animals	Walsh & Bossart (1999)
Isoflurane		End expired concentrations no lower than 1.0% to 1.3% to ensure no purposeful movement to surgical stimulus	
Ketoprofen 1–2 mg/kg IM		Analgesia for severe abdominal pain Authors' note: Caution in dehydrated animals, side effects not well documented in this species	Ball (pers. comm., 2011)
Lidocaine 2%		Local analgesia, local infusion to effect Recommend preservative-free lidocaine for any epidural use	
Meperidine 0.5–1 mg/kg IM		Sedation/analgesia for minor surgical procedures	Bossart (2001)
Meperidine up to 1 mg/kg IM	Naloxone (dosage not noted)	In combination with midazolam for more painful procedures or anesthetic induction	Walsh & Bossart (1999)
Meperidine	Naltrexone 5 mg/1 mg meperidine IM	Equal volume of reversal when meperidine 10 mg/mL and naltrexone 50 mg/mL used	
Midazolam 0.02–0.05 mg/kg IM	Flumazenil 1 mg/10–20 mg midazolam IV	Mild to moderate sedation	Murphy (2003)
Midazolam 0.045 mg/kg IM	Flumazenil equal volume as midazolam (5 mg/mL) IM	Sedation for 60–90 minutes, can also use in conjunction with meperidine for more painful procedures or anesthetic induction Flumazenil may require re-dosing after long procedures	Walsh & Bossart (1999)
Midazolam 0.05–0.072 mg/kg IM		Sedation for 20–30 minutes at peak effect for endoscopy, freeze branding, or noninvasive procedures	Ball (pers. comm., 2011)
Midazolam 0.08 mg/kg IM	Flumazenil equal volume as midazolam (5 mg/mL) IM	For anesthetic induction with use of 20-L facemask with isoflurane	Walsh & Bossart (1999)

Table 42.2 (Continued)

Drug Combination	Reversal	Comments	Reference
Midazolam 0.08 mg/kg IM, followed by midazolam 0.008–0.017 mg/kg IV	Flumazenil equal volume as total midazolam dose (5 mg/mL) IM	Anesthetic induction Authors' note: Used in at least six anesthesias in two manatees	
Midazolam 0.08 mg/kg IM, meperidine up to 1 mg/kg IM	Flumazenil equal volume to midazolam (5 mg/mL) IM Naltrexone 0.2 mg/kg IM	Anesthetic induction	MT Walsh et al. (pers. comm., 1992)
Midazolam 0.1 mg/kg, butorphanol 0.04 mg/kg[a]	Flumazenil equal volume as midazolam (5 mg/mL) IM, Naltrexone 0.0275 mg/kg	Induction assisted with 20-L mask with isoflurane (single case)	A Bukowski & MT Walsh (unpubl., 2010)
Midazolam 0.1 mg/kg IM, butorphanol 0.06 mg/kg[a]	Flumazenil equal volume as midazolam (5 mg/mL) IM Naltrexone 0.013 mg/kg	Intubation without mask induction; for reproductive examination (single case)	A Bukowski & MT Walsh (unpubl., 2010)
Midazolam 0.1 mg/kg IM, butorphanol 0.06 mg/kg IM[a]	Flumazenil equal volume as midazolam (5 mg/mL) IM Naltrexone 0.029 mg/kg IM followed by 0.014 mg/kg IM	Moderate effect, reacted to initial intubation then induced with 20-L mask with isoflurane for intubation (single case)	A Bukowski & MT Walsh (unpubl., 2010)
Midazolam 0.1 mg/kg IM, butorphanol 0.1 mg/kg IM[a]	No reversal, euthanized	Fractious animal with pyothorax (single case) Profound effect from sedation, intubated without mask induction	A Vigani et al. (unpubl., 2010)
Midazolam 0.08–0.1 mg/kg, butorphanol 0.1 mg/kg IM	Flumazenil 0.001–0.0018 mg/kg IM, naltrexone 0.1–0.5 mg/kg IM	Moderate to marked sedation, intubation often possible without mask induction Authors' note: Performed in at least 14 procedures in three manatees	
Sevoflurane		Similar settings as in domestic animals End expired concentrations no lower than 1.8–2% to assure no purposeful movement to surgical stimulus in manatees	
Xylazine 0.05–0.1 mg/kg IM	Yohimbine 1 mg/5–10 mg xylazine IV/IM or atipamezole 1 mg/20 mg xylazine IV	Moderate sedation, beware of narrow therapeutic index	Murphy (2003)
Xylocaine 1%, dosage not noted	Epidural anesthetic	Epidural used in one case for vertebral fracture surgery	Bossart (2001)

IM, intramuscular; IV, intravenous.
[a] Series of five anesthesias in three manatees; butorphanol dosage adjusted to try to achieve intubation without mask induction.

benzodiazepines was initially used in the development of sedation and anesthesia protocols for more fractious individuals and surgical procedures. In recent years, butorphanol has replaced the use of meperidine in manatee anesthesia. In managed environments, after administration of these sedatives, animals are often placed back in shallow water pools to allow the agent to take effect and minimize the effects of restraint overriding the sedative, in particular the benzodiazepines. Sirenians are monitored closely with higher sedative dosages for evidence of hypoventilation or reduced ability to surface to breathe. Butorphanol (0.05–0.1 mg/kg IM) has been used in combination with midazolam (0.05–0.1 mg/kg) to achieve deeper planes of anesthesia and allow intubation. At higher dosages, patients must be closely monitored for respiratory depression. A combination of detomidine (0.017 mg/kg IM) and butorphanol (0.017 mg/kg IM) resulted in marked respiratory depression in a 700-kg female Florida manatee (D. Neiffer & A. Stamper, pers. comm.). Intravenous administration of yohimbine/naltrexone/supplemental atipamezole reversed the respiratory effects. Manatees have subsequently been

sedated with lower dosages of detomidine (0.0085 mg/kg IM) and butorphanol (0.0085 mg/kg IM) without adverse side effects detected by limited monitoring (D. Neiffer & A. Stamper, pres. comm.). In one instance of a manatee sedated with this detomidine/butorphanol combination, an additional 0.017 mg/kg midazolam IV was administered to achieve adequate sedation for intubation.

Local infiltration of 2% lidocaine at a surgical site is effective, in conjunction with sedation, for analgesia in minor procedures. Epidural administration of 1% lidocaine has been reported once in a manatee undergoing spinal surgery for a vertebral fracture (Bossart 2001); preservative-free lidocaine is recommended for epidural use. Other analgesic agents used in sirenians include nonsteroidal anti-inflammatory drugs such as ketoprofen, but care is taken to avoid gastrointestinal upset and elevations in kidney enzymes, including creatinine and symmetric dimethylarginine, with these drugs. Adverse effects can be reduced by minimizing dosage and frequency of use, as well as avoiding use in dehydrated young animals or those prone to or having existing gastric ulcers or kidney disease. Butorphanol has also been administered for analgesia either intra- or postoperatively in West Indian manatees.

Endotracheal Intubation

Manatees can occasionally be intubated under midazolam (0.1 mg/kg IM) sedation, but often require additional supplementation with midazolam IV or butorphanol IM to achieve adequate muscle relaxation. The combination of midazolam (0.1 mg/kg IM) and butorphanol (0.05–0.1 mg/kg IM) has been used successfully by the authors for smooth intubation; some animals may still require higher dosages.

With use of lower dosages of preanesthetics, additional anesthetic induction with midazolam intravenously or an inhalant administered by mask may be required for endotracheal tube placement. Breath-holding by a manatee can prolong mask inductions and so administration of supplemental injectable sedatives is often preferred. When performed, mask administration has historically been done with a modified 20-L (5-gallon) clear plastic water jug with the bottom removed. The edges are padded for a tighter fit over the animal's head (Walsh & Bossart 1999). A large mask allows adequate tidal volume exchange with less resistance to rapid inspiration. Small masks, covering only the nares, have been used in patients but are generally not recommended by the authors; monitoring is recommended to identify any hypercapnia and hypoxemia that may result. When breath-holding occurs during mask induction, the manatee patient may require stimulation, such as rocking side to side, to facilitate additional respirations. Animals inadequately sedated for intubation will often respond to sound, open their eyes partially, or move their head when stimulated with partial tube insertion into the nasal cavity.

For intubation, a manatee's glottis and trachea are best accessed from the nasal cavities. Oral intubation is generally unsuccessful because of the poor visualization of the caudal pharynx and larynx due to the curved angle of the tongue, the narrow width of the buccal cavity, and the long soft palate. Tubes have occasionally been passed blindly into tracheas of manatees, but dependable tracheal intubation is best accomplished with rhinoscopic assistance. This visualization helps in wild sirenians that are commonly infested with mild to heavy loads of nasopharyngeal trematodes and occasionally have severe rhinitis or tracheitis (Beck & Forrester 1988; Bossart 2001). Use of scopes also aids in maneuvering around caudal pharyngeal tissue that can impede glottal visualization during breath-holding in heavily sedated manatees.

In Florida manatees, it is recommended to use cuffed elongated foal endotracheal tubes (8–14 mm internal diameter, based on the size of the animal) for intubation. Breath-holding and the periodic, brief opening of the glottis in a sedated manatee can result in multiple attempts for successful intubation. Placing lidocaine gel or spray in the nares as well as the glottis, prior to attempting to pass the tube, can help facilitate intubation. Stylets may be used to assist passage of the tube into the laryngeal opening if using the scope separately (Walsh & Bossart 1999; Murphy 2003), though pre-placing the endotracheal tube over the end of a bronchoscope usually results in quicker intubation and confirmation of accurate placement. The improved visualization allows the anesthetist to guide the tube past the loose nasopharyngeal tissues into the trachea even when the glottis is closed, allowing efficient and minimally traumatic intubation. Due to the short length of the manatee trachea, intubation of a single bronchus can occur; bronchoscopy can confirm proper positioning of the endotracheal tube cranial to the carina (Fig. 42.6).

The endotracheal tube is secured to the muzzle with white waterproof tape strips secured to white tape encircling the muzzle, caudal to the oral disk (Fig. 42.7). Periodic suctioning of endotracheal tubes is required to remove mucous that accumulates in the tube (Walsh & Bossart 1999). Once intubated, sirenians can be maintained with isoflurane or sevoflurane levels similar to those used in domestic animals (Table 42.2). Phenylephrine nasal spray can be used to address nasal edema that may develop with recumbency and circumferentially encircling the muzzle with tape to hold in the endotracheal tube.

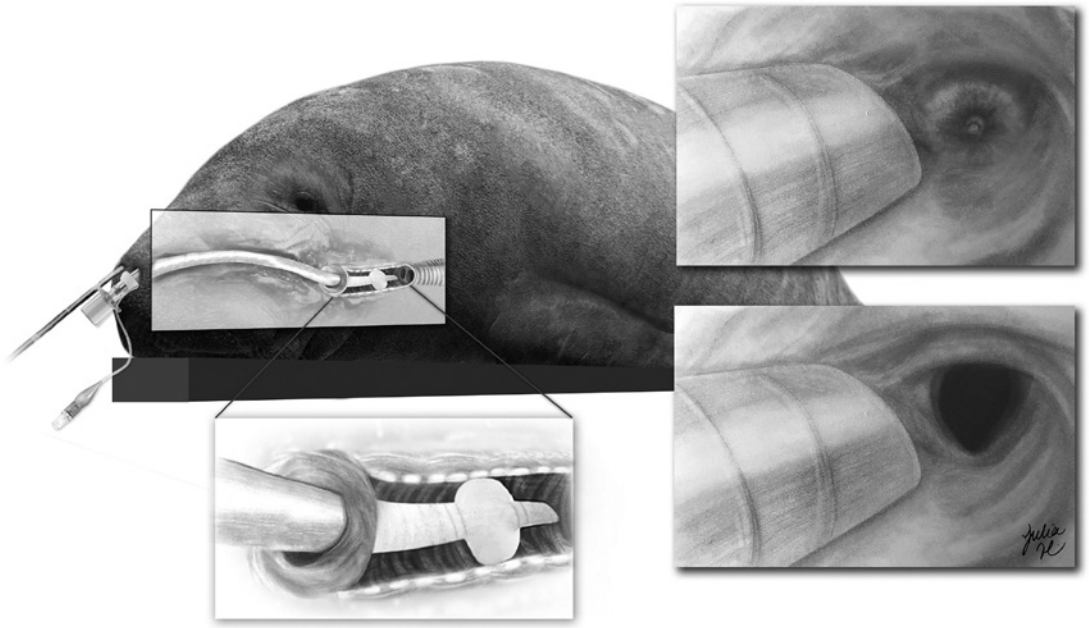


Figure 42.6 Rhinoscopic-assisted nasal intubation of the Florida manatee (*Trichechus manatus latirostris*). Endoscope placement through the nasal passage allows visualization of the glottis to time intubation with glottal opening. Note the final positioning of the endotracheal tube tip cranial to the carina after advancement of the endotracheal tube into the trachea.

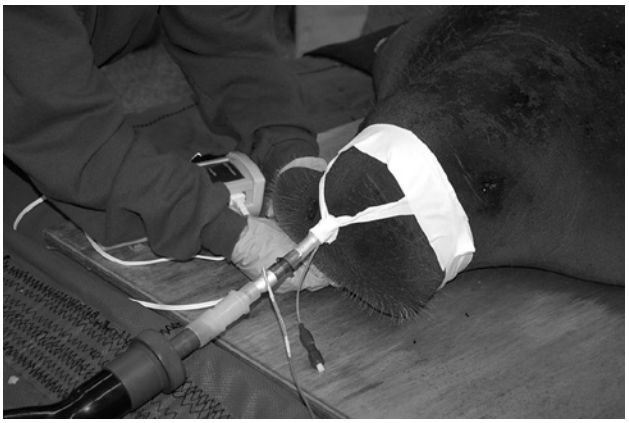


Figure 42.7 Endotracheal tube securing on muzzle of a Florida manatee (*Trichechus manatus latirostris*).

Ventilation

Understandably, many investigators have an interest in how marine mammal species can sleep and breathe in aquatic environments. In addition, the superficial appearance of sleep and anesthesia has led many investigators to compare drug-induced unconsciousness with that of sleep, despite significant differences between the two states. The first attempts to characterize sleep and breathing in the Antillean (Caribbean) manatee (*Trichechus manatus manatus*) by Sokolov produced interesting, but inconclusive electrophysiologic data (Sokolov & Mukhametov 1982). Later, Mukhametov recorded the EEG over a 5-day period from a single Amazonian manatee (*Trichechus inunguis*) after surgical implantation of electrodes under diazepam sedation (0.7 mg/kg IM every 2 hours) and local anesthesia (Mukhametov et al. 1992). The results demonstrated a circadian rhythm for sleep and wakefulness, and similar slow wave sleep to that evident in other aquatic species. For this one manatee, unihemispheric slow waves occupied approximate one quarter and bihemispheric slow waves characterized the majority of sleep. The sleep of both this Amazonian manatee, as well as the Antillean manatee of Sokolov, were characterized by short arousals for the act of respiration, followed by a rapid return to sleep during respiratory pauses.

Anesthetic agents appear to depress respiration in manatees, such that even subanesthetic dosages may cause significant respiratory depression or apnea. The degree of respiratory depression in mammals at equipotent dosages of anesthetic appears to be species dependent. Indeed, breathing does deteriorate in manatees with induction and deepening of anesthesia by mask. Carbon dioxide is the primary driver for respiration in manatees, but they tolerate elevated CO_2 levels (Gallavan 1980). In fact, the arterial partial pressure of CO_2 ($PaCO_2$) must rise very high to trigger spontaneous ventilation even at light planes of anesthesia. This respiratory depression is such that manual or mechanical ventilation is necessary for appropriate ventilation during surgical levels of general anesthesia of manatees.

Mechanically assisted ventilation is preferred over manually assisted ventilation during general anesthesia to maintain adequate lung volumes, gas exchange, and oxygenation. For shorter sedative procedures without general anesthesia, oxygen supplementation of spontaneous respiration is accomplished with an oxygen demand valve. When mechanically ventilating a manatee, some unique anatomical and physiological traits need be considered. First, the narrow nasotracheal tube diameter is at most half the tracheal diameter and will produce resistance leading to prolonged passive expiration, and must be taken into account. Also, mechanical ventilation does not mimic the sirenian respiratory cycle of inspiration closely following expiration. Rather, it reverses the cycle with a lengthy expiratory period following inspiration. There is a growing interest by clinicians and investigators in attempting to mimic the normal respiratory pattern by applying alternative modes of ventilation. The apneustic plateau ventilation mode used in early dolphin ventilation and the novel apneustic anesthesia ventilation (AAV) mode are discussed in Chapter 43 on cetacean anesthesia. The potential advantages when compared to conventional controlled mechanical ventilation (CMV) are lower mean intrathoracic (pleural) pressure, augmented venous return, improved cardiovascular performance, and better distribution of inspired gas flow resulting in improved ventilation-perfusion matching. The AAV mode has been applied to three Florida manatees, but there is currently insufficient data to specify any specific advantage or disadvantage to this novel mode of ventilation.

In manatees combined chest wall and lung compliance may be reduced with removal of the patient from the water and organ displacement. In dorsal recumbency, abdominal organs and ingesta put pressure directly on the lungs. In sternal recumbency, the ventilator must also contend with limited lateral mobility of the pachyostotic ribs and ventral pressure from abdominal organs. Lung compliance can also be reduced by loss of lung function from any concurrent respiratory disease (e.g., severe pyothorax, pneumothorax, or pulmonary fibrosis or adhesions secondary to thoracic trauma). In these cases it may be difficult to alleviate hypercapnia or hypoxemia due to loss of functional tissue. In some cases, whether due to disease or patient positioning, the peak inspiratory pressure of the ventilator when using the CMV mode of ventilation must be adjusted above 30 mmHg to achieve lung expansion, oxygenation, and carbon dioxide exchange. Interestingly, the AAV mode of ventilation is specifically indicated in patients with low lung and thoracic compliance, such as appears to be the case in the beached, anesthetized manatee. Close monitoring of physiological variables will determine the most appropriate ventilatory settings. The ventilatory rate is initially set at 6 breaths per minute (Murphy 2003). Doxapram (IV, IM) has been administered to improve respiration in sedated and anesthetized manatees but this approach should not be considered a substitute for proper ventilation management and only increases cerebral oxygen consumption in the face of potential hypoxemia.

Monitoring

Manatees are closely monitored during sedation and anesthesia using standard techniques or modalities used in domestic animals (Chapter 3). Monitoring of manatees has often relied on noninvasive methods (electrocardiograph, temperature, pulse oximetry, capnography, and other inspired/expired gases), however the authors have been successful with invasive blood pressure monitoring in three adult Florida manatees. The heart rate can be monitored with an electrocardiograph (ECG) as in other mammalian species. Scholander recorded the ECG on the Florida manatee in the 1940s (Scholander & Irving 1941) and Sokolov documented the electrocardiogram waveform in his electrophysiologic studies of the Antillean manatee in 1982 (Sokolov & Mukhametov 1982). Based on the works of, and in consultation with, Hamlin in 1994 (Hamlin et al. 1970, 1972), we proposed a type 2 pathway of ventricular activation with a primary axis of depolarization dorsad, cranial, and sinistrad in the Florida manatee and a diffuse, arborized, and penetrating Purkinje fiber network to the level of the epicardium as evident in the horse (Bailey et al. 1998). Indeed, the heart of sirenian species with its deep interventricular cleft (double ventricular apex) could benefit from the coordination of rhythm produced by a type 2 Purkinje network. However, it was not until 2006 that Siegal-Willott more thoroughly examined the ECG of two subspecies of manatees (*Trichechus manatus latirostris* and *T. m. manatus*) and demonstrated a mean electrical axis of depolarization "similar to that recorded for horses and pinnipeds" (Siegal-Willott et al. 2006). Interestingly, Hamlin reported as early as 1970 that the close relative of manatee, the elephant, differed slightly with a mean electrical axis dorsad, craniad, and dextrad.

Echocardiography parameters have been published for the Florida manatee (Gerlach et al. 2013, 2015). For clinical monitoring, esophageal leads or pad/needle placement of leads on skin is used. If esophageal leads are inserted orally, care is taken to prevent the probe inadvertently being advanced into the trachea instead of the esophagus. It may be prudent to verify placement with a bronchoscope.

Anesthetic depth is determined by assessing blink response, jaw tone, resistance to limb movement, and response to noxious stimuli such as pain from needle or

catheter placement. Eye position is often difficult to assess due to recession of the globe into the orbit during anesthesia.

Anesthetic gas monitoring can facilitate monitoring appropriate anesthetic levels. The amount of inhalation anesthetic agent necessary to prevent 50% of animals from responding to noxious stimuli (minimum alveolar concentration [MAC]) has not yet been determined for manatees, so comparison of equipotent concentrations to other species is imprecise at best. However, the efficacy of inhalation anesthetic agents is well preserved across the many species tested and the amount of inhalation anesthetic needed for manatees will not differ significantly from that required for other mammalian species. The MAC may be estimated at 1.3% isoflurane and 2.3% sevoflurane. It requires 1.2–1.5 times the MAC to assure the majority of subjects do not respond to a surgical stimulus. Addition of other drugs and hypothermia contribute to reductions in the amount of inhalation anesthetic needed. Reviewing cases over the past few decades with similar preanesthetic drugs and body temperature, an end-expired isoflurane concentration no lower than 1.0–1.3% and sevoflurane no lower than 1.8–2.0% were necessary to ensure no gross purposeful movement to surgical stimulus of manatee. Monitoring expired gases into recovery will assist in assessing anesthetic washout and timing of reversal and other interventions.

The physiological variables of the Florida manatee are listed in Table 42.3. Heart rates are calculated by listening to the heart with a stethoscope, placing a Doppler on the skin near the heart, performing electrocardiography, or observing the pulsation of the skin overlying the heart when animals are positioned on their backs. Placement of a pulse oximetry probe on the tongue is difficult because of the short, thick shape and reduced mobility of sirenian tongues and their firm attachment to the lower jaw (Yamasaki et al. 1980; Levin & Pfeiffer 2002). Pulse oximetry readings are occasionally collected from the nasal septum, buccal mucosa, or rostral gingival ridge of the lower jaw. Rectal reflectance pulse oximetry probes can be placed in the nostril to obtain saturation readings. Gingival capillary refill time is generally ≤2 seconds in manatees.

Table 42.3 Physiological parameters for the Florida manatee (*Trichechus manatus latirostris*).

Parameter	Range
Respiratory rate	Variable, average 2–4 breaths per 5 minutes in water, 3–15 breaths per 5 minutes out of water
Heart rate	40–60 beats per minute (can be as low as 30 with diving)
Body temperature	35.5–36°C[a] 35–35.8°C[b]
Tidal volume	2.9% of body weight[c]
Lung volume	Approximately 5% of total body weight

Sources: Scholander & Irving (1941), Pabst et al. (1999), Walsh & Bossart (1999), Murphy (2003), and Martony et al. (2020).
[a] Oral temperatures. Note that body temperatures are dependent on environmental water temperatures as well as site of thermometer placement.
[b] Esophageal temperatures. Based on Martony et al. (2020), $N = 20$.
[c] Based on Scholander and Irving's work, $N = 2$.

Body temperature is measured with a rectal, oral, esophageal, or nasal probe. Flexible rectal thermometers are difficult to place due to high sphincter tone and the fibrous consistency of feces obstructing advancement into the colon. Rectal temperatures may read lower than core temperatures for these reasons (Irvine 1983). Nasal passage of flexible probes is relatively easy, but inhalation can result in spurious results due to inadequate tissue contact. Oral placement of thermometers alongside the caudal buccal mucosa appears to give fairly accurate results, though also lower than core body temperature. Equipment damage from the molars or accidental advancement into the trachea must be avoided. Correct placement of a temperature sensor in the distal esophagus can be used in awake or anesthetized manatee patients to more accurately measure core body temperature (Martony et al. 2020).

End-tidal carbon dioxide ($ETCO_2$) levels follow those of other mammals, yet no scientific study has been reported, to the authors' knowledge, to correlate results with arterial blood gases. Samples for blood gas analysis have been collected from manatees, but the arteriovenous plexus in the pectoral flipper makes interpretation difficult. Venous or mixed samples are still diagnostically valuable when the animal is used as its own control during the procedure. Arterial catheters placed by the authors in three manatees have documented limited arterial blood gases. When applying the CMV mode of ventilation there is an $ETCO_2$ to $PaCO_2$ difference of 10–15 mmHg, suggesting significant dead-space ventilation; when applying the AAV mode of ventilation this problem appears reduced. For those not able to perform arterial catheterization, intermittent venous or arterial blood gas samples are still very informative.

Recovery Considerations

Following recovery from anesthesia, manatees are not placed in water until they are appropriately responding to stimuli and breathing voluntarily. In addition to

monitoring signs of waking, monitoring of expired gas anesthetic concentrations can facilitate the postoperative assessment. The expired anesthetic concentration must drop below 0.4% isoflurane and 0.8% sevoflurane before most animals will begin to wake. At this point reversal of preanesthetic agents can be considered. If possible, animals are moved to shallow water (≤1 m) so they are able to surface to breathe by pushing off the pool floor with their pectoral flippers. Attendants should be present in the pool to aid the animal in surfacing if needed.

The unique anatomy, physiology, and aquatic environment of sirenians make sedation and anesthesia challenging. Continued efforts to develop knowledge of sirenian anesthesia are important to advance conservation efforts and improve our ability to treat sick and injured animals.

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43

Cetaceans

James E. Bailey and Chris Dold

We dedicate this chapter to the memory of Dr. Sam Ridgway, senior author, mentor, friend, and leader in the development of cetacean anesthesia.

Introduction

Cetaceans (whales, dolphins, and porpoises) are mammals whose ancestors developed on land. Around 55 million years ago these ancestors went back to the water (Gingerich et al. 1983) and evolved anatomically, physiologically, and behaviorally for a completely aquatic existence. Most clinical experience has been with the bottlenose dolphin (*Tursiops truncatus*, *Tursiops truncatus gilli*, and *Tursiops truncatus aduncus*) since it is the species most commonly found in display, research, and rehabilitation facilities. Other odontocete species have been successfully managed in zoos and aquaria for many years, including killer whales (*Orcinus orca*), beluga or white whales (*Delphinapterus leucas*), Pacific white-sided dolphins (*Lagenorhynchus obliquidens*), false killer whales (*Pseudorca crassidens*), rough-toothed dolphins (*Steno bredanensis*), as well as several hybrid delphinoid species (Nishiwaki & Tobayama 1982; Zornetzer & Duffield 2003) such as the rare so-called "wholphin" (*Tursiops* and *Pseudorca* cross). Increases in the longevity of cetaceans in managed care have resulted in a growing amount of clinical experience with these species. Dolphins 50 years of age or more are not uncommon in managed care, with subjects over 40 years old being considered geriatric (Venn-Watson et al. 2007, 2011). The high median age of these managed populations (32 years) compared to that of free-ranging dolphins (19.9 years) demonstrates the overall health of the population (Venn-Watson et al. 2015). This statistic is due, in part, to advancements in the medical and surgical interventions employed to maintain the well-being of this mature and closed population of marine mammals. As diagnostic and interventional capabilities continue to improve, the need for and use of advanced surgical procedures increases, in turn leading to increasingly frequent need for sedation and general anesthesia of cetaceans.

Dolphin Sleep and Breathing

As the 1956 Nobel laureate in Medicine, Dr. Dickenson Richards, once said, "Breathing is truly a strange phenomenon of life, caught midway between the conscious and the unconscious, and peculiarly sensitive to both" (Richards 1953).

Bottlenose dolphins, like all cetaceans, have an apneustic breathing pattern. Even when resting at the water surface, dolphins typically take one to three breaths per minute. Each breath is deep, and rapidly fills the lungs to 80% or 90% of capacity (Irving et al. 1941; Ridgway et al. 1969; Scholander 1940). Expiratory flow rates are also very rapid and empty the lung almost completely (Kooyman & Cornell 1981). Thus, the effort of breathing, even at rest, appears much more pronounced than that of humans and other terrestrial mammals.

Given their need to swim and breathe air with these deep breaths, it is not surprising that many biologists and veterinarians have wondered how dolphins sleep in the water. In the early 1900s, Townsend (1914) noted captive bottlenose dolphins "are very lively and keep swimming day and night." Then in the 1960s, John Lilly (1964) observed bottlenose dolphins slept with one eye open and proposed what we now know as unihemispheric sleep. He never, however, produced any electroencephalograms (EEGs) to support this hypothesis. From behavioral observations, Lilly (1962) stated:

> "In regard to lateralization of the sleep pattern, these animals sleep with one eye closed at a time. The eye closures are 180 degrees out of phase; it is rare to

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> have both eyes closed at once. The accumulated sleep for each eye runs from 120 to 140 minutes per day. The sleep occurs in brief periods between each respiration running from 20 to 40 seconds per eye closure. A dolphin wakes up in order to take each breath. Alternate sides are rested alternately."

However, as early as the 1940s it had been observed that cetaceans can sleep with both eyes closed, suggesting they maintain reflex regulation of breathing (McBride & Hebb 1948; Tomilin 1955). Later, in the 1960s, McCormick conducted extensive behavioral observations of dolphins acclimated to large tanks held either alone or in small groups. He observed dolphins resting at the water surface, virtually immobile, with both eyes closed and breathing in an "automatic fashion" for periods of greater than or equal to 1 hour. McCormick (1967, 1969) concluded "respiration in the porpoise can be automatic or can be brought under voluntary control, just as in other mammals." These studies also implied that properly acclimated dolphins may spend more time in bihemispheric sleep when they are held under familiar, comfortable, and safe conditions.

In the 1970s Serafetinides reported the first EEG evidence of unihemispheric sleep in cetaceans using subcutaneous needle electrodes during a one-night recording from a pilot whale (*Globicephala scammoni*) (Serafetinides et al. 1972). Mukhametov recorded many 24-hour periods of EEGs from multiple dolphins using screw electrodes inserted through the skull in a multichannel array with a low-noise wire system that allowed a degree of free movement around a small, shallow pool (Mukhametov et al. 1977; Mukhametov 1984). These dolphins—held in isolation—demonstrated the vast majority of their slow waves were unihemispheric (with the contralateral eye held open), and appeared first in one hemisphere and then the other. Remarkably, each hemisphere appears to accumulate a separate sleep debt. When one hemisphere was deprived of slow wave sleep for several days, only that hemisphere showed the typical sleep rebound; the nondeprived hemisphere continued to alternate its slow wave sleep by the usual amount (Oleksenko et al. 1992). Using a small implantable telemetry unit, Ridgway (2002) replicated these earlier unihemispheric EEG findings and also recorded symmetrical EEGs in both hemispheres during thiopental/halothane anesthesia and recovery. Short periods of EEG slow waves were identified days later in both hemispheres during the unanesthetized state (Fig. 43.1).

Sleep might be simply defined as a state of immobility that is rapidly reversible and is best conducted in a place perceived as comfortable and safe. Laboratory polysomnography (sleep study) of humans has proven sufficiently uncomfortable that home methods have been developed to address this barrier to accurate study (Zancanella et al. 2022). Cetacean laboratory sleep studies involving electroencephalography were often performed in subjects which were wild caught and minimally acclimated, held in isolation in a very restricted space (Serafetinides et al. 1972; Mukhametov et al. 1976), and frequently under the influence of barbiturates (Mukametov & Supin 1986), benzodiazepines (Mukhametov 1984; Howard et al. 2006), or propofol (Howard et al. 2006) to induce a sleeplike state (Wang et al. 2014). Even in these uncomfortable and abnormal conditions, cetacean subjects clearly demonstrated global or bihemispheric sleep (Serafetinides et al. 1972; Mukhametov et al. 1977; Mukhametov 1984; Howard et al. 2006; Supin & Mukhametov 1978; Ridgway 2002), including slow wave, and in no instance did any subject go into respiratory arrest. In fact, as Mukhametov reported, "The whole sequence of respiratory movements of dolphins may be observed during bilateral intermediate EEG synchronization without arousal" (Mukhametov et al. 1977; Mukhametov 1984). However, it is true that many investigators could only induce so-called "deep" slow wave bihemispheric sleep in dolphins through the use of anesthetic drugs, which did stop respiration (Howard et al. 2006; Supin & Mukhametov 1978). Nevertheless, it must be noted that there are clear differences in brain function between sleep and anesthesia. Sleep involves brainstem and frontal lobe function, while anesthetic drugs, like propofol, have widespread or global influence on the brain (Li et al. 2018). Indeed, as early as 1978 Supin noted that the EEG synchronization of the dolphin brain under the influence of pentobarbital "is a widely generalized process that covers simultaneously large regions of the cerebral cortex" (Supin & Mukhametov 1978).

In hindsight, answers may be more obvious than they were at the outset. It is easy to sit in judgement of past works when we have decades of cumulative observations at our disposal. Even so, we are obligated to note that John Lilly described how in 1955 he injected a dolphin with pentobarbital (30 mg/kg Nembutal®) intraperitoneally (IP) (Lilly 1961). This dosage we now know to be sufficient to induce general anesthesia with global cerebral depression and a high likelihood of apnea in many mammals. Without advanced knowledge of how to support ventilation in this dolphin, the animal died. Lilly proceeded to use pentobarbital (10.3 mg/kg IP) with a similar result. Two more dolphins were anesthetized with pentobarbital, but this time with some early failed attempts at intubation and ventilation. Finally, despite clear evidence in the anesthesia literature of the time indicating many deaths had occurred after injection of even small doses of paraldehyde by "paralysis of the respiratory center" (Springer et al. 1943), Lilly attempted to substitute an unknown amount of

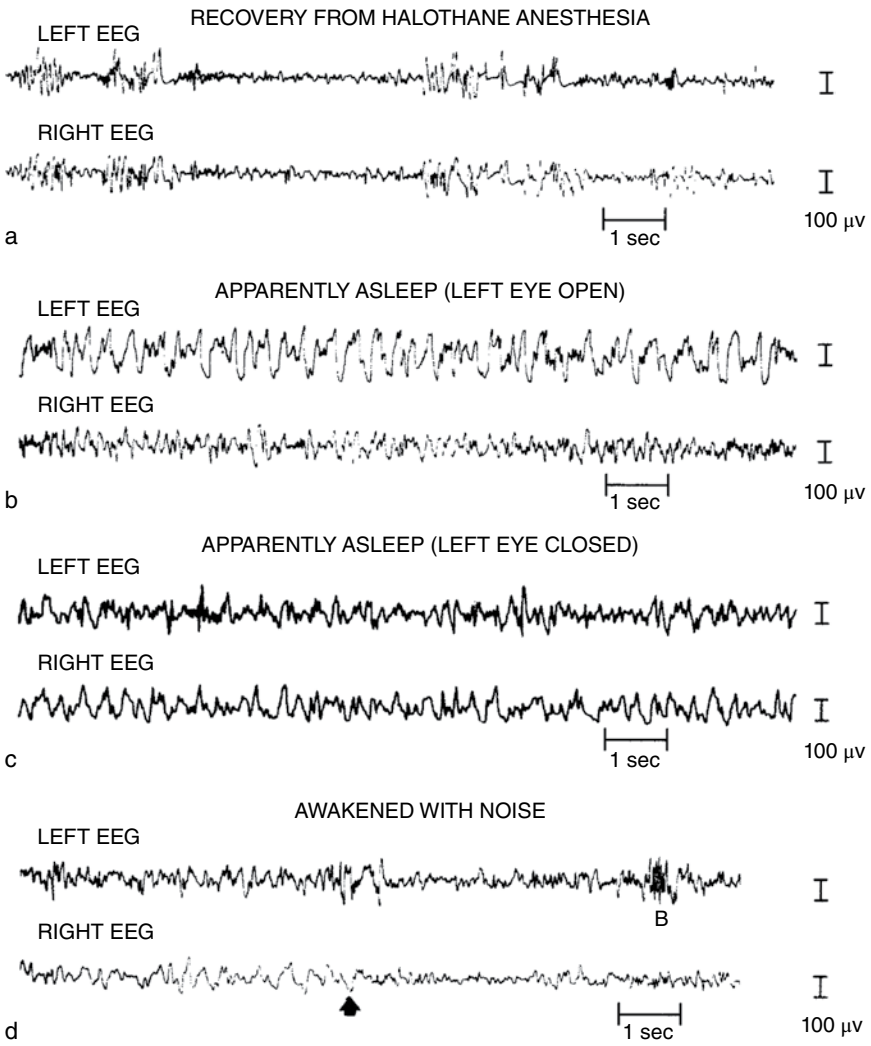


Figure 43.1 Electroencephalogram (EEG) of the bottlenose dolphin (*Tursiops truncatus*) in four different conditions. Records are not continuous. (a) Dolphin awake with both eyes open recorded while the dolphin was recovering from thiopental-halothane anesthesia. (b) Recorded 2 weeks after (a) when the dolphin had recovered from surgery and could be placed in the small recording pool. (c and d) Recorded a day later in the same small recording pool. At the arrow in (d) the animal was awakened with a loud clap of two wooden planks brought together smartly. At point B in (d) the dolphin took a breath. Short periods of EEG slow waves were identified in both hemispheres (bihemispheric) during waking from anesthesia (a) and an unanesthetized restful state (d). Reproduced with permission from Ridgway (2002).

paraldehyde to induce "anesthesia" of another dolphin. In all, five dolphins were dead of what could only be described as anesthetic-induced respiratory arrest at a marine park now unhappy with the visiting researcher (Lilly 1961). From this Lilly incorrectly concluded dolphins "lack our unconscious, automatic, self-sustaining breathing system...so this function is almost if not fully voluntary. Therefore, a drunken dolphin dies when he passes out. It seems a sure bet that there are no alcoholic porpoises!" (Lilly 1958). Later, Lilly did implant electrodes into the skull of dolphins under local anesthesia (Lilly & Miller 1962) in an attempt to validate this opinion, believing he found that "respiration is controlled in the nucleus ellipticus of the thalamus" (Lilly 1964). Misinformed and misguided, many still reference Lilly believing dolphins only breath voluntarily and must "wake" for every breath. Instead, the existing literature supports McCormick's conclusion respiration in cetaceans is automatic or involuntary, albeit sensitive to anesthetic drugs.

However, McCormick also observed that unlike the bottlenose dolphin, the Dall porpoise (*Phocoenoides dalli*) swam continuously without ever stopping to rest or become immobile (McCormick 1967, 1969). Mukhametov also observed that Azov porpoises (*Phocoena phocoena*), in the same family as the Dall porpoises, swim continuously. From these behavioral observations it might be easy to conclude that Dall porpoises and Azov porpoises never sleep. Mukhametov fitted three Azov porpoises with EEG recording equipment (Mukhametov & Poliakova 1980). The animals swam continuously around their pool. Unihemispheric slow waves alternated between the hemispheres while the porpoises continued to swim, therefore stopping to rest or becoming immobile is not an absolute requirement for sleep in cetaceans. Although bottlenose dolphins and the largest member of the dolphin family, killer whales, often rest at the surface as described by McCormick, both mother and calf are known to swim constantly for several weeks after the birth (Lyamin et al. 2005).

Thus, if the mother and calf of these delphinid species are sleeping, it must occur while they are continuously swimming (Hill et al. 2008).

Spontaneous breathing does cease in dolphins with induction of anesthesia (Ridgway 2002; Mukhametov et al. 1976; Supin & Mukhametov 1978; Lilly 1961; Ridgway & McCormick 1971). Early in the evolution of dolphin anesthesia, Ridgway intubated dolphins while awake and induced anesthesia with the inhalation anesthetic agent halothane and an apneustic plateau ventilator. These dolphins would undergo "swimming movements" and variable periods of "tube bucking" or attempts to spontaneously ventilate as anesthesia deepened to the point that all reflexes were quietened (Ridgway & McCormick 1967). In the late 1930s Irving documented the relative insensitivity of diving mammals to carbon dioxide (CO_2) when compared to terrestrial mammals (Irving 1938), later noting that dolphin "sensitivity of respiratory control to carbon dioxide must be quite different from the sensitivity of land animals" (Irving et al. 1941). Using controlled mixtures of CO_2, oxygen (O_2), and nitrogen (N_2) in the air breathed by conscious dolphins, McCormick demonstrated an increased respiratory rate in response to increased CO_2 and decreased O_2 inhaled in a manner similar to other mammals, but noted "tolerance to CO_2 in the blood is greater due to increased buffering capacity" (McCormick 1969). It has long been known that inhalation anesthetics depress the response of mammals to carbon dioxide in a dose-dependent fashion (Fourcade et al. 1971; Hickey & Severinghaus 1981). We now know Phox2B transcription factor expressing neurons of the retrotrapezoid nucleus (RTN) located in the ventrolateral brainstem are sensitive to changes in CO_2 and pH levels, and Phox2B is critical to the triggering of breathing. It is theorized here that since Phox2B varies by species (Albersheim-Carter et al. 2016; Nomaksteinsky et al. 2013) and anesthetic drugs appear to change cellular localization of Phox2B, thus affecting the protein's ability to trigger breathing in response to rising blood carbon dioxide levels (Dubreuil et al. 2009; Coghlan et al. 2018), anesthetic-induced depression of the response to CO_2 will vary between species. This depression of the response to CO_2 appears clinically to vary between mammalian species following the trend hominid $\cong$ canid $<$ equid $<$ otariid $<$ phocid $\cong$ delphinid (Colitz & Bailey 2019). The shift in the response to carbon dioxide is such that moderately anesthetized otariids will not spontaneously ventilate until the arterial partial pressure of carbon dioxide ($PaCO_2$) has climbed to 60–80 mmHg. In addition, the anesthetic effect of CO_2 has been recognized since the early 1800s, and the reduction in inhalation anesthetic requirement with introduction of carbon dioxide is well established in terrestrial mammals (Eisele et al. 1967; Brosnan et al. 2007). It appears the shift in the response of dolphins to $PaCO_2$ while under anesthesia is sufficient that it must rise very high, to the point of becoming an anesthetic itself (CO_2 narcosis, $PaCO_2 > 95$ mmHg), and therefore dolphins will be unlikely to spontaneously ventilate even at moderate to light planes of inhalation anesthesia.

As it stands, dolphins appear to breath involuntarily and the amount of time they spend in unihemispheric or bihemispheric sleep may well be determined by the need for vigilance based on the perceived safety of the sleep environment, and the needs of the animal grouping or pod. Species other than aquatic mammals also capable of both bihemispheric and unihemispheric sleep demonstrate variable use of unihemispheric sleep, seemingly based on such need. Given unihemispheric sleep was first identified in birds, they provide well-established examples and a model for study. EEG and behavioral evidence of frigate birds (one of many species known to remain in flight for days, weeks, or months without landing) demonstrate that, although they are able to engage in all types of sleep when in flight, they primarily engage in unihemispheric sleep in flight (Rattenborg et al. 2019), perhaps to avoid collisions with other birds (Rattenborg 2017). EEG and behavioral evidence of Mallard ducks sleeping on the ground at the edge of a group show they spend a greater proportion of time in unihemispheric sleep than ducks in the center of the group, and do so with one eye open facing away from the other ducks and toward the direction of predation risk (Rattenborg et al. 1999). On the contrary, at night Pacific white-sided dolphins appear to instead maintain visual contact with their neighbors in the pod, rather than scanning the environment for potential predators in the dark in order to maintain a cohesive group (Goley 1999). As we improve our approach to EEG study of dolphin sleep and become able to evaluate them grouped in comfortable, safe environments and apply minimally invasive remote methods, we will likely find some dolphins in a pod will maintain greater vigilance (Ridgway et al. 2006a), spending more time in unihemispheric sleep and acting as sentries or supervisors, while others will be allowed to undergo a greater degree of bihemispheric, slow wave sleep. In addition, we can anticipate we will discover significant differences in the various cetacean species and individual animal uses of bihemispheric sleep.

History of Dolphin General Anesthesia

The physiology of anesthesia is different from that of sleep, especially in cetaceans. The superficial appearance of these two physiological states, however, gives rise to the common comparison of administering general anesthesia with

inducing sleep. Although there are many differences, unconsciousness in these two different physiologic states has historically been considered somewhat similar in humans and other land mammals. However, the phenomenon of unihemispheric sleep in cetaceans makes the direct comparison between sleep and anesthesia even less applicable in these species. Moreover, in all mammals, arousal from sleep by noxious stimuli has a relatively low threshold, whereas arousal from anesthesia may only be possible after recovery.

The first attempt to anesthetize a dolphin was made in the 1930s by Langworthy, who administered "ether by cone" held over the blowhole. The dolphin stopped breathing and died (Langworthy 1932). After Lilly's attempts to employ intraperitoneal barbiturate anesthesia also resulted in dolphin deaths (Lilly 1961), Nagel successfully developed an endotracheal intubation method and induced a state where the dolphins were "largely insensitive to noxious stimuli" with 70% nitrous oxide and O_2 delivered by a ventilator (Nagel et al. 1964). Although nitrous oxide appeared safe, it was wholly inadequate for major surgery. Ridgway and McCormick (1967, 1971) used the inhalation anesthetic agent, halothane, and later intravascular thiopental for induction followed by halothane for maintenance of anesthesia sufficient for major surgery. Other early work in cetacean anesthesia has been reviewed in French by Lecuyer (1983). More recently, intravenous (IV) propofol has been the choice for anesthetic induction followed by intubation and maintenance of anesthesia with the inhalation anesthetic agents isoflurane or sevoflurane (Linnehan & MacMillan 1991; Bailey 2013a, 2016, 2021).

When under general anesthesia, dolphins do not breathe spontaneously, and "deep" slow waves appeared on the EEG of both brain hemispheres (Ridgway 2002; Mukhametov et al. 1976; Howard et al. 2006; Supin & Mukhametov 1978; Ridgway & McCormick 1967, 1971). As such, all successful general anesthesia of dolphins has required intubation and the use of a ventilator. Naturally this finding obligates further discussion found later in this chapter (see the section on ventilation). Historically, a Bird Corporation, Mark 9 large animal ventilator fitted with an apneustic control device (Bird 1975) has been employed to mimic normal respiration of dolphins (Ridgway & McCormick 1967, 1971; Nagel et al. 1964). More recently, alternative modes of ventilation have been applied.

Anatomy and Physiology Relevant to Anesthesia

Specific anatomic and physiologic adaptations of the respiratory and cardiovascular systems, although beneficial for a purely aquatic existence, pose challenges to the clinician for sedation and general anesthesia of the cetacean patient. Much of the physiological and anatomical knowledge discussed here was gained from work on bottlenose dolphins. Fortunately for the clinician, most of the adaptations are well conserved among the other odontocete species commonly encountered in zoos and aquaria. The most obvious adaptation of the respiratory system is the blowhole, the external nasal opening of cetaceans. It is positioned on top of the head rather than at the front of the face as it is in all other mammals. Immediately ventral and lateral to the blowhole internally are right and left lateral vestibular sacs. One can readily palpate these sacs by placing a finger through the blowhole directed to the left or to the right, with the right sac being larger. Paired internal nares can be seen below the nasal plug when it opens. The paired nasal cavities, separated by the nasal septum, extend from the nares ventrally along the cranial aspect of the calvarium to the nasopharynx just above the elongate larynx. Because of its semblance in shape to the beak of a goose, the larynx has been given the common name "goosebeak" (see Fig. 43.7). The goosebeak is an elongation of epiglottal and cricoarytenoid cartilages supported laterally by arytenoepiglottal muscles (Green et al. 1980). It is held in its dorsally oriented position by the nasopharyngeal sphincter muscle located in the dorsal oropharynx. Foods, usually swallowed whole, course laterally around the larynx. The larynx is not permanently affixed in this position. It can be displaced voluntarily by the animal or when swallowing large food items, and by the clinician manually when intubating the animal. The larynx leads to a short, robust trachea with a large lumen. Preceding the carina and mainstem bronchi is a right-sided accessory (tracheal) bronchus (Green 1972), which is an important consideration when intubating these species because this separate right tracheal bronchus is required for inflation of a portion of the right lung. Since cetaceans must be intubated and ventilation must be controlled for general anesthesia, the anatomy relative to the endotracheal intubation process is especially important.

Compared with terrestrial mammals, cetaceans have more extensive pulmonary support structures, including complete tracheal and bronchial cartilagenous rings that extend beyond the mainstem bronchi into deep bronchioles, as well as plates and rings of cartilage that extend all the way to the junctions of alveoli. Smooth-muscle, sphincter-like narrowings occur at the terminal bronchioles (Simpson & Gardner 1972). The lungs contain a large amount of elastic tissue. A dense elastic visceral pleura 1 mm or so in thickness covers each nonseptate, nonsegmented lung. As previously mentioned, conscious cetaceans have a specialized respiratory cycle with short, rapid exchange phases followed by long inspiratory apneustic

plateaus. They take fewer and deeper breaths than their terrestrial counterparts. Bottlenose dolphins breathe an average of two to three times per minute and have a tidal volume of 5–10 L, which may represent 80% or more of their total lung capacity (Ridgway 1972).

Anatomic adaptations of the cardiovascular system to support deep diving, long breath holds, and temperature conservation in the cold ocean include large, distensible veins, venous sinuses, venous valves in the lungs, portal triads of the liver, and a venous sphincter in the common hepatic vein at the junction of the inferior vena cava below the diaphragm. A highly developed meshwork of arteries and veins between the thoracic vertebral bodies, the rete mirabile, as well as the peri-arterial venous rete, represent temperature countercurrent exchange systems that allow cetaceans to peripherally vasoconstrict and still perfuse the brain with warm, oxygenated blood even under the great pressure and temperature extremes experienced at depth (McFarland et al. 1979). Finally, cetaceans have a profound respiratory sinus arrhythmia that is normal, the heart rate speeding up with each breath and slowing down between breaths (see Fig. 43.10a).

Physical Restraint

With practitioner experience in cetacean sedation and anesthesia still being relatively limited, clinically relevant procedures are currently more frequently performed with physical restraint alone or with modest sedation. Physical restraint of small cetaceans is common practice, but requires multiple personnel to accomplish safely. Even then it can still result in injury to both people and patient due to the substantial size and strength of most small cetaceans. It is recommended, therefore, that physical restraint be performed under the supervision of trained, experienced personnel. Animals requiring care can be separated from pool mates either under voluntary control, or with the use of nets or stranding devices. Care must be taken when introducing a net into the water. If animals become entangled, they must be quickly assisted to the surface so that they can breathe. Many facilities have medical pools designed to strand animals out of the water for clinical procedures without the need for nets, slings, or stretchers. Clinical procedures have been performed on dolphins and other odontocetes out of the water suspended in fitted slings, watertight boxes, or most commonly on soft foam rubber pads on the ground or on large animal surgical tables. When not suspended in stretchers or slings, animals are commonly positioned onto closed-cell foam padding. Personnel are then positioned on both sides of the animal with one or two people to restrain the tail

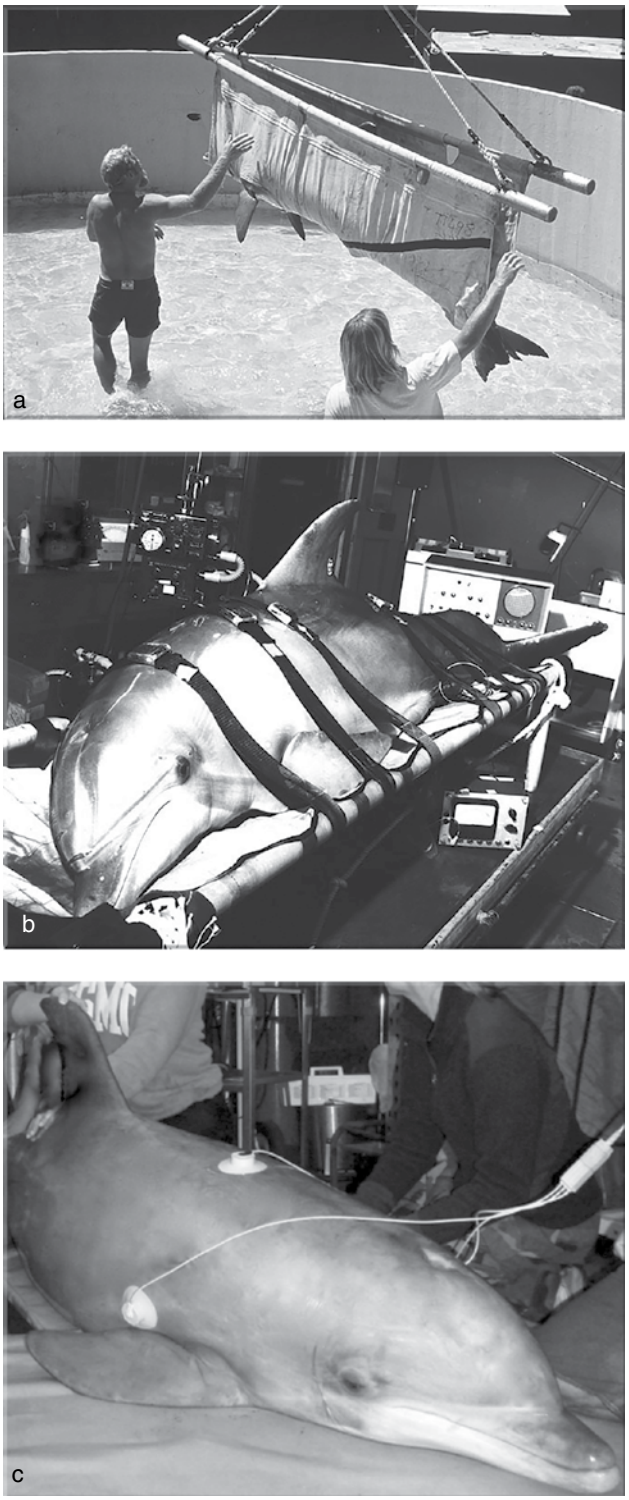


Figure 43.2 (a) A dolphin is lifted from its pool in a fitted sling. (b) Prior to induction of anesthesia, a dolphin rests on a special table held loosely by seat-belt straps. US Navy photograph. (c) Dolphin on soft medium-density closed-cell foam pad on the ground with electrocardiograph electrodes attached per Ridgway standard. US Navy photographs.

fluke, and one or two people positioned at the shoulder to control head and upper body movement. For animals that are relaxed out of water, simple support by only one or two people may be all that is required. For more fractious animals, multiple people may be needed to provide adequate restraint.

Due to the challenges associated with physical and chemical restraint in these animals, operant conditioning and training have resulted in many small cetaceans being conditioned to voluntarily participate in clinical procedures (e.g., blood sampling, ultrasound, radiographs, and endoscopy). Whenever the cetacean patient is out of the water, its skin must be kept moist for temperature control and prevention of drying. Special attention should be paid to the eyes to prevent injury or drying. During anesthesia it is best to apply a lubricating ophthalmic ointment to prevent drying of the eyes. Special tables or tanks (Fig. 43.3) have been constructed to maintain the dolphin patient in the proper position for monitoring and surgery.

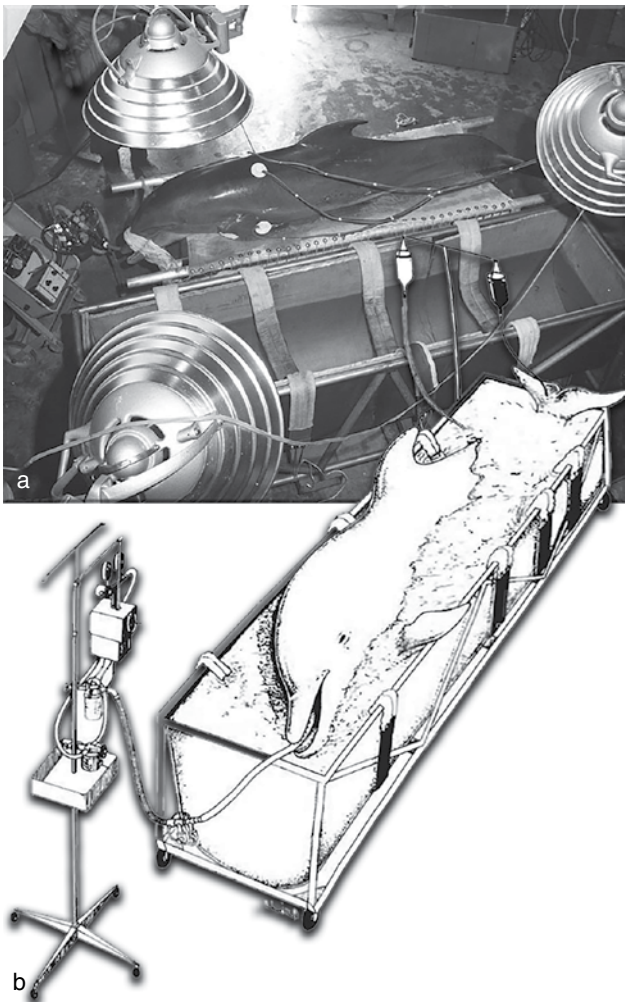


Figure 43.3 (a) The dolphin is anesthetized and ventilated with a Bird (Bird 1975) respirator through an oral endotracheal tube. White rubber suction cups hold surface electrodes for monitoring the electrocardiogram (ECG). The suction cups provide insulation for the electrodes to allow the ECG to be recorded while the animal is immersed. The dolphin will be supported by the warm water and padded straps in the adjacent tank during the surgical procedure. For long procedures, a nebulizer is placed in the line for humidification of respiratory gas. US Navy photograph. (b) Drawing showing the surgical tank with a dolphin in the customary position used for ear surgery. Reproduced with permission from Ridgway (1974).

Translocation

Most facilities housing cetacean species do not have sufficient resources on sight to manage major surgery or specialty diagnostic imaging, particularly on an emergency basis. As such, it has been, and will continue to be, necessary for such facilities to transport a patient a considerable distance for certain diagnostic and surgical procedures. Ideally, considerable planning to address logistics and assign responsibilities takes place prior to long-distance transport of cetaceans. A plan should be in place, ready on an emergency basis, for this eventuality. Where logistically feasible, the animals should be afforded time to acclimate and recover from the fatigue of transport prior to any procedure. At locations which do have adequate facilities to preform major surgery, local transport for short distances of limited time can be accomplished with open-cell foam mats and personnel positioned on both sides of the animal, or supplemental side mats to control animal movement (e.g., tri-fold mats). In addition, nets, slings, or stretchers are used as appropriate for translocation of the animal. Wetting with spray bottles may be sufficient for maintenance of skin condition and thermoregulation during these brief, local transports.

The transport of dolphins for long distances was first proposed over 100 years ago, using long boxes filled with cool water (Townsend 1914). Lilly refined this method using fiberglass contoured boxes to reduce the water volume and thus the total weight of the transport (Lilly 1961). The disadvantages of this water suspension method of transport include the considerable weight of the container, the danger that the animal might crash against the side of the box through inertia when the transport vehicle accelerates or stops, the sloshing and spillage of water, urine, and feces in the water necessitating water changes, and the possible difficulties in breathing due to splashing of the befouled water from inertia and animal movement.

In the early 1960s evolution of dolphin transport techniques, animals were placed on their sides in shallow boxes lined with open-cell foam padding material. Though this technique was historically used rather extensively, there

was considerable overheating on the underside of the animals. In addition, if the attendants were not careful, by the end of the transport the animals were lying in and perhaps breathing their own urine and feces (Ridgway 1972).

Today, the most frequently used method of long-distance transportation consists of suspending the animal in a hammock-like sling on a framework to evenly distribute its weight and allow for a maximum possible amount of evaporative cooling. The dolphin slings are equipped with padded pectoral holes to allow the flippers to hang at a normal angle, padded genital and anal slits to allow the drainage of urine and feces, and occasionally tail pockets to support the tail fluke. The hanging sling is mounted on a framework such that the animal and sling rest lightly on medium-density open-cell foam for additional support and cushioning. Alternatively, the sling is suspended in cool water, similar to early iterations of transport. The US Navy, which transports dolphins halfway around the world during deployments, has special fleece-lined slings in transport containers that contain water up to the eye level of the dolphin (Fig. 43.4) (Ridgway 2008). Regardless, the framework is surrounded by flexible vinyl material or is mounted in a watertight rigid container to capture water and collect waste. An added disadvantage to air transport versus land transport by this method involves the difference in atmospheric pressure. Aircraft cabin pressure is optimally held at or below a 3520-feet altitude equivalent (Yip & Dold 2018), but should not exceed a 6000-feet altitude equivalent. As such, cetaceans being transported in nonpressurized aircraft should stay below this maximal elevation limit to avoid respiratory distress thought to be similar to high-altitude sickness.

Terrycloth covers for the body, dorsal fin, and pectoral flippers with water sprayed, poured, or sponged over the body assist in keeping the animal cooled and the skin moist. Ventral skin surfaces and the pectoral flipper axilla may be generously coated with zinc oxide ointment to prevent rubbing injury. Some also add packed ice around the tail flukes or the entire body, or spray with ice water to further reduce overheating, particularly when transporting larger species, such as killer whales (Ridgway 1972).

Assessment

A voluntary preanesthetic health assessment of subjects from managed populations where medical behaviors can be cultivated provides an overview of the animal's current health status prior to anesthesia. Where possible, this should include complete blood count, serum chemistry panel, and physical examination. Further information can be garnered from urinalysis, radiographs, ultrasound, and echocardiography where appropriate. Unfortunately, useful medical behaviors may be lost when there is pain and discomfort, changes in vision or other sensory capabilities, or cognitive changes associated with extreme physiologic imbalance caused by the medical condition of concern. Trainers must be vigilant to maintain necessary medical behaviors, and preoperative analgesia or other physiologic

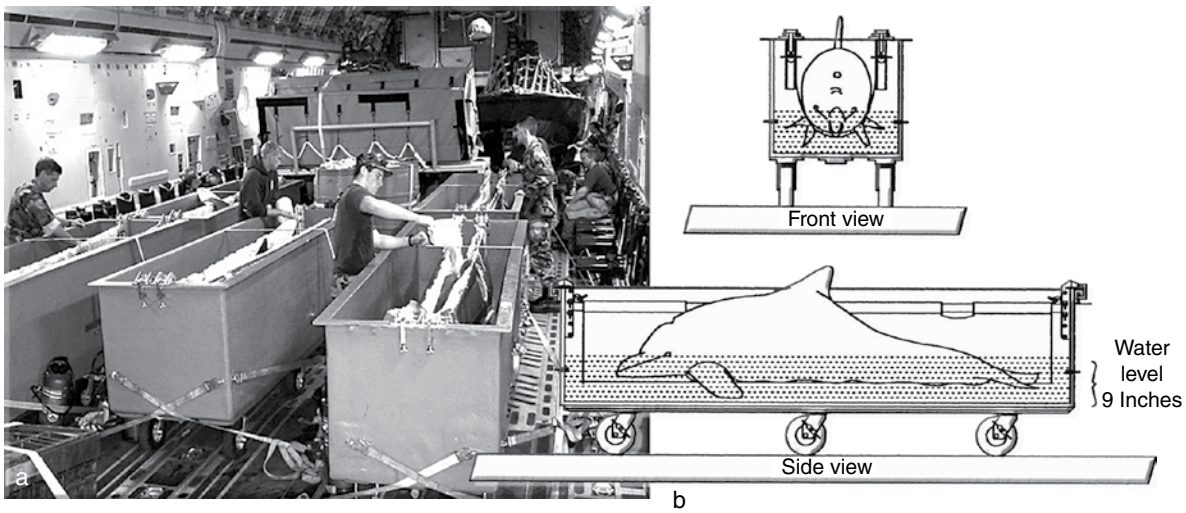


Figure 43.4 (a) Scene inside a US Air Force transport plane at 12,000-m altitude. Cabin pressure is maintained under 2000 m for dolphin comfort. Navy dolphins rest inside fleece-lined slings, in water, in their blue fiberglass transport pools as handlers watch over their animals. A staff veterinarian and veterinary technician always accompany transports along with the animals' experienced handlers. Reproduced with permission from Ridgway (2008). (b) Diagram of dolphin hanging in a sling mounted on a framework suspended in cool water at the appropriate depth of approximately 9 inches. The sling may be raised or lowered independently at each corner to maximize comfort. US Navy diagram.

intervention may be necessary to support the effort of the trainers. Given more surgical procedures are being performed on geriatric patients in managed populations, the preanesthetic health assessment is imperative to identify other potential underlying disease states.

Anesthesia of cetaceans requires a balance of behaviors, physical restraint, and anesthetic drugs. The practitioner must consider the patient species, size, age, demeanor, training, as well as the working environment to best tailor the anesthetic protocol. Desensitization training and voluntary medical behaviors contribute in no small part to positive outcomes. These voluntary medical behaviors may also reduce the need for manual or mechanical restraint. Excessive reliance on physical restraint may lead to physical injury, hyperthermia, or exertional myopathic conditions in the patient. With proper desensitization training, appropriate chemical sedation, and judicious use of physical restraint, the safety of anesthetic procedures for both the patient and the animal handlers will improve and eliminate undue added risk. Again, since more and more surgical procedures on cetaceans are elective and are performed on geriatric patients, we emphasize here that quality trainers and animal handlers are necessary for safe anesthesia and they must be given both the opportunity and time to train subjects whenever possible. These voluntary medical behaviors may also reduce the need for repeated anesthetic procedures and will assist with postsurgical medical treatment and follow-up procedures. Trainers, and the time necessary to train, are key to positive anesthesia procedure outcomes of managed populations of all marine mammals.

Vascular Access

There are several peripheral sites from which blood may be collected. The arteriovenous nature of the peripheral vasculature, however, means very few of these sites allow rapid drug or fluid administration or clear differentiation of arterial and venous blood. Consequently, true venous and arterial access is desirable and has become increasingly attainable as imaging and vascular access methodology has improved. In this section we describe both peripheral and central access sites for blood sampling and catheter placement.

Braun's 1905 X-ray angiograms of the arteries of the fluke and pectoral flipper of the harbor porpoise helped begin documentation of the extensively branching network of the peripheral vasculature of cetaceans (Braun 1905). In 1941 the complex nature of the arterial and venous blood supply of dolphins and manatee was described by Fawcett (1942), and Tomilin (1951) first described the closely adhering venous reticulum associated with the arteries that he called "complex vessels" involved in temperature regulation. We now know these as the periarterial vascular rete (PAVR). Shortly thereafter, Scholander and Schevill (1955) first hypothesized the countercurrent heat exchange function of this "artery-within-vein arrangement" of the PAVR. In 1974, Elsner further detailed the radiographic, gross, and histologic anatomy and produced corrosion casting of the PAVR (Fig. 43.5) (Eisner et al. 1974).

Armed with this knowledge, it must be noted that when performing "venipuncture" at a PAVR location, it is the artery surrounded by the venous reticulum (periarterial venous rete) that is most probably penetrated by the needle. This may be evidenced by a rapid passive outflow of blood. Depending on the location and angle of incidence, the needle lumen may communicate with the artery, venous reticulum, or the perivascular space or channel through the firm collagenous matrix surrounding the PAVR. This imprecise positioning and the likelihood of migration lead to venous admixture and possible perivascular leakage. With proper aseptic technique, this is acceptable for blood collection and delivery of isotonic crystalloid fluids, but caution is advised in delivering any medication. It is well known that arteries are muscular and will respond to medications of extreme pH, osmolarity, direct cytotoxicity, or known vasopressor activity with vasospasm and thrombosis after a variable degree of vascular injury. There are a number of anecdotal reports of fluke vascular injury and circumferential sloughing after delivery of medications, such as insufficiently diluted antibiotics, into the peduncle or fluke PAVR (Lowenstine et al. 1990). It is well documented that anesthetic drugs of extreme pH, such as the barbiturate thiopental, will cause vascular injury and severe complications when injected into arteries (Sen et al. 2005). Ridgway was able to deliver thiopental (10 mg/kg IV of 50 mg/mL) in the peduncle PAVR without complication on multiple occasions (Ridgway & McCormick 1967, 1971; Ridgway et al. 1974; Ridgway 1965). These injections, however, were normally delivered in crystalloid perioperative fluids, thus diluting the drug prior to entry into the PAVR (S.H. Ridgway, pers. comm., 2020). There are some reports of vasculitis and vascular impairment after intra-arterial delivery of midazolam in human subjects, but symptoms resolved without sequelae with no specific intervention. Propofol is well known to cause pain on injection, but it has not been associated with any vascular injury when inadvertently delivered intra-arterially. If true venous access is not acquired for anesthetic drug delivery, we advise careful drug selection and use of crystalloid fluids during induction for the purpose of dilution. True venous access in the lateral subcutaneous caudal vein is now routine and enhances safety.

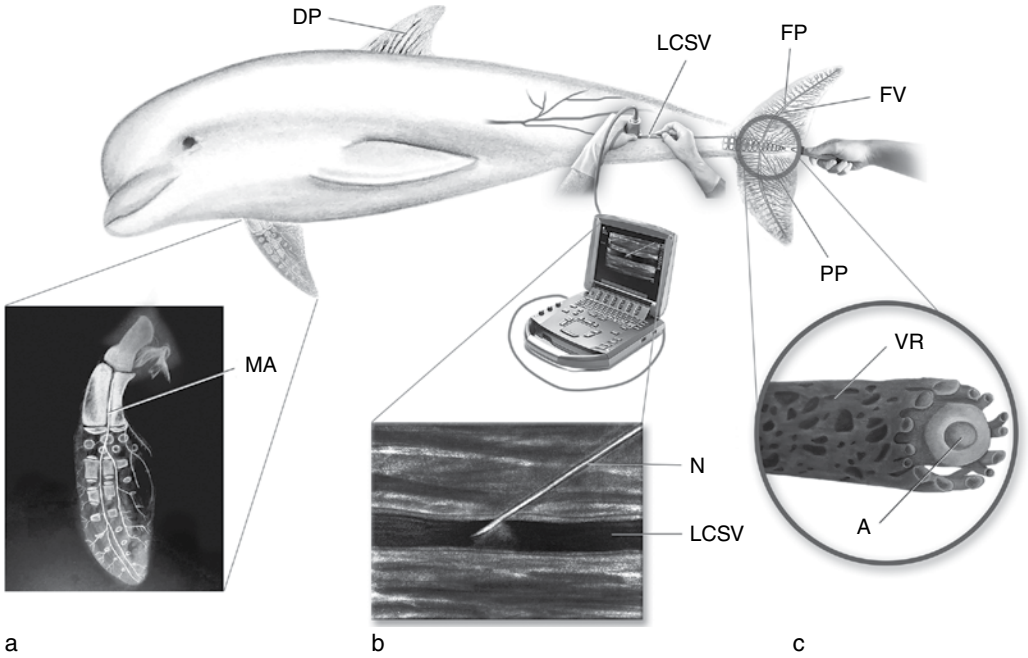


Figure 43.5 Vascular access locations. (a) Angiography of the median artery (MA) of the pectoral flipper. Adapted from Braun (1905). (b) Longitudinal plane ultrasound image of the lateral caudal subcutaneous vein (LCSV) with echogenic needle (N) placed. (c) Peri-arterial venous rete (VR) surrounding artery (a) often taken together in the literature as the peri-arterial vascular rete (PAVR). Adapted from Elsner 1974. DP, dorsal fin PAVR; LCSV, lateral caudal subcutaneous vein; FP, fluke PAVR; FV, fluke vein; PP, peduncle PAVR. Reproduced with permission from Bailey (2020).

Dorsal and Ventral Fluke PAVR

The ventral fluke PAVR is most commonly used for routine venipuncture in odontocete species (Ridgway 1965). In dolphin collections, animals are often trained to allow venipuncture in this site under voluntary stimulus control. After application of proper aseptic technique, blood can be collected with 19–23-gauge and 2–4-cm (0.75–1.5-inch) needles, depending on the size of the subject. Intravascular antibiotics and fluids can be administered into this site, but the size and microanatomy of the vessel, the accuracy of the needle stick, and the dynamic nature of the peripheral blood vessels can limit successful administration. Blood from this site (Fig. 43.5) is most commonly a mix of arterial and venous blood (venous admixture) and rarely purely arterial or venous.

Peduncle PAVR

This venipuncture site is located on the ventral aspect of the terminal vertebral bodies. The landmarks for injection are the ventral peduncle ridge, immediately proximal to the confluence of the right and left fluke PAVR. Venipuncture at this site is best performed with needles longer and larger than those used for fluke vessel venipuncture in the same animal. Needles 18–21-gauge, 3–5-cm (1.5–2-inch) and larger may be required. The site may be accessed from voluntary fluke presentations or in animals out of the water for examinations and procedures (Fig. 43.5). The larger diameter of the artery at this site allows for rapid collection of large volumes of arterial, or more likely venous, admixed blood. With proper aseptic technique, the site has been successfully used for repeated phlebotomy to treat iron overload in bottlenose dolphins (Johnson et al. 2009). The larger vessels also make the site convenient for intravascular injection of select appropriately buffered substances. With proper positioning and a degree of restraint of the fluke, the needle may be left indwelling in this site during longer procedures for continuous infusion of fluids, as well as repeat blood samples for venous admixture blood gas analysis. Arterial blood pressure has been measured at this site (Ridgway & McCormick 1971; Ridgway et al. 1974), however, needle placement and movement must be carefully monitored because shifts may lead to values that are not necessarily reflective of the patient's status. Some individuals have expressed anxiety for any venipuncture at this site out of concern for a possible vascular accident leading to severe fluke ischemic injury and sloughing. As such, even those comfortable with venipuncture at this site have yet to pursue catheterization of the artery for accurate blood pressure monitoring and arterial blood collection for blood gas analysis, though clearly feasible.

Dorsal Fin PAVR

Although a challenging site for venipuncture in smaller cetaceans, this location is useful for larger species such as killer whales (Fig. 43.5). For dolphins, it is usually reserved for fractious animals that will not allow access to the flukes or peduncle. It is also a second site for blood collection during medical procedures. The dorsal fin PAVR has all of the same anatomical challenges as the fluke PAVR (Rommel & Lowenstine 2001). When considering IV drug administration, it is important to remember blood from this site flows directly to a rete around the animal's gonads. The authors usually access this site with needles similar to those used for fluke PAVR venipuncture.

Hemal Arch/Caudal Vascular Bundle

The caudal vascular bundle runs longitudinally along the ventral midline of the caudal vertebral bodies within an arch formed by the chevron bones. In an adult bottlenose dolphin, a 9-cm (3.5-inch) spinal needle is advanced transversely into the ventral intervertebral space, ventral and parallel to the lateral processes of the caudal vertebral bodies in the mid- to caudal peduncle region. The caudal vascular bundle is a low-pressure, mostly venous system. This area has been cannulated (Van Bonn et al. 1996) and, when accessed, it appeared appropriate for IV fluid and drug administration. However, this is a venous rete and the rate of absorption drugs and fluids may be more variable and delayed compared with administration into other sites.

Common Brachiocephalic Vein

The common brachiocephalic vein (CBV) is a true vein that is not part of the PAVR (Fig. 43.6) (Ridgway et al. 2006b; Dold et al. 2005). It is therefore a site to collect purely venous blood samples and to measure venous blood pressure when the catheter is advanced more centrally. It is large enough to allow catheterization, and indwelling catheters in this site have historically assisted in anesthetic monitoring and support capabilities. Drugs and fluids delivered into the CBV would have more predictable and rapid distribution and effect than those injected into peripheral sites that are part of PAVRs. However, accessing the brachiocephalic vein is challenging. In bottlenose dolphins, it lies 10–12 cm deep under skin, blubber, and muscle, and runs in a transverse plane. The actual site for access is large: 2–3 cm wide and 2 cm thick. Slight misdirection at the skin, however, can translate into significant misdirection of the long needles at the level of the vessel. The transverse orientation of the vessel also makes catheterization difficult. As such, there have been significant mishaps in application of this method, making it a less clinically useful technique currently.

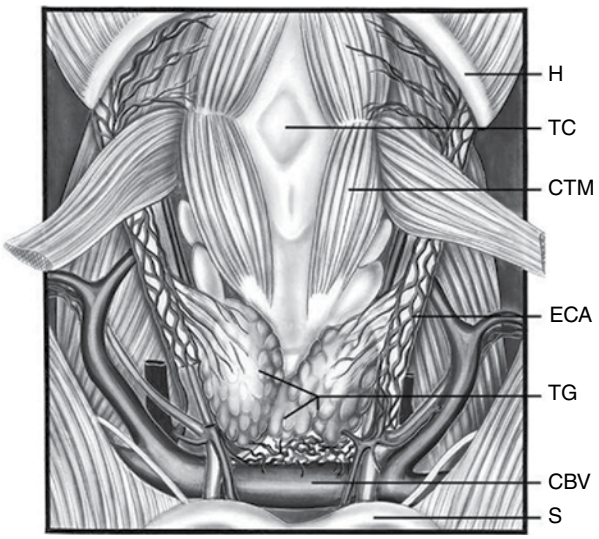


Figure 43.6 Drawing from a dissection of the ventral neck of a bottlenose dolphin. H, hyoid; TC, thyroid cartilage; CTM, cricothyroid muscle; ECA, external carotid artery; TG, thyroid gland; CBV, common brachiocephalic vein; S, sternum. Note that the ECA is covered by a meshwork of veins. Drawing by Barbara Stolen Irvine. Reproduced with permission from Ridgway (1971).

The common brachiocephalic vein should be approached with ultrasound guidance for safety (Ridgway et al. 2006b). Catheter placement benefits from two people working together; one person guides the ultrasound probe and holds the image steady, while the other person performs the venipuncture. For classical catheterization, a 14-gauge, 16-cm (6-inch) needle would be passed into the vein, and a 60-cm polyurethane catheter fed through it to a depth of approximately 25 cm. For short-term access (IV drugs, bolus fluids), only a needle is used and no catheter. The stylet from an equine 16-gauge, 14-cm (5.5-inch) radiopaque catheter (Abbocath Hospira, Inc., Abbocath T 16-g × 5.25-inch long, product code 390C54300) is a sharp disposable needle currently available for such use. The animal is positioned in lateral recumbency for the procedure. We have evidence placing the animal in right lateral recumbency is more anatomically appropriate for catheterization. Right lateral recumbency, along with the natural tendency of the phlebotomist to orient the needle tip toward the floor, encourages the catheter to feed toward the heart (with left to right flow in the vessel). In left lateral recumbency, the catheter tends to feed toward the venous return from the rete (against flow). Successful catheterization, however, can also be performed with the animal in left lateral recumbency.

Lateral Subcutaneous Caudal Vein or Lateral Caudal Subcutaneous Vein

The lateral caudal subcutaneous vein (LCSV) is also historically referred to as the caudal ventral peduncle, caudal superficial peduncle, or superficial caudal peduncle and superficial lateral peduncle vein. First proposed in 1997 and attempted in 1998 by Stetter (Stetter et al. 1997; Dover et al. 1999), catheterization of the LCSV was not perfected until 2011 (Ivančić et al. 2015). LCSV is now the first choice for true venous access in the dolphin and is a routine procedure performed in sternal recumbency with a slight lateral tilt to expose the area of interest (Fig. 43.5). The authors have had the greatest success accessing the LCSV with ultrasound guidance using a linear transducer (10–5 MHz) and single lumen, 4–5 French (F) micro-introducer catheter kits (Innovative Veterinary Medicine, Inc micro-introducer kits 4F (KIT-076-00) and 5F (KIT-076-01) × 10 cm Stiffen (018 × 40 cm NiTi/SSCoil, 21-gauge × 7 cm) standard echogenic needle using a modified Seldinger method (Seldinger 1953). When necessary, longer peripherally inserted central catheters (PICCs) with one or more lumen can be placed. In a transverse ultrasound view, the ventral branch of the LCSV lies just dorsolateral to the *levator ani m.* (*pubocaudalis m.*) and ventromedial to the *hypaxialis lumborum m.* (*supracoccygeus m.*). In the longitudinal view, the vein travels caudal to cranial under the blubber, getting larger and diving deeper as it travels craniad. Further caudad, the vessel diameter becomes smaller and the subdermal sheath connective tissue thickens, making catheter placement more difficult. Stiffened micro-introducer dilator cannula are preferred for this method of placement through this dense connective tissue. For patient comfort, sedation and local anesthesia are applied prior to catheter placement. Warm wet towels and local anesthetic block placed in advance, as well as pressure cranial to the site of venipuncture, may help increase the diameter of the vessel and facilitate cannulation.

Median Artery

It is feasible to catheterize many arteries of the cetacean PAVR. Used for collection of blood in early studies (Medway & Geraci 1964), the median artery of the pectoral flipper of dolphins is now a commonly acceptable location for cannulation (Ivančić et al. 2014). Well illustrated by Braun (1905), the median artery sits snuggly between the radius and ulna, slightly palmar, under the dense connective tissue of the flipper (Fig. 43.5). Doppler flow probes and ultrasound can facilitate identification and cannulation of the median artery, but the location is also digitally palpable. The authors have had the greatest success catheterizing the median artery with ultrasound guidance using a linear transducer (10–5 MHz) and 4–5F micro-introducer catheter kits utilizing a modified Seldinger (1953) method similar to those used for venous access. In a transverse ultrasound view across the palmar surface of the flipper, the artery sits slightly superficial to the notch formed by the coming together of the radius and ulna. To maintain patency of the cannula, 2–5 unit/mL heparinized normal saline is used to regularly flush the catheter. Modern disposable blood pressure transducers with integrated, pressurized flush mechanisms can be used to simplify maintenance of the catheter. The transducer is zeroed to the level of the right atrium (physiologic zero) and blood pressures are continuously monitored.

Preanesthetic Sedation and Anesthetic Induction

Cetaceans have been mechanically restrained and intubated without sedation for inhalant anesthetic delivery (Ridgway & McCormick 1967), however a balanced anesthetic approach may be more appropriate. Balanced anesthesia involves the use of a combination of drugs, with each drug delivered in an amount sufficient to produce the desired effect while keeping undesirable effects to a minimum. The practitioner may induce anesthesia using conscious intubation under behavioral control, but it may be wise to supplement the anesthetic event with analgesic agents, muscle relaxants, or other appropriate inhalation anesthetic sparing drugs once the subject is intubated and monitored. More often now, dolphins are induced to anesthesia by rapid sequence induction using intravenous anesthetic agents, such as propofol, balanced with preanesthetic agents, such as midazolam and meperidine or butorphanol.

Drugs that have been reported or used by the authors for sedation and local or general anesthesia of several cetacean species are presented in Tables 43.1 and 43.2. The authors wish to caution, in most instances, that the number of animals exposed to these drugs is small and the potential for unpredictable or as yet unrevealed drug reactions is possible if not probable. Also, to provide perspective, we estimate that general anesthesia in cetaceans has been performed at most 100 times. However, cetaceans have been safely, and in some instances repeatedly, sedated or anesthetized with the listed drugs. The benzodiazepines midazolam and diazepam, and the opioids butorphanol and meperidine have been most often used for sedation of cetaceans.

Anticholinergics

Historically, atropine 0.02 mg/kg intramuscular (IM) was routinely given as a preanesthetic agent to dolphins undergoing anesthesia in an attempt to prophylactically prevent

Table 43.1 Thirty-four anesthesia events involving 27 different individual small cetaceans. Bottlenose dolphin Tt = *Tursiops truncatus*; Ttg = *Tursiops truncatus gilli*, and Tta = *Tursiops truncatus aduncus*. Common dolphin Dc = *Delphinus capensis*. Pacific white-sided dolphin Lo = *Lagenorhynchus obliqidens*. Cumulative dosages of the drugs: AT = atropine; ATRA = atracurium; B = butorphanol; D = diazepam; E = edrophonium; F = flumazenil; Iso = isoflurane; Mp = meperidine; T = tramadol; M = midazolam; Nalx = Naloxone; Nalt = naltrexone; ; propofol = P; Sevo = sevoflurane. PO = per os; IM = intramuscular; IV = intravenous. FeAgent = fraction expired inhalation anesthetic. Anesthesia duration was documented as the time from injection of IV induction agent until the vaporizer was turned off and the anesthetic circuit was flushed with oxygen to minimize inhalation anesthetic for recovery phase to begin. CMV = conventional controlled mechanical ventilation; AAV = apneustic anesthesia ventilation; PIP = peak inspiratory pressure; P_{high} = plateau pressure or pressure high; LSCV = lateral subcutaneous caudal vein; CP = caudal peduncle vein; MAP = mean arterial blood pressure (Note: parenthesis indicate MAP in semi-conscious and spontaneously ventilating subject during recovery phase with arterial catheter maintained until extubation). Time of detection of hypotension generally coincided with the time of placement of the arterial catheter. Reversal agent dosages were total dosages that include repeat dosing. Temp = temperature as measured at end of anesthesia. Extubation = time to extubation was measured from the point the anesthetic circuit was initially flushed with oxygen to minimize inspired inhalation anesthetic until extubation. (Reproduced with permission from Bailey J. Innovative Veterinary Medicine Inc.: 101 Marketside AVE, STE 404-402, Ponte Vedra, FL 32081-1541, 2021).

	Species	Date	Sex	Age (yrs)	Wt (kg)	Procedure	Premed (mg/kg)	Induction (mg/kg)	Inhalant	FeAgent (%) Range	Position	Duration Anesth (min)	Heart Rate Range	Resp Rate (br/min) Range	PIP or Phigh (cmH20)	Vein	Artery	MAP (mmHg) Range	Reversal Agents (mg/kg)	Temp (C)	Extubation Time (min)
1	***Tt***	1998	F	21	150	Laproscopic Renal Biopsy	D0.27 PO AT 0.02 IM	P 3.5 IV	Iso	0.6–1.1	Right Lateral Oblique	107	87–102	4 to 6 CMV	20–30	CP	none	n/a	F 0.001 IV F 0.002 IM	35.4	52 plus reintubate for 21 min
2	***Tt***	2011	M	31	179	Laproscopic ureteroscopy	M0.08 IM AT 0.02 IM	P 5.6 IV	Sevo	1.7–2.1	Left Lateral	276	58–95	8 to 13 CMV	20–30	CP LSCV	none	n/a	n/a	n/a	Humane euthanasia
3	***Tt cross Ttg***	2013	F	7.5	180	Scleral Mass OS	D0.26 PO	M0.06 IV P 5.48 IV	Sevo	2.0–2.8	Right Lateral	54	64–110	4 to 7 CMV	20–27	CP	none	n/a	F 0.025 IV F 0.025 IM	35.7	62
		2016		10	185	Scleral Mass OS	B 0.108 IM M 0.054 IM M 0.027 IM	M 0.027 IV P 2.4 IV ATRA0.1 IV; repeat 0.05 IV	Sevo	1.0–1.4	Right Lateral	109	77–115	4 to 5 CMV	25–30	LSCV	none	n/a	F 0.032 IV E 0.5 IV	96.5	26
4	***Tt***	2013	F	39	175	Lythotrypsy	M0.07 IM	M 0.06 IV P 3.6 IV	Sevo	2.1–2.3	Left Lateral	96	90–99	8 to 10 CMV	25–30	CP LSCV	Median	57–117 (132–155)	F 0.024 IV	34.7	124
5	***Tt***	2014	F	29	174	Cervical Abscess	M0.07 IM Mp 0.5 IM	M 0.04 IV P 2.0 IV	Sevo	1.6–2.7	Dorsal	132	105–121	6 to 8 CMV	25–30	LSCV	Median	44–55 (57–131)	F 0.04 IV Nalx 0.02 IV Nalt 0.05 IV	35.6	97
6	***Tt***	2015	F	24	206	Parital Glossectomy	D0.24 PO M0.05 IM	M 0.024 IV P 4.0 IV	Sevo	1.7–2.3	Sternal	62	57–72	5 to 9 CMV	18–27	CP LSCV	Median	63–81	F 0.017 IV F 0.01 IM	34.3	20 plus re intubate for 47 min
7	***Tt cross Dc***	2015	F	21	130	Parital Glossectomy	D0.23 PO	M 0.038 IV P 3.1 IV	Sevo	2.2–2.7	Sternal	54	58–112	4 to 6 CMV	20–25	CP LSCV	none	n/a	F 0.023 IV	35.7	24

(*Continued*)

Table 43.1 (Continued)

	Species	Date	Sex	Age (yrs)	Wt (kg)	Procedure	Premed (mg/kg)	Induction (mg/kg)	Inhalant	FeAgent (%) Range	Position	Duration Anesth (min)	Heart Rate Range	Resp Rate (br/min) Range	PIP or Phigh (cmH20)	Vein	Artery	MAP (mmHg) Range	Reversal Agents (mg/kg)	Temp (C)	Extubation Time (min)
8	***Tt***	2015	M	36	263	Oral Surgery	M0.08 IM	M 0.02 IV P 3.8 IV	Sevo	1.5–2.1	Sternal	120	82–105	4 to 7 CMV	22–30	LSCV	Median	31–67 (94–136)	F 0.01 IV	35	37
		2016		37	241	Oral Surgery Stem Cell Tx	M0.08 IM	M 0.04 IV P 4.3 IV Mp 0.4 IM	Sevo	1.4–2.5	Left Lateral	110	83–99	4 to 8 CMV	25–31	LSCV	Median	29–75 (60–125)	F 0.02 IV Nalx 0.01 IV Nalt 0.05 IV	34.9	66
		2017		38	234	Oral Surgery	M0.08 IM	M 0.03 IV P 5.5 IV Mp 0.25 IM	Sevo	1.4–2.0	Left Lateral	119	84–104	6 to 10 CMV	28–35	LSCV	Median	73–84 (111–141)	F 0.012 IM/IV Naît 0.05 IV	35	50
9	***Lo***	2015	F	22	125	Exploratory Laparotomy	M0.1 IM	M 0.06 IV P 4.8 IV B0.04 IV	Sevo	1.6–2.2	Right Lateral	140	86–128	6 to 10 CMV	25–30	CPLSCV	none	n/a	F 0.023 IV	36	51 plus re intubate 3X for total 50 more min
10	***Tt***	2015	F	15	180	Corneal Mass OS	D0.25 PO M0.08 IM	P 2.78 IV ATRA 0.1 IV; repeat 0.05 IV	Sevo	1.6–2.6	Right Lateral	61	65–98	3 to 6 CMV	-25–30	CP	Median	67–91 (96–181)	F 0.011 IV F 0.003 IV E 0.5 IV	35.5	12
		2016		16	190	Corneal Mass OS	D0.21 PO M 0.05 IM	M 0.026 IV P 2.9 IV ATRA 0.1 IV	Sevo	1.8–2.8	Right Lateral	67	52–89	3 to 6 CMV	25–30	LSCV	none	n/a	F 0.013 IV F 0.013 IV E 0.53 IV	34.7	26 plus re intubate for 34 more min
11	***Tt***	2016	M	17	184.5	Corneoscleral Mass OD	D0.22 PO M 0.054 IM	M 0.027 IV P 2.87 IV ATRA 0.1 IV	Sevo	2.0–2.4	Left Lateral	78	65–83	4 to 5 CMV	~25–30	LSCV	none	n/a	F 0.01 IV E 0.5 IV	34.9	68
12	***Tt***	2016	M	18	220.5	Mandibular Sequestrum	D0.18 PO M0.05 IM	M 0.023 IV P 1.5 IV	Sevo	1.2–2.0	Sternal	60	83–98	4 to 8 CMV	30	LSCV	Median	25–35	F 0.026 IV Nalx 0.02 IV Naît	34	60 plus re intubate for 3 more min

13	***Tt***	2017	M	15.5	195	Bronchoscopy	D0.1 PO M0.08 IM	P 4.0 IV Mp 0.25 IM	Sevo	1.3–2.2	Sternal	70	101–114	6 to 8 CMV	28–32	LSCV	Median	50–64 (70–94)	F 0.15 IV Nalx 0.01 IV Natx 0.05 IV	36	50	
		2019		17	202	Ophthalmologic surgery	D 0.2 PO M0.07 IM Mp 0.25	P 2.23 IV M0.03 IV Cis-ATRA 0.1 IV	Sevo	1.4–2.0	Right Lateral	40	94–109	6 to 8 CMV	28	LSCV	Median	(84–87)	F 0.01 IV Nalx 0.01 IV Natx 0.05 IV	36.7	27	
14	***Tt***	2017	M	45	215.5	Parital Glossectomy & Lymph node	D0.23 PO M0.08 IM	P4.0	Sevo	1.0–1.8	Sternal	155	85–118	6 to 8 CMV	25–30	LSCV	Median	44–87 (111–112)	F 0.019 IV	36.2	58	
15	***Tt***	2017	F	35	160.5	Laparoscopic Exploratory	M0.09 IM	Awake Intubationdue to apneaCis-ATRA0.1 IV	Sevo	1.1–1.9	Dorsal oblique	242	84–104	6 to 8 CMV	28–35	LSCV	Median	30–114	F 0.01 IV	35.8	Humane euthanasia	
16	***Tt***	2018	F	35	245	Parital Glossectomy	D0.25 PO M0.05 IM	M 0.02 IV P 2.0 IV	Sevo	. . .	Sternal	90	75–95	5 to 9 CMV AAV for recovery onlv	~25–30	CP LSCV	None	. . .	F 0.02 IV	35.4	53 plus reintubate for 10 more min	
17	***Tt***	2018	F	37	256	Parital Glossectomy	D 0.2 PO T 1.0 PO	M0.02 IV P 3.05 IV	Sevo	1.4–2.1	Sternal	112	82–111	4 to 5 CMV	28–30	LSCV	Median	66–86 (73–150)	F 0.03 IV Nalx 0.023 IV	34.8	41	
		2019		38	243	Corneal Repair OS	D0.25 PO M0.14 IM	P 1.0 IV ATRA 0.3 IV	Sevo	1.2–2.1	Right Lateral	79	80–95	6 to 7 CMV	~25–30	CP LSCV	None	. . .	F0.037 IV	35.3	27 plus reintubate for 22 moremin	
18	***Ttcross Ttg***	2018	F	27	225	Parital Glossectomy	D0.25 PO M0.05 IM	M 0.02 IV P 1.15 IV AT 0.02 IM	Sevo	. . .	Sternal	115	77–98	6 to 8 CMV	~25–30	CP	Median	98–120 (110–130)	F 0.022 IV	36.3	34	
19	***Tt***	2018	F	20	190	Parital Glossectomy	D0.25 PO M0.05 IM	M 0.02 IV P 2.1 IV	Sevo	. . .	Sternal	61	73–95	5 to 6 CMV	~25–30	LSCV	Median	33–65 (62–75)	F0.025 IV	35.5	38	
20	***Tt***	2018	F	5	106	CSF Tap	D0.28 PO M0.05 IM	M 0.02 IV P 2.0 IV	Sevo	1.4–2.2	Right Lateral	67	114–125	5 to 6 AAV	~25–30	LSCV	Median	93–122 (110–202)	F 0.02 IM	36.2	75 plus reintubate for 22 more min and again for 11 more min	

(*Continued*)

Table 43.1 (Continued)

	Species	Date	Sex	Age (yrs)	Wt (kg)	Procedure	Premed (mg/kg)	Induction (mg/kg)	Inhalant	FeAgent (%) Range	Position	Duration Anesth (min)	Heart Rate Range	Resp Rate (br/min) Range	PIP or Phigh (cmH20)	Vein	Artery	MAP (mmHg) Range	Reversal Agents (mg/kg)	Temp (C)	Extubation Time (min)
21	***Tta***	2019	M	49	140	Lymph node removal	M0.20 IM	M 0.035 IV P 1.5 IV	Sevo	1.3–2.6	Right Lateral	150	77–110	5 to 8 CMV	~25–30	LSCV	Median	24–53	F 0.021 IV Nalx 0.04 IV	35.6	45 plus reintubate for 15 more min
22	***Tta***	2019	M	12	117	Gastric foreign body	M0.10 IM	M 0.042 IV P 2.141V ATRA 0.2 IV	Sevo	1.4–3.0	Sternal	96	95–108	6 to 7 CMV	~25–30	LSCV	Median	76–119 (53–130)	F 0.016 IV NalT0.2 IV NaIX 0.017 IV	35.9	65
23	***Tt***	2019	F	46	210	Parital Glossectomy	D0.24 PO M0.02 IM	M 0.02 IV P 2.95 IV	Sevo	0.8–1.4	Sternal	68	84–101	4 to 6 AAV	23–34	LSCV	. . .	. . .	F 0.03 IV	35.5	214
24	***Tt***	2020	F	38	187.5	Oral Surgery & eye exam	M0.08 IM Mp0.1 IM	M 0.02 IV P 2.29 IV	Sevo	1.4–2.3	Sternal	216	78–86	6 to 7 CMV 4 to 6 AAV	23–29 19–26	LSCV	Median	73–96 (86–149)	F 0.015 IV Nalx 0.02	35.2	107
25	***Tt***	2020	M	8	196	Bronchoscopic dilation	D0.2 PO M0.08 IM Mp0.1 IM	M 0.03 IV P 3.0 IV	Sevo in 30–35% O_2	1.81–2.36	Sternal	227	85–109	4 to 8 AAV	23–35	LSCV	Median	62–84 (105–169)	F 0.02 IV Nalx 0.02 IV	35.4	18
26	***Tt***	2020	M	22	171	Eye surgery	D0.1 PO M0.09 IM Mp 0.2 IM	M 0.02 IV P 3.0 IV	Sevo	1.3–1.9	Right Lateral	90	96–120	5 to 6 CMV 6 AAV	19–24 20–21	LSCV	Median	60–115	F 0.018 IV Nalx 0.03 IV	34.8	21
27	***Tt***	2020	M	15.5	181	Parital Glossectomy	D0.25 PO M0.05 IM	M 0.02 IV P 1.65 IV	Sevo	1.4–1.8	Sternal	71	93–101	6 to 8 CMV 6 AAV	~25–30	CP	Median	39–42 (42–54)	F 0.022 IV	35.2	200

Table 43.2 Chemical sedative and anesthetic agents used in bottlenose dolphins (*Tursiops truncatus*).

Category	Drug Name	Dosage	Route	Comments	Reference
Premedication	Atropine	0.02 mg/kg	IM		Ridgway & McCormick (1971)
Sedatives	Diazepam	0.1–0.2 mg/kg	IM		Reidarson (2003)
		0.25–1.0 mg/kg	PO	Larger doses reserved for research or for animals that may have become refractory to smaller oral doses of diazepam Keep flumazenil available for reversal	Ridgway (pers. obs.)
		0.26–0.36 mg/kg	PO		Schroeder et al. (1986)
	Midazolam	0.05–0.15 mg/kg	IM	Provides a good plane of sedation lasting about 45–60 minutes **Caution when using in species other than *Tursiops truncatus***	McBain & Walsh (pers comm.); Ridgway & Dold (pers. obs.)
	Flumazenil	0.005 mg/kg	IM, PO, IV, sublingual	Can be given at equal volume of midazolam when midazolam is 5 mg/mL and flumazenil is 0.5 mg/mL Usually titrate dose to effect	McBain & Walsh (pers. comm.); Ridgway & Dold (pers. obs.)
	Butorphanol	0.05–0.15 mg/kg	IM	Provides sedation adequate for bronchoscopy and other minor procedures Possible drug reactions seen when combined with bronchodilators	Chittick et al. (2006)
	Meperidine	0.1–2.0 mg/kg	IM	Given in combination with midazolam can produce a deep level of sedation that is reversible	Joseph & Cornell (1988); Reidarson (2003); Ridgway (1965)
	Tramadol	0.15–0.2 mg/kg	PO	Given in combination with diazepam (0.15 mg/kg) provides sedation adequate for tooth extraction	Schmitt (pers. comm.)
	[Naloxone]	5–10 mg/kg	IM/IV	Butorphanol and meperidine reversal	Reidarson (2003)
	[Naltrexone]	0.005 mg/kg	IM/IV	Opiod reversal	Chittick et al. (2006)
Induction agents	Ketamine	1.75 mg/kg	IM	Single case only	Reidarson (2003)
	Medetomidine	10–40 mg/kg	IM/IV	Abolishes sinus arrhythmia and causes respiratory depression, decreased central venous pressure	Reidarson (2003); Ridgway & Dold (pers. obs.)
	[Atapamazole]	50–200 mg/kg	IM/IV	Equal volume of medetomidine for reversal; medetomidine is 1 mg/mL and atapamazole is 5 mg/mL	Ridgway & Dold (pers. obs.)
	Thiopental	10–15 mg/kg	IM	Requires additional inhalant anesthesia for full induction	Ridgway & McCormick (1971)
	Propofol	0.5–3.5 mg/kg	IV	Onset and duration of effect are injection-site dependent	Linnehan & MacMillan (1991); Ridgway & Dold (pers. obs.); Van Bonn (pers. comm.)
Inhalational agents	Isoflurane	0.5–2.0%	IH	Higher dose for induction, lower maintenance dose	Linnehan & MacMillan (1991); Ridgway & Van Bonn (pers. obs., 1991–2005); Dover et al. (1999)
	Nitrous oxide	70%	IH	Light anesthesia	Nagel et al. (1964)

IH, Inhalation; IM, intramuscular; IV, intravenous; PO, per os.

bradycardia during anesthesia (Howard et al. 2006; Bailey 2016; Ridgway et al. 1974; Reidarson 2003). However, it may be better to individualize treatment and take into account the procedure being performed, the anesthetic and other medications used, and the historical individual response. In general, atropine at appropriate dosages is minimally toxic, but it has not been without consequence in cetaceans. Repetitive doses of atropine (0.01 mg/kg IM) caused symptoms suggestive of atropine toxicity in one pygmy sperm whale (Manire et al. 2002). Interestingly, unihemispheric EEG effects are inducible pharmacologically, and atropine IM was found to cause profound cerebral signal asymmetry in one subject (Howard et al. 2006). In addition, preanesthetic fasting and anesthesia both tend to promote development of ileus postoperatively. Atropine may add to the potential for this postanesthetic complication. As such, the general response has shifted to only giving atropine if required, not routinely, and first eliminating possible causes of bradycardia, such as excessively deep anesthesia, prior to use of atropine (Brock 2001). However, there are still situations when atropine or other anticholinergic agents would be given prophylactically, such as prior to anticholinesterase use or procedures strongly triggering vagal reflexes such as the oculocardiac reflex associated with retraction of the eye during enucleation procedures.

Benzodiazepines

Diazepam and midazolam are frequently administered for light sedation per os (PO) and parenterally, respectively. Diazepam (0.55–0.60 mg/kg PO) has been used to help trained dolphins remain still for 35–45-minute functional imaging scans such as positron emission tomography. Diazepam (0.5 mg/kg PO) combined with tramadol (0.5 mg/kg PO) results in an enhanced sedation, as well as providing some analgesia. This combination has been used successfully for tooth extractions in combination with local anesthesia in white whales (T. Schmitt, pers. comm., 2011). Midazolam (0.05–0.1 mg/kg IM or IV) is effective and generally safe in Atlantic bottlenose dolphins (*T. truncatus*). Caution has been advised by some when working with species other than Atlantic bottlenose dolphins as profound sedation resulting in respiratory and cardiac depression was witnessed in Pacific bottlenose dolphins (*T. truncatus gilli*) and Atlantic/Pacific hybrids (C. Smith, pers. comm., 2005). In the case of benzodiazepine overdose, flumazenil may be given via oral (Votey et al. 1991), intramuscular or intravascular routes depending on the urgency (Geller et al. 1988; White et al. 1989). Full reversal of midazolam requires 1 part flumazenil for every 13 parts of this benzodiazepine (Pawson 2008). Although irrelevant at these practical clinical dosages, some studies suggest flumazanil may have intrinsic benzodiazepine partial agonist or inverse agonist activity in certain animal models. For this reason, repeat and copious dosing of flumazenil should not be considered limitless.

Opioids

Historically opioids were not recommended for dolphin sedation and anesthesia because, at least with morphine, excitement was observed (Ridgway 1965). However, meperidine did gain favor for use in dolphins in the not-so-distant past (Joseph & Cornell 1988). For a time, and in some species, the use of meperidine was supplanted by the use of butorphanol, and several marine mammal clinicians developed a comfort level with butorphanol as a sedative that provided some analgesia, safe light sedation, and was easily reversible with naloxone or naltrexone (Chittick et al. 2006; Walsh et al. 2006). Meperidine, however, is currently being revisited for perioperative use as a full agonist opioid analgesic to better balance the anesthetic drug approach for major surgery (Bailey 2013b). Unfortunately, the respiratory depressive nature of opioids can necessitate partial or full reversal for return of optimal and timely spontaneous breathing by the patient in the recovery period after anesthesia.

Alpha-2 Agonists

Medetomidine has been used in rare instances in dolphins, but little or no physiologic data is published (Reidarson 2003). One dolphin undergoing monitoring during medical procedures (Dold et al. 2005) was first given diazepam PO prior to 0.01 mg/kg medetomidine IV, but only monitored for 10 minutes prior to reversal with 0.05 mg/kg atipamezole IV. With a CBV catheter already in place, central venous pressure (CVP) was noted to decrease, as did the respiratory rate, subjective quality of ventilation, and venous saturation of oxygen, while the end-tidal CO_2 increased. Alpha-2 adrenergic agonists, such as medetomidine and dexmedetomidine, will provide profound sedation, analgesia, and muscle relaxation, and are reversible. Unfortunately, they also cause bradycardia, interfere with contractility of the heart, and cause peripheral vasoconstriction leading to increased afterload. The reversibility of alpha-2 agonists is enticing, however, sudden reversal and reduction in afterload could lead to cardiovascular collapse in patients with limited cardiovascular reserve. For this reason, it is considered unwise to introduce the reversal agent (atipamezole) IV. The practitioner will need to carefully weigh the risks and benefits of this drug choice.

Parenteral Anesthetics

Thiopental (pentothal) and propofol have been used for induction of general anesthesia. Over this past decade, propofol IV, given slowly over 3–5 minutes has been the method of anesthetic induction. Supplemental midazolam given concurrently with propofol helps to reduce the muscle fasciculations induced by propofol and reduce the total propofol dose. Reidarson reported the use of ketamine and medetomidine for the successful intubation and maintenance of anesthesia in one animal (Reidarson 2003). The authors have limited experience with ketamine in cetaceans, but consider it worthy of further investigation. As an N-methyl-D-aspartate (NMDA) glutamate receptor antagonist, ketamine provides an alternative method of pain management and contributes to a balanced anesthetic and analgesic approach. In addition, alfaxalone is worthy of examination for induction of anesthesia of cetaceans, although the only advantage to current preparations of this drug over propofol is the ability to deliver alfaxalone IM.

Inhalant Anesthetics

Anesthesia of dolphins has been maintained with the inhalation anesthetics halothane (Ridgway & McCormick 1967; Ridgway 1965; Medway et al. 1970), isoflurane (Linnehan & MacMillan 1991; Dover et al. 1999; Reidarson 2003), and more recently sevoflurane (Bailey 2016) in oxygen. Sevoflurane is currently the inhalational anesthetic of choice following induction of anesthesia by propofol IV, but isoflurane is an acceptable option as well. Both isoflurane and sevoflurane are low-solubility agents with most of the drug being eliminated by exhalation. The amount of these inhalation anesthetic agents needed to have 50% of animals show no response to noxious stimuli (Minimum alveolar concentration) has not yet been determined, so comparison of equipotent concentrations to other species is imprecise. However, since the effect of inhalation anesthetic agents is well preserved over the wide variety of mammalian species tested, the amount of inhalation anesthetic for dolphins will not differ much from other mammalian species. The MAC can be estimated at 1.3% isoflurane and 2.3% sevoflurane. It requires 1.2 to 1.5 times the MAC to assure the majority of subjects do not respond to a surgical stimulus when inhalation anesthetic is used as the sole anesthetic drug. Addition of other drugs and hypothermia contributes to significant reductions in the required inhalation anesthetic for surgery. Based on cases over the past decade applying similar preanesthetic drug dosages, one will find the end-expired sevoflurane will need to be maintained at no lower than 1.8–2.0% to assure no gross purposeful movement to surgical stimulus of dolphins (Bailey 2021).

Neuromuscular Blocking Agents

Atracurium 0.1 mg/kg IV has been used to produce neuromuscular blockade in dolphins undergoing ophthalmologic procedures to properly relax and centralize the eye for surgery (Schmitt et al. 2014). Long ago it was reported that delphinids lack plasma cholinesterase (Nagel et al. 1964), and it was recommended the depolarizing neuromuscular blocker, succinylcholine, not be used in delphinids (Ridgway & McCormick 1967). Over time, false dogma developed suggesting this meant all neuromuscular blocking agents could not be used. Atracurium, which undergoes simple Hofmann degradation (elimination) based on body pH and temperature, has been successfully used for neuromuscular blockade in marine mammals including dolphins. Even though easily eliminated from cetaceans, any residual muscle weakness caused by atracurium can be antagonized by delivery of the anticholinesterase, edrophonium. Delivery of edrophonium should be done slowly, while still monitoring to avoid or detect bradycardia that may develop. Atropine can be given prior to the anticholinesterase to prevent bradycardia and may be considered mandatory for certain anticholinesterase drugs (e.g., neostigmine). The need for edrophonium can be assessed in part by use of nerve stimulators, but the method is not well defined for dolphins and sufficiently imprecise to fully clarify any residual paralysis. The new selective relaxant binding agent, suggammadex, a structurally unique cyclodextrin designed to selectively bind to the neuromuscular blocking agents rocuronium or vecuronium, will likely replace the use of atracurium and anticholinesterases in cetaceans in the near future.

Analgesia and Local Anesthesia

Postoperative pain can be minimized by analgesics if they are given before surgical manipulation. Preemptive analgesia means minimizing postoperative pain by preventing exorbitant nociceptive signal transmission to the central nervous system, thereby preventing establishment of central sensitization. The term preemptive analgesia may be misleading because simply providing nociceptive blockade before stimulation does not ensure complete blockade, nor is it enough to prevent sensitization. Postoperative pain is best managed by pre-, intra-, and postoperative analgesic agents. Peripheral nociceptors, sensory nerve inflow, and central nervous system structures must all be addressed. Analgesia can be provided by nonsteroidal anti-inflammatory agents, local anesthetics, alpha-2 adrenergic agonists, opioids, and ketamine administered orally, locally, epidurally, intrathecally, and parenterally, alone or in

Table 43.3 Analgesic drugs used in cetaceans.

Category	Drug Name	Species	Dosage	Route	Comments	Reference
Nonsteroidal anti-inflammatory drugs	Flunixin meglamine (banamine)	*Tursiops truncatus, Orcinus orca*	0.25–0.5 mg/kg SID	IM	Caution with use in cetaceans as gastric ulcers are common	McBain (pers. comm.)
	Carprofen	*Tursiops truncatus*	0.5 mg/kg SID	PO	Gastric ulceration seen	Schmitt (pers. comm.)
	Acetaminophen	*Tursiops truncatus, Orcinus orca*	3–5 mg/kg SID	PO	Monitor transaminases	Walsh (pers. comm.)
Opioids	Butorphanol	*Tursiops truncatus, Orcinus orca*	0.05–0.13 mg/kg	IM	Possible excitatiory repsponse seen in one dolphin.	Chittick et al. (2006)
	Tramadol	Multiple (bottlenose dolphin, common dolphin, rough tooth dolphin, spinner dolphin, spotted dolphin, and pygmy and dwarf sperm whales)	0.1–0.4 mg/kg BID	PO	Titrate up to least effective dose Produces good analgesia without change in appetite Drowsiness seen at 0.73 mg/kg (Can be used IM or IV as well)	Manire (pers. comm., 2006)

BID, twice a day; IM, intramuscular; IV, intravenous; PO, per os; SID, once a day.

combination. Central sensitization is related to inflammation from surgical manipulation. The use of minimally invasive surgical techniques where possible will minimize surgical manipulation, inflammation, and postoperative pain. Taken together, all of these maneuvers are perhaps better described as "preventive analgesia."

While there is little published data on anesthetic drugs used in cetaceans, there is even less for analgesics. The greatest challenges to cetacean pain management are the difficulty in effective assessment of pain, measurement of response to therapy, and assessment of potential drug reactions. Several marine mammal clinicians have encountered acute, negative side effects after the use of nonsteroidal anti-inflammatory drugs in cetaceans (J. Mcbain, pers. comm., 2005). With that caveat, Table 43.3 lists several analgesic and anti-inflammatory agents that have been used in cetaceans. Again, the clinician must consider this with caution as the number of animals exposed to these drugs is relatively small and there is the potential for as yet unidentified drug reactions.

Local Anesthesia

Lidocaine (xylocaine) 2% has frequently been used for infiltrative block in minor dental procedures and superficial cutaneous surgical procedures. Blocking the infra-alveolar nerve, a branch of the mandibular nerve, with lidocaine infiltration has also been effectively employed for dental procedures (Ridgway et al. 1975). Bupivacaine and long-lasting liposomal bupivacaine have also been used in bottlenose dolphins (Bailey 2021).

Endotracheal Intubation

Endotracheal intubation of adult bottlenose dolphins and larger odontocete species is usually performed by an oral approach to the larynx (Fig. 43.7). This can be accomplished when the animal is either awake (in an emergency situation) or following sedation or anesthetic induction. Large animal endotracheal tubes with inflatable high-volume, low-pressure cuffs (16–30 mm internal diameter) are appropriate for most adult bottlenose dolphins. Intubation usually requires multiple personnel in addition to those providing physical restraint: one or more people to hold the animal's mouth open with soft rolled towels and another to pass the endotracheal tube. The oral approach is performed blindly by palpation. Intubation requires manual removal of the larynx ("goosebeak") from the nasopharyngeal sphincter to orient it in a rostral direction. Once the tip of the larynx is positioned rostral, two fingers can be placed into the glottis and the endotracheal tube guided through the glottis into the short trachea. The trachea is very short in most odontocetes and there is a right-sided accessory bronchus (Green 1972) that precedes the carina. Care must be taken not to advance the endotracheal

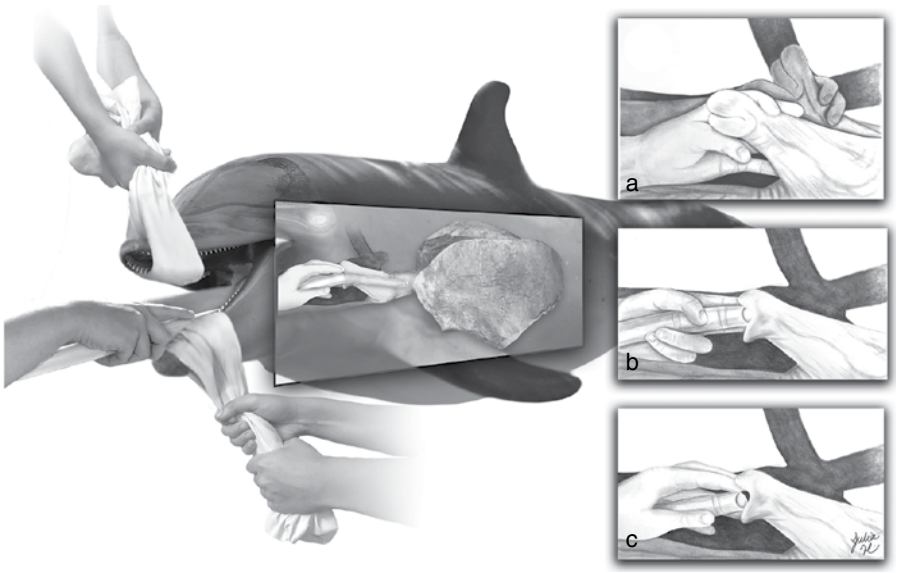


Figure 43.7 Example endotracheal intubation of a dolphin beached and positioned on appropriate foam padding in sternal recumbence as anesthesia is induced with intravenous medications. Blowhole response to touch and palpebral reflex are continuously monitored during the onset of anesthesia. The palpebral reflex diminishes, the blow hole relaxes and leaks, and the jaw tone relaxes progressively with the slow delivery of anesthetic drug intravenously. Were the intravenous drug to be delivered too quickly the patient could become apneic prior to adequate relaxation. Usually, two assistants then place two soft towels in the mouth over the mandible and maxilla to hold the mouth open for intubation. As the assistants hold the mouth open with towels, a hand of the anesthetist is inserted into the oropharynx. (a) The larynx, resembling the beak of a goose (goosebeak), is gently grasped and pulled from its location in the nasopharynx down into the oropharynx. (b) Usually, one or two fingers are inserted into the glottis to guide endotracheal tube placement, as the endotracheal tube is passed over the palm of the hand. The endotracheal tube is pushed forward and advanced by the second hand still outside the mouth. Using two fingers, the anesthetist can spread the fingers apart to open the larynx further. This method may be mandatory for conscious or inadequately anesthetized patients having excessive muscular control of the larynx. Unfortunately, this approach involves fingers that in part obstruct the larynx and thus may limit endotracheal tube size options. (c) Alternatively, in the adequately relaxed patient, a single digit can depress the epiglottis without entering the larynx. This author depresses the epiglottis with the fourth digit (ring finger) as the first, second, and third digits (thumb, index, and middle fingers, respectively) control the tip of the endotracheal tube to redirect and position the beveled edge of the tube and facilitate advancement into and through the larynx. Keeping fingers out of the larynx may allow for larger endotracheal tube placement. The endotracheal tube can be rotated to position the Murphy-eye of the tube to the right to minimize the likelihood of obstructing the accessory bronchus. An intubation endoscope can be used to facilitate intubation and ensure proper positioning, avoiding endobronchial intubation or obstructing the accessory bronchus. The X-ray view above demonstrates this positioning relative to the trachea and lungs. Reproduced with permission from Bailey (2020).

tube too far and block the separate right bronchus. Use of a flexible endoscope can facilitate intubation and ensure proper placement of the endotracheal tube in the trachea.

The oral approach to intubation may not be possible in some smaller odontocetes due to their small mouths and oropharynx. Intubation in these animals can be accomplished with a small endotracheal tube placed through the blowhole. This approach is more complicated than the oral approach due to redundant tissue and muscular folds used for vocalization and echolocation located between the larynx and the blowhole. The tube must be inserted through either the right or left nasal cavities. This limits the size of the tube that can be used. This approach to intubation is greatly facilitated by the use of a flexible endoscope for both visualization of the laryngeal opening and as a stylet to guide advancement of the endotracheal tube through the glottis. A possible adverse effect of prolonged intubation by this method is abnormal function of the blowhole, which would be problematic once the animal is returned to the water. To our knowledge, however, prolonged blowhole intubation has not yet been performed. Blowhole intubation was used in small dolphins (*Stenella styx* and *Delphinus delphis*) under experimental conditions at sea (Rieu & Gautheron 1968). Lidocaine (xylocaine 2%) was applied to the blowhole, nasal passages, and larynx using a small metal cannula prior to passing the uncuffed endotracheal tube to produce laryngeal anesthesia for conscious intubation.

Ventilation

The rhythm for breathing is generated by a complex neural network in the brainstem involving both excitatory and inhibitory circuits. The medulla oblongata is the lower half of the brainstem and contains the dorsal and ventral respiratory groups. In vivo and in vitro experiments point to a site in the rostral ventrolateral medulla, the preBötzinger complex (preBötC), as the sight of excitatory neurons driving inspiration (Smith et al. 1991) and generating the respiratory pattern (Kam et al. 2013). Expiratory activity is regulated primarily by the Bötzinger complex (BötC), containing mostly inhibitory neurons. Also located in the rostral ventrolateral medulla, the BötC has direct projections to and from the preBötC and from the RTN. Although the overall central respiratory network is actually far more complex than we will describe here, it should be clear that perturbations of the function of this network severely disrupt breathing.

It has long been recognized that exogenously administered opioids are potent depressants of respiration (Weil et al. 1975) and significantly alter the response to both hypercapnia and hypoxemia (Pattinson 2008). Opioids depress respiration by a number of mechanisms, and at multiple neuronal sites within the central respiratory network. This opioid-induced respiratory depression is due to activation of opioid μ receptors in the central respiratory network, and is reversible with μ receptor antagonists (Dahan et al. 2001). The end result of opioid exposure is decreased respiratory rate, tidal volume, and response to hypercapnia and hypoxemia, as well as loss of control of the upper airway (swallowing, prevention of aspiration). Interestingly, the respiratory depression of inhalation anesthetic agents is, at least in part, due to the influence of endogenous opioids (Dahan et al. 2001). Clearly, further investigation of the endogenous opioid systems (β-endorphins, enkephalins, and dynorphins) and opioid receptors (μ, δ, and κ) of cetaceans is warranted.

γ-aminobutyric acid (GABA) is the most abundant inhibitory neurotransmitter in the mammalian central nervous system. With the global abundance of $GABA_A$ receptors ($GABA_AR$) functioning throughout cortical and subcortical areas, the receptor's importance to memory, awareness, and consciousness becomes evident. We may generalize and say that most modern anesthetic agents enhance the function of the $GABA_AR$ and the inhibitory neurotransmitter, GABA, which is important to both anesthesia and emergence from anesthesia (Garcia et al. 2010; Kelz et al. 2019). $GABA_AR$ are also present in the preBötC inspiratory neurons and $GABA_AR$ stimulation can depress breathing, in part explaining the respiratory depressive effects of anesthetic drugs (Montandon et al. 2017).

Not all anesthetic agents, however, exert their effect though action on GABA. Ketamine does have some GABA effects, but primarily acts through the NMDA glutamate receptors. Clinically we find that ketamine, though prone to altering the respiratory pattern, infrequently interrupts spontaneous breathing at clinically relevant dosages. Unfortunately, ketamine was not approved for use in the United States until 1970, so it was not available to the early dolphin researchers, and still has not been thoroughly evaluated in cetaceans. In addition, ketamine enhances cortical cholinergic tone and may be associated with higher-frequency electroencephalographic activity that did not meet early investigators' needs for emulating sleep in dolphins. However, Ridgway has delivered ketamine at a subanesthetic dosage (2.76 mg/kg IM) by hand-thrown dart in one free-swimming dolphin and observed slow swimming with continued spontaneous respirations as the subject came to no longer resist restraint (S.H. Ridgway, pers. comm., 2020). Ketamine has also been used to induce anesthesia of dolphins on a few occasions (Reidarson 2003; Walsh et al. 2006). Given the ability of ketamine to modulate pain through NMDA glutamate receptor inhibition, and perhaps producing less respiratory depression than opioids, we should investigate the use of ketamine in cetaceans further.

The RTN of the central respiratory network contains pH-sensitive neurons which express the transcription factor paired-like homeobox 2b (Phox2b). Subjects with naturally occurring or induced mutations of Phox2b do not respond to CO_2 or the pH change induced by CO_2 (Marina et al. 2010). As such, these Phox2b-expressing neurons are fundamental to the generation and coordination of inspiration and expiration related to chemosensory control of breathing. Anesthetic drugs appear to change the folding of the Phox2B protein structure as well as its subcellular localization and aggregation, thus affecting this protein's ability to trigger breathing in response to rising blood carbon dioxide levels (Dubreuil et al. 2009; Coghlan et al. 2018). It has long been recognized that the inhalation anesthetic agents produce dose-dependent depression of respiration (Munson et al. 1966), with a shift in responsiveness to blood carbon dioxide levels as the anesthetic concentration rises. Phox2B has been identified in the medulla of a wide variety of species (Albersheim-Carter et al. 2016; Nomaksteinsky et al. 2013), but it is theorized here that the degree of Phox2B expression, the intrinsic functionality of Phox2B, or the degree of protein structural change and localization when exposed to anesthetic agents may vary by species, thus altering each species' responsiveness to blood carbon dioxide levels during equipotent anesthetic exposure.

To summarize, anesthetic agents depress respiration such that even subanesthetic dosages may cause

significant respiratory depression or apnea. The degree of respiratory depression at equipotent dosages of anesthetic appears to be species dependent. Indeed, spontaneous breathing does cease in dolphins with induction of anesthesia (Ridgway 2002; Mukhametov et al. 1976; Supin & Mukhametov 1978; Ridgway & McCormick 1971). As such, manual or mechanical ventilation is mandatory to general anesthesia of cetaceans. The normal conscious breathing pattern of dolphins involves rapid exhalation followed immediately by rapid inhalation and a breath hold or apneustic interval. Historically, investigators chose to attempt to mimic this normal respiratory pattern by applying an apneustic plateau during the ventilator cycle (Ridgway & McCormick, 1967, 1971; Nagel et al. 1964; Ridgway et al. 1974; Ridgway 1965).

Mechanical Ventilation

As others have recently commented, there is a paucity of information published on the respiratory mechanics of dolphins (Fahlman et al. 2011, 2015), particularly for those undergoing anesthesia. The elastic properties of excised lungs of marine mammals have been examined and the static inflation and deflation, pressure–volume curves measured. Inflation curves of excised lungs for the dolphins and sea lion studied were similar to those measured in the dog (Fahlman et al. 2011; Denison et al. 1972; Ponganis 2011). However, the deflation curves for the dolphins (Fahlman et al. 2011; Kooyman & Sinnett 1979) demonstrates greater recoil with smaller residual volumes than in terrestrial mammals (Fahlman et al. 2011). It has been suggested that the difference may be due to the greater abundance of elastic fibers and muscle in the supportive tissue of the lung and conducting airways in the dolphins, but possible biochemical differences must still be examined. Regulation of pulmonary surfactant production and the unique bronchiolar myoelastic sphincters (Simpson & Gardner 1972) of dolphins certainly require further investigation.

In general, there is a tendency for the lungs and chest wall of mammals to return to their original shape after being inflated mechanically, secondary to elastance. For air to flow into the lungs, the elastic resistance of the lungs and the chest wall must be overcome. This elastic impedance of the lungs and chest wall is additive. The inverse of elastance is compliance, or the ease with which the chest wall and lungs are distended. When chest wall and lungs are very stiff and resist expansion (low compliance), there is a greater tendency of the lungs and thorax to collapse, and extra work is necessary to deliver a normal volume of air to the apneic patient when using a mechanical ventilator.

Pulmonary morphology and mechanics of actively breathing dolphins have recently been reviewed (Piscitelli et al. 2013), further demonstrating the absence of data on the mechanics of ventilation for the unconscious dolphin. The extensive cartilaginous reinforcement of the airways from the trachea to the level of the alveolar sac (respiratory bronchioles absent) of dolphins should allow higher flow rates and faster gas exchange during the brief surface intervals of these animals (Ponganis 2011), but they contribute to the elastic recoil and alter total compliance in the anesthetized, mechanically ventilated animal. This overall elastic recoil is so profound that it is the sole driving force for expiration in the surfacing pilot whale (expiration is not active) (Olsen et al. 1969). Others have recently noted the chest wall of the dolphin appears to be much less compliant than that of terrestrial large animals (Fahlman et al. 2011; Moore et al. 2011). Although studies are needed to confirm these observations of low total compliance, the low compliance is clinically evident in anesthetized dolphins out of water. Specific respiratory mechanical data of unconscious dolphins, both beached and neutral buoyant, is needed. It is theorized here that total compliance will be significantly increased where cetaceans can be maintained near-neutral buoyant under anesthesia (Fig. 43.3).

Controlled mechanical ventilation (CMV) is the current mechanical ventilation method available on nearly all veterinary anesthesia ventilators and has often been treated as merely a convenience, taking the place of squeezing the anesthetic reservoir bag by hand to deliver a breath. However, new modes of ventilation, previously used only in intensive care units, are becoming available not only to mechanically ventilate the anesthetized patient, but to make the anesthesia ventilator a therapeutic tool. The conventional CVM mode begins the ventilator cycle at ambient pressure and elevates airway pressure to deliver an appropriate tidal volume (Fig. 43.8). Disadvantages of CMV include the need for application of relatively high peak inspiratory pressures with resultant higher mean intrathoracic pressure, reduced venous return and cardiac output, as well as poor distribution of inspired gas flow with subsequent ventilation-perfusion mismatch. The addition of extrinsic positive end-expiratory pressure to CMV in an attempt to reopen closed airways has been applied to large animal patients, but has proven minimally effective except at very high pressures that significantly reduced cardiac output (Hubbell 1991). Early dolphin researchers attempted to overcome the inadequacy of CMV for dolphin anesthesia by mimicking the normal respiratory pattern of dolphins with the apneustic plateau ventilation (APV) mode (Ridgway & McCormick 1967, 1971; Nagel et al. 1964; Ridgway et al. 1974; Ridgway 1965; McCormick & Ridgway 2018). Although a significant

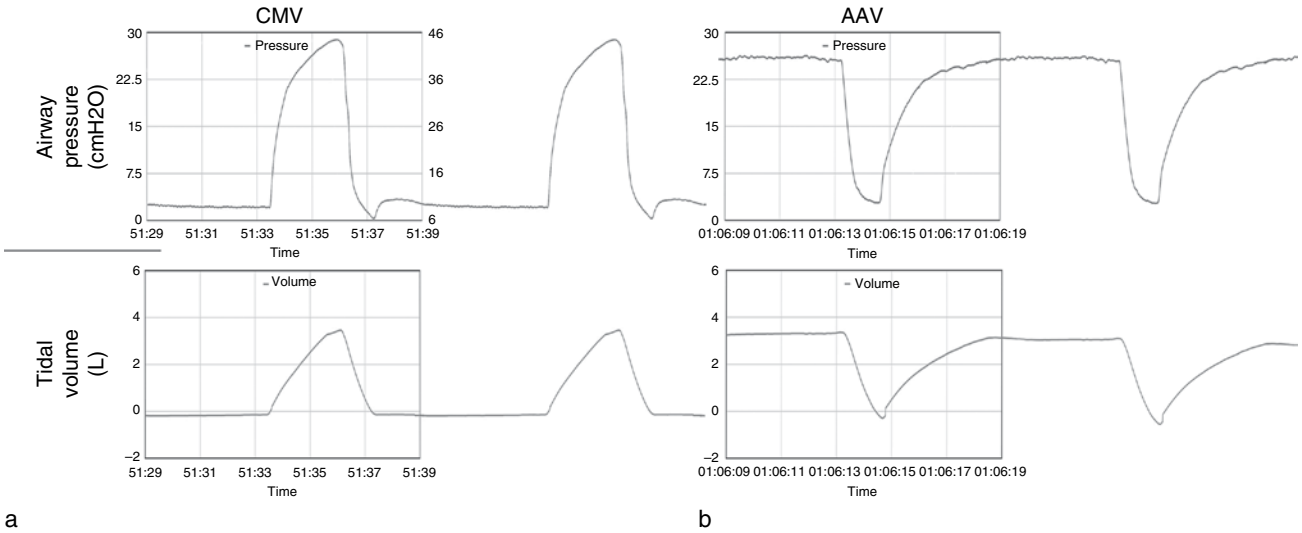


Figure 43.8 Controlled mechanical ventilation (CMV) versus apneustic anesthesia ventilation (AAV) mode spirometry waveforms. Adapted from Bratzke. Example of the change in airway pressure and lung volume during the CMV mode (left column) and during the AAV mode (right column) when applied to the same 190-kg adult bottlenose dolphin. In applying CMV the airway pressure increases from residual or ambient pressure to the peak pressure of 29 cmH_2O (range 20–30 cmH_2O in anesthetized dolphins) to generate a 3.5-L tidal volume. In contrast, when applying AAV the pressure is released from the selected upper level (P_{high}) to the lower level (P_{low}). In this instance, when P_{high} is 26 cmH_2O and P_{low} is 2 cmH_2O it will generate the same 3.5-L tidal volume. CMV increases up from the functional residual capacity (FRC) or lower over time, where AAV decreases down from the selected elevated plateau value to a level slightly above FRC. Following the release time of AAV, the lung volume is rapidly reestablished by reapplication of P_{high}. Reproduced with permission from Bailey (2020).

improvement in ventilation methodology, APV still failed to mitigate the development of atelectasis (Ridgway & McCormick 1971).

Unlike CMV, airway pressure release ventilation (APRV) employs an elevated baseline pressure followed by a drop in airway pressure to accomplish proper tidal ventilation. As first described by Downs and Stock (Downs & Stock 1987; Stock et al. 1987), APRV involves continuous positive airway pressure (CPAP) with an intermittent pressure release phase, but is better described as applying continuous airway pressure (P_{high}) identical to CPAP to maintain adequate lung volume and promote alveolar recruitment, with a time-cycled release phase to a lower pressure (P_{low}) very transiently. Mechanically, this is not too dissimilar from the early APV mode used on dolphins by Ridgway (Ridgway & McCormick 1967, 1971; Nagel et al. 1964; Ridgway et al. 1974; Ridgway 1965; Medway et al. 1970). However, APV uses a P_{low} of 0 cmH_2O pressure and allows a brief period of time for alveoli to collapse. APRV, as described by Downs and Stock (1987), was developed to maintain functional residual capacity at a level that would optimize gas exchange and lung compliance in the spontaneously ventilating patient in respiratory failure. Functional residual capacity (FRC) is the volume of gas left in the lung after a normal expiration. Unfortunately, when APRV is applied to the unconscious patient not spontaneously ventilating, it allows lung volume to drop below FRC and allows atelectasis to develop.

The apneustic anesthesia ventilation (AAV) mode was developed to maintain lung volume at a level slightly greater than FRC. In this mode, ventilation occurs when airway pressure is transiently reduced from P_{high} (CPAP) to the lower pressure P_{low} (the release pressure), allowing lung volume to decrease to no lower than FRC (Fig. 43.9). Immediate reapplication of P_{high} causes lung volume to increase. This intermittent drop and expansion of lung volume permits tidal breathing to occur without allowing atelectasis to occur. Appropriate levels of P_{high} and P_{low} are determined by optimizing compliance and the desired tidal volume. Note that mechanically, the AAV and APV modes of ventilation are similar. However, the key distinction is that exhalation to lower airway pressures ($P_{low} = 0$ mmHg) during APV can result in atelectasis, decreased compliance, derangement of ventilation/perfusion (V/Q) relationships throughout the lung, and progressive hypoxemia. During AAV, V/Q matching is maintained at normal levels in anesthetized patients and lung mechanics are normalized (Bratzke et al. 1998; Downs et al. 2014). The AAV mode is specifically indicated in patients with low lung and thoracic compliance, such as appears may be the case of the beached, anesthetized dolphin. The advantages of AAV over other modes of ventilation include lower mean intrathoracic (pleural) pressure, augmented venous return, improved cardiovascular performance, and better distribution of inspired gas flow resulting in improved

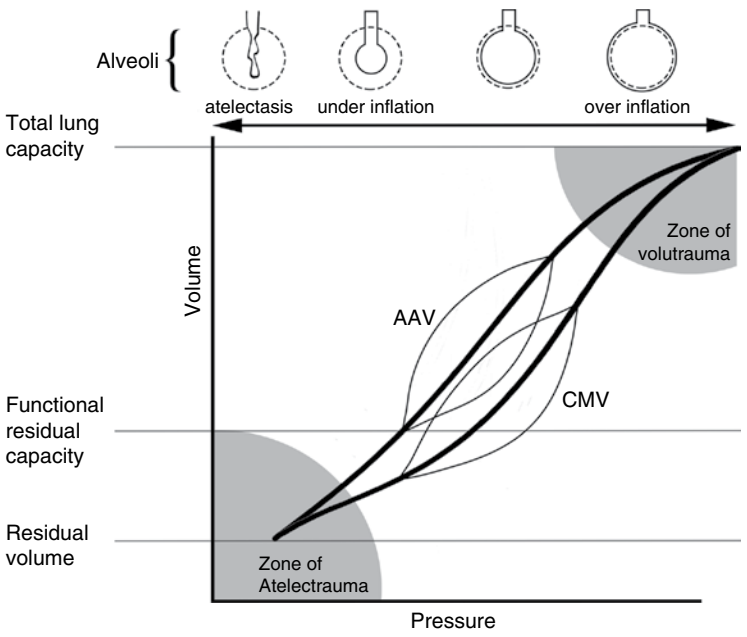


Figure 43.9 Graphical representation of conventional mechanical ventilation (CMV) and apneustic anesthesia ventilation (AAV) superimposed on individual pressure–volume curves. The AAV mode preserves lung architecture and compliance. On the contrary, compliance decreases over time as atelectasis develops during the CMV mode, shifting the compliance curve to the right. To achieve the same tidal volume, higher pressures are required during CMV.

ventilation-perfusion matching (Downs 1996). APV, APRV, and AAV will each mimic the breathing patterns of conscious, actively breathing dolphins, but AAV would be anticipated to provide superior ventilatory support to the anesthetized, nonspontaneously ventilating dolphin.

In summary, while the APV mode used in early dolphin ventilation (Nagel et al. 1964; Ridgway 1965) was designed in an attempt to mimic conscious dolphin breathing patterns and proved superior CMV, it still allowed for development of atelectasis (Ridgway & McCormick 1971). APRV was developed to improve ventilation of patients with low thoracic compliance and AAV was designed to normalize the pulmonary physiology of all mammals while under anesthesia. Although both APRV and AAV mechanically mimic the breathing patterns of conscious marine mammals, the objective of mechanical ventilation of the anesthetized dolphin is also to provide physiologically appropriate ventilation that supports cardiopulmonary function. The advantages of each of these potentially beneficial modes of ventilation for anesthetized dolphins can only be determined through live subject testing in the target population. Such testing is currently underway and is producing promising results in both terrestrial (Bukoski et al. 2022) and marine mammal species (McCormick & Ridgway 2018; Bailey & Ridgway 2020; Le-Bert et al. 2020).

Permissive or Intentional Hypercapnia

Blood gas data should be continuously monitored and interpreted throughout the procedure to assess the effectiveness of ventilation (Bailey & Pablo 1999). In theory, lung protective ventilation strategies, such as the AAV mode, that deliver lower tidal volumes and avoid atelectasis would be ideal for cetacean ventilation. However, implementing such lung protective strategies necessarily leads to hypercapnia. As such, when properly performed, the lung protective AAV mode of ventilation will produce a degree of *intentional hypercapnia*. A more common term present in the medical literature regarding hypercapnia and lung protective ventilation modes is *permissive hypercapnia* (Bailey & Pablo 1999). In the past decade the respiratory depression of dolphins has usually been managed by the conventional CMV mode of mechanical ventilation to maintain a $PaCO_2$ of 40 mmHg and a pH of 7.40 (as measured at 37°C). To accomplish this, an increased inspiratory pressure, respiratory rate, and/or tidal volume have been necessary. If a patient has lung disease, ventilation with conventional tidal volumes may cause alveolar overdistention and lung injury. If CMV mechanical inspiratory pressures or tidal volumes are intentionally limited to diminish possible alveolar overdistention, hypercapnia may develop. Be it intentional hypercapnia, where hypercapnia is intentionally implemented as part of the ventilation mode as in AAV, or permissive hypercapnia, which involves accepting variable levels of hypercapnia in avoidance of potentially negative effects produced by other forms of mechanical ventilation, both are generally well tolerated.

Before using intentional or permissive hypercapnia, its effects must be understood. High blood levels and alveolar concentrations of CO_2 can contribute to hypoxemia. The alveolar gas equation, $PAO_2 = (PB - PH_2O)F_IO_2 - PaCO_2/R$,

in which PAO_2 is the alveolar partial pressure of oxygen, PB is the barometric pressure, PH_2O is the vapor pressure of water, F_IO_2 is the fractional inspired oxygen concentration, $PaCO_2$ is the arterial partial pressure of carbon dioxide, and R is the respiratory quotient ($VCO_2/VO_2 = 0.8$), demonstrates this effect. However, hypoxemia may be remedied by administering supplemental oxygen. Hypercapnia may cause tissue acidosis, resulting in decreased intracellular pH and altered transmembrane electrolyte transport, glucose utilization, and structure-function relationships of amino acids. Neurologic sequelae of hypercapnia include sympathetic nervous stimulation with release of epinephrine and norepinephrine, significant increases in cerebral blood flow, and elevation of intracranial pressures. Hypercapnia also leads to increased cardiac output, decreased peripheral vascular resistance, and increased arterial blood pressure. As pH falls, left ventricular contractility is decreased in canine models, but cardiac output is still increased (Walley et al. 1990). Decreasing pH also causes a shift in the oxyhemoglobin dissociation curve to the right, promoting release of oxygen from hemoglobin. Cardiac arrhythmias are reported with $PaCO_2$ levels above 80 mmHg, but this observation may vary with species (Rasmussen et al. 1978). Type I hearts (canid, felid, hominid) tend to be more arrhythmic than type II hearts (equid, otariid, delphinid) (Bailey & Pablo 1999). Maintaining eucapnia may be more important when there is significant atelectasis of one lung (e.g., lateral recumbence, down or dependent lung compression). Hypocapnia may directly inhibit normal hypoxic pulmonary vasoconstriction of the nonventilated lung. Hypercapnia may increase pulmonary vascular resistance of the ventilated lung. Both would lead to increased shunt.

Allowing a degree of intentional or permissive hypercapnia will allow implementation of lung protective ventilatory strategies, tending to lead to increases in cardiac output and promoting downloading of oxygen to tissues if held to a reasonable level. If intentional or permissive hypercapnia is used, the $PaCO_2$ should be maintained below 80 mmHg, the pH above 7.2, and the PaO_2 well above 70 mmHg. A blood gas analyzer should be considered mandatory for prompt, accurate decision making when implementing such protocols.

Positioning, Support, and Padding

Dolphins, accustomed to a near-neutral buoyant, relative weightless environment, experience significant gravity-induced stressors on their respiratory and circulatory systems when out of water (Ridgway & McCormick 1971). This compromise appears clinically to be more severe when positioned in lateral or dorsal recumbence. Where dorsal recumbence is required, but table design does not allow, the dorsolateral oblique position (dorsal fin off the table edge) can often suffice (Dover et al. 1999). Dolphins on padded tables during historical dolphin anesthesia events did not fare well for lengthy procedures (Ridgway 1965). Where padding is the chosen method of cushioning, thick (4–8-inch) medium-density, open-cell foam padding similar to that used for large terrestrial mammals is necessary to prevent both myopathy and neuropathy from developing during longer procedures (Bednarski 1991). However, with the insulating effect of foam padding, one must guard against overheating of contact points with the patient. Waterproof closed-cell foam provides little if any cushioning and should be reserved for short, waterside beaching procedures. Regardless of method, time out of water should be monitored and limited. An alternative approach to surgery padding, also used historically, involved use of a frame with the dolphin supported by a yielding fabric containing a cutout for the dorsal fin. This framed support structure allowed for positioning of the dolphin in multiple ways (Fig. 43.2b) (Ridgway & McCormick 1967; Ridgway 1965). Further improvement was achieved by immersion of the dolphin in a tank of temperature-controlled water such that little of the dolphin's weight rested on the tank bottom (Fig. 43.3) (Ridgway et al. 1974). Such near-neutrally buoyant procedural approaches should be revisited, particularly as we move forward with cetacean anesthesia of larger species.

Anesthesia Support and Vigilance Monitoring

Although still applied infrequently, sedation and anesthesia of certain species of managed and free-ranging cetaceans has become an acceptable risk for medically necessary procedures. Historical failures and limited experience had led to myths and misconceptions about anesthesia of cetaceans. The relative difficulty with invasive support and monitoring in these species added to apprehension in performing needed surgeries, only increasing the probability of negative outcomes and further perpetuating these misconceptions. Advancements in both invasive and noninvasive monitoring methods have improved the care and safety of cetaceans undergoing sedation and general anesthesia. These advancements in monitoring and support have led to improved outcomes and acceptance of anesthesia of cetaceans for procedures deemed advantageous to the patient, but less urgent in nature.

Clearly, anesthesia monitoring and support are just as critical in cetaceans as in terrestrial mammals, if not more

so. A comprehensive approach to monitoring and support should be applied to the cetacean patient and, since reported drug protocols are frequently limited to experience with only a few individual animals, the anesthetist should always be on alert for the possibility of profound and unexpected drug reactions. Applying anesthesia monitoring equipment to patients out of the water without sedation is as important as applying it to sedated or fully anesthetized patients, if for no other reason than it can help to build the clinician's familiarity with the individual animal's normal heart and respiratory rates, core temperatures, and reflexes.

Since spontaneous ventilation, circulation, and perfusion in cetaceans normally take place with the animals' bodyweight supported by the buoyancy forces exerted by the water column, simply removing the patient from the water for a clinical procedure may place them at a cardiopulmonary disadvantage. A collapsible thorax and the animals' mass under the influence of gravity combine to increase respiratory effort and compress muscles and vessels. With normal thermoregulatory mechanisms disadvantaged, changes in temperature and pressure may cause hyper- or hypothermia from abnormal vasoconstriction or vasodilation and resultant blood shunts. This can happen even before any respiratory, cardiovascular, or central nervous system depressing anesthetic drugs are given.

Respiratory support in sedated animals that are still spontaneously ventilating may not be necessary. Many marine mammal clinicians, however, will still provide supplemental oxygen to dolphins that are out of the water, particularly if sedated. For general anesthesia in dolphins, successful mechanical ventilation has historically been performed with use of a Bird Mark 9 respirator with an apneustic plateau modification to allow for prolonged inspiratory hold in the ventilation cycle with a respiratory rate of 2–4 breaths per minute generally employed (Ridgway & McCormick 1967, 1971; Ridgway et al. 1974). These early experiences suggested that general anesthesia lasting longer than 4 hours without modification of the ventilation mode resulted in reduced lung expansion and alveolar inflation, and associated respiratory acidemia and cardiovascular depression (Ridgway & McCormick 1971). However, a summary from 2003 suggested that the apneustic plateau ventilatory cycle might not be necessary for shorter procedures (Reidarson 2003). Even so, review of other historical cases up until only a decade ago, though anecdotal in nature, suggested altering the mode of ventilation from the conventional mode was beneficial in any dolphin anesthesia greater than 1 hour (S.H. Ridgway, pers. comm., 2020). It is only through the active and ongoing testing of such ventilation modes that mechanically mimic the breathing patterns of conscious marine mammals that we can establish any benefit to marine mammal species (McCormick & Ridgway 2018; Bailey & Ridgway 2020; Le-Bert et al. 2020).

Monitoring is often noninvasive (electrocardiography, temperature, pulse oximetry, capnography, and other inspired/expired gases), but invasive blood pressure monitoring has become a standard of care for dolphins (Bailey 2013a, 2016). Heart rate can be monitored with an electrocardiograph (ECG), as in other species. Where possible, the authors recommend placing the ECG leads before the animal has received any drugs to establish baseline readings. Applying the McFee's orthogonal lead system as modified for veterinary medicine (McFee & Parungo 1961), in 1970 Hamlin defined the type 2 pathway of ventricular activation with a primary axis of depolarization left and cranial in the dolphin (very similar to the horse) (Hamlin et al. 1970). The diffuse, arborized, and penetrating Purkinje fiber network to the level of the epicardium in the dolphin leads to more instantaneous depolarization of the ventricles and an ECG waveform with a positive, bifid, or biphasic P-wave, small positive R-wave (Q-wave absent), large negative S-wave, and small positive T-wave. Anderson (1969) also documented this waveform as early as 1964. To simplify lead placement on dolphins positioned sternal out of water, in 1968 Ridgway standardized the three-lead system by positioning the left arm electrode in the left axilla, the right arm electrode in the right axilla, and the left leg electrode at the center dorsum of the thorax in the same transverse plane as the other leads (Fig. 43.2c) (Ridgway 1968). With the ECG monitor set to Lead II the left leg electrode is positive and the right arm electrode is negative. Electrodes imbedded in silicone suction cups allowed nontraumatic and uncomplicated attachment. Given the type 2 ventricular activation very similar to the horse, a simple alternative, and perhaps more representative, lead placement for clinical use in dolphins is a base-apex, bipolar lead. In this instance, with the monitor set to Lead II, the left leg electrode (positive) is placed on the left at the apex of the heart as close to midline as achievable and the right arm electrode (negative) with the left arm electrode are placed on the dorsum caudal to the blowhole (Fig. 43.10).

In the 1940s, Scholander and Irving noted that the resting heart rate of bottlenose dolphins varied rhythmically with breathing, reaching a minimum just before each breath and a maximum shortly after (Scholander 1940; Irving et al. 1941). Indeed, clinically normal dolphins have a significant resting sinus arrhythmia (Fig. 43.10a) whether shallow diving, resting at the surface, or out of water. However, this arrhythmia becomes exaggerated when subjects are beached and experience what appears tantamount to a Valsalva maneuver. Some animals that are anxious or stressed may override the arrhythmia and

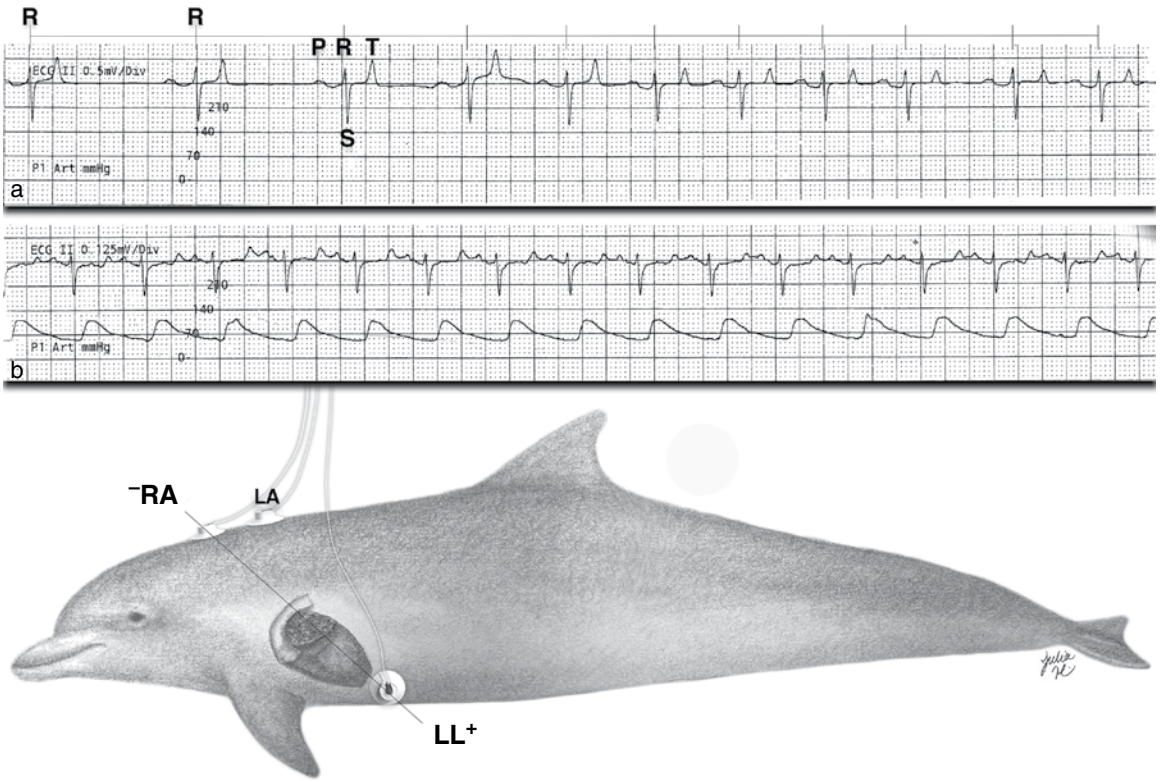


Figure 43.10 Example base–apex lead electrocardiogram (ECG) waveform of an adult dolphin undergoing anesthesia with the ECG monitor set to Lead II, making the left leg electrode positive and the right arm electrode negative. The positive, bifid P-wave, small positive R-wave (Q-wave absent), large negative S-wave, and small positive T wave demonstrate the type 2 pathway of ventricular activation with a primary axis of depolarization left and cranial. (a) The regular variation in the R–R interval demonstrates the common and significant resting respiratory sinus arrhythmia evident in the dolphin. (b) General anesthesia results in abolition of this sinus arrhythmia. The associated arterial blood pressure wave (median artery.) is presented as well. LA, left arm; LL+, left leg; −RA, right arm. Reproduced with permission from Bailey (2020).

maintain a steady, mildly tachycardic rate (100–120 beats per minute [bpm]). Additionally, general anesthesia results in abolition of the sinus arrhythmia (Ridgway et al. 1974; Ridgway 1972) (Fig. 43.10b). Published reports also suggest that a heart rate of less than 60 bpm may be a cause for concern in anesthetized dolphins (Ridgway & McCormick 1971).

Body temperature has been monitored with a flexible thermometer probe placed rectally to a depth of 15–25 cm depending on animal size (Ridgway & McCormick 1967; Nagel et al. 1964; Ridgway et al. 1974; Ridgway 1965). Clinicians should be aware that countercurrent heat exchange systems for internal gonads may interfere with thermometer readings if the probe is placed too deep or too shallow, and lead to misinterpretations of core body temperature readings (Rommel et al. 1992, 1993). In the awake animal, out of the water, one must especially guard against development of hyperthermia. After induction of anesthesia, under standard operating room conditions, dolphins more often become hypothermic (Bailey 2016). Low body temperatures reduce the inhalation anesthetic requirement for anesthesia and may lead to prolonged recoveries.

During anesthesia, body heat is lost through radiation, conduction, convection, and evaporation and may be exacerbated by peripheral vasodilation. Conductive and convective heat loss can be minimized by various methods of insulation. Evaporative heat loss can be more difficult to control, such as losses to the breathing of dry anesthetic gases. Warming of replacement fluids generally has an absolute minimal effect on patient warming, but delivery of cold fluids is of no benefit. Several types of patient-warming devices are available, but few are useful for dolphins. The most effective systems are likely the warm circulating air-blanket systems, although these would be inappropriate for dolphins. Core body temperature-controlled, body-wrap circulating water blankets system designed for human subjects are under review for use on dolphins. Historically patients held neutrally buoyant for surgery and exposed to temperature-controlled water

experience improved temperature control over current methods (Fig. 43.3). The need for warming will depend on the working environment, but the majority of patients in an appropriate surgical environment will arrive normothermic and quickly become hypothermic after induction of anesthesia. This is particularly true where the surgical environment is temperature controlled to the needs of the surgeon. It is important to remember that the dosage of inhalant anesthetic gas necessary to produce anesthesia is reduced by hypothermia, and recovery is prolonged by hypothermia. It is also important to know that cardiac contractility is reduced in hypothermia. Most patients do not benefit from hypothermia and it should be avoided.

Studies have demonstrated an increased detection of hypoxemia, hypoventilation, and endobronchial intubation with pulse oximetry. However, it must be understood that the pulse oximeter only estimates the saturation of blood with oxygen and it is based on human hemoglobin. The transmittance pulse oximeter sensor (probe) sends red (660 nm) and infrared (910 or 940 nm) light from two light-emitting diodes through the tissues to a photodetector measuring at several hundreds of samples per second. Oxygenated blood does not absorb (or reflect) red light and absorbs infrared light, where deoxygenated blood does the opposite. With each beat of the heart there is an increase in the amount of arterial blood under the sensor and a pulsatile change in light absorption. The ratio of red to infrared light reaching the photodetector is then used in an algorithm based on empirical data collected from normal volunteers (almost exclusively from human beings). The result is an estimate of the arterial blood oxygen saturation (SaO_2), indicated as SpO_2. However, species differences, patient motion, low perfusion, pigmentation, dysfunctional hemoglobins, intravascular dyes, light interference, and improper sensor placement will all affect accuracy. Some pulse oximeter manufacturers include special microprocessor-controlled programming, providing additional accuracy when their devices are used under conditions of motion and low perfusion. Perhaps more importantly, pulse oximetry is not a "set-and-forget" device. The sensor clip itself will squeeze the tissues and reduce blood flow to the area over time, thus requiring regular repositioning. Pulse oximetry by a transmittance probe placed on the tongue of an anesthetized dolphin is commonplace (Linnehan & MacMillan 1991). In sedated and anesthetized animals, the authors have attempted to place reflectance probes rectally or within the genital slit of some patients with rather limited success.

Monitoring respiratory CO_2 (capnography) provides information about the cardiovascular system, metabolism, and adequacy of ventilation of the patient. It will also warn the anesthetist about the most common anesthesia mishaps and breathing circuit problems. Capnography can forewarn of esophageal intubation, tracheal intubation and extubation, disconnection of breathing circuit from the endotracheal tube, airway obstruction, apnea, ineffective CO_2 elimination, incompetent unidirectional valve(s), hypo- and hyperventilation, increased and decreased CO_2 production, and increased dead space ventilation. Monitoring end-tidal carbon dioxide ($ETCO_2$) is recommended for dolphins undergoing general anesthesia and may be helpful even with dolphins under sedation (not intubated). For nonintubated animals, the sampling device (side-stream or mainstream) can be held in the blow stream above the blowhole. Although such measurement will be inaccurate, trends in $ETCO_2$ may be monitored (van Elk et al. 2002). Only side-stream capnography is available for monitoring of intubated adult dolphins attached to large animal breathing circuits (mainstream is diameter limited, increase resistance). $ETCO_2$ measurements should always be checked against the $PaCO_2$ to determine the adequacy of ventilation. It must be understood that the $ETCO_2$ is not equivalent to the alveolar or arterial CO_2. When applying the CMV mode of ventilation in the dolphin there is an $ETCO_2$ to $PaCO_2$ difference of 10–15 mmHg indicating significant dead-space ventilation. When applying the AAV mode of ventilation, the $ETCO_2$ to $PaCO_2$ difference is greatly reduced and the $ETCO_2$ will be more representative of blood levels of CO_2. Blood flow to the lungs for gas exchange is also important to $ETCO_2$ such that in critically low cardiac output states the $ETCO_2$ will fall and will rise again with resuscitation.

First demonstrated in a horse in 1714 (Hall 1987), arterial blood pressure has proven the most reliable clinical indicator of the adequacy of circulation (Wagner & Brodbelt 1997) and it has been recommended for managing marine mammals under anesthesia (Bailey 2013a). Mean arterial blood pressure was monitored and reported by Ridgway in the 1970s in anesthetized bottlenose dolphins and pacific white-sided dolphins (Ridgway & McCormick 1971; Ridgway et al. 1974). These measurements were recorded from an indwelling needle within the ventral peduncle PAVR. The authors have also successfully measured CVP in several bottlenose dolphins through an indwelling IV catheter placed in the CBV. CVP can also be measured from a lengthy PICC line placed via the hepatic vein (Johnson et al. 2010) or from the lateral subcutaneous caudal vein into the caudal vena cava under ultrasound guidance. It is now standard practice to place arterial catheters in cetaceans (see the vascular access section). Doppler flow probes and ultrasound can facilitate cannulation of the median artery of the pectoral flipper of cetaceans as well as other peripheral arteries of the PAVR (Fig. 43.5) (Bailey 2016; Ivančić et al. 2014). Hypotension cannot be

detected if it is not measured. The purpose of monitoring blood pressure is to obtain an objective measure of the adequacy of the systemic circulation.

Uninterrupted direct blood pressure monitoring through full recovery and extubation has demonstrated to the authors the similarity of dolphin blood pressures to those of ruminants (unpub. data). The mean arterial blood pressure in ruminants has long been recognized at approximately 20 mmHg higher than in humans and other domestic species (Doyle et al. 1960). In general, hypotension in mammals may be defined as a mean arterial blood pressure of less than 60 mmHg. However, for species with a normally higher resting mean arterial pressure, a low of 60 mmHg may be considered excessively low for proper maintenance of cerebral, vital organ, and muscular blood flow. It would be wise to intervene through supportive measure where mean arterial blood pressure approaches 70 mmHg in cetaceans. Drug-induced vasodilation and both sensible and insensible fluid losses are generally addressed by delivery of crystalloid fluids at 10 mL/kg/h, unless contraindicated. Use of colloid solutions in dolphins has been brought into question (hetastarch; C. Smith, pers. comm., 2011), but low molecular weight varieties may be acceptable if colloid solutions are necessary and plasma is unavailable. Where anesthesia is the sole cause of hypotension, the appropriate response would involve reducing the level of anesthesia where possible, balancing the anesthetic technique with less cardio-depressive drugs (e.g., opioids), volume loading with fluids where appropriate, inotropes such as dobutamine (0.2–2.0 μg/kg/min IV) or ephedrine (0.05–0.1 mg/kg IV), and then, possibly, vasopressors such as phenylephrine (1 μg/kg/min IV) or norepinephrine (0.1–0.5 μg/kg/min IV). It should be noted that the recommended dobutamine rates are well below the rates used in most domestic species as the drug has been observed to lead to tachycardia at higher rates in dolphins. In addition, lower dosages of phenylephrine (0.01 μg/kg/min IV) or norepinephrine (0.01 μg/kg/min IV) are being applied more routinely with the inotrope dobutamine as we investigate management of perceived anesthetic induced engorgement of rete mirabile (Bailey 2021). Noninvasive methods of estimating blood pressure have yet to be established for dolphins and current methods are not feasible given the unique anatomy.

Blood gases can be measured as in other animals, and normal ranges appear similar to other mammals. Due to cetacean vascular anatomy, collecting a purely arterial or purely venous sample is possible, but less likely than collecting an arteriovenous admixture when sampling from peripheral sites by needle puncture. It is now common practice to collect arterial blood from a catheter in the median artery and venous blood from a catheter in the LCSV.

Depth of anesthesia can be determined through assessment of reflexes as in other mammals. Palpebral and corneal responses, response to manipulation of the blowhole, jaw tone, and swallow reflexes are all appropriate, though typically only evident at very light planes of anesthesia. Ridgway and McCormick (1971) reported loss of swimming motion in the tail flukes as the most reliable indicator that a surgical plane of anesthesia has been reached when inducing anesthesia by inhalation anesthetic alone. Future advances in assessing anesthetic depth may be achieved through application of EEG monitoring and detection of the effect of anesthetic agents on the irregularity of the EEG signal (brain entropy).

Postanesthesia Care and Recovery

Perhaps greater than the challenges posed by induction and maintenance of general anesthesia in cetaceans are those encountered on recovery (Ridgway 1965). This is due in part to the need for replacement of the goosebeak back into the nasopharynx. This must be timed with the return of spontaneous breathing concurrent with adequate voluntary muscular control over the blowhole in these obligate nasal breathing species. In general, the dolphin patient may leave the operating room for the recovery area if they have a patent airway, adequate ventilation, and stable hemodynamics. The location for recovery should be a temperature-controlled, quiet, dimly lit area where multiple experienced animal handlers are afforded adequate space for proper control of the patient. Mechanical ventilation is necessarily continued into the recovery period due to the degree of drug-induced respiratory depression in these species. Any neuromuscular blockade not yet reversed should be addressed. Monitoring and supportive care established during anesthesia is continued into the recovery period until the patient is fully alert and sufficiently physiologically stable for return to an aquatic environment. Vascular access is maintained during the postoperative period to allow emergency administration of drugs and fluids, and may be maintained in the subsequent aquatic environment after protective covering (Johnson et al. 2010; Daly et al. 2013) if necessary. Given recovery can be slow, proper positioning and padding, as well as wetting with spray bottles sufficient for maintenance of skin condition and thermoregulation are just as necessary as during the anesthetic procedure. Put simply, anesthesia, and the necessary support associated with anesthesia, does not end when the vaporizer of the anesthesia machine is turned off. It must continue as long as necessary until the patient can demonstrate physiologic stability through self-regulation. As such, it may simplify logistics to recover the

patient to the point of being safely extubated while still on the surgery table or on a padded floor location as near to the surgery as reasonably possible.

Reflexes suggestive of return to consciousness are continuously monitored in the recovery phase. Blowhole muscular tone and response to touch, palpebral reflex or eyelid tone, and jaw tone will progressively increase with washout of anesthetic gas. Monitoring of expired gas anesthetic concentrations can facilitate this postoperative assessment. The expired anesthetic concentration must drop to around 0.3 times the MAC to ensure the majority of subjects will show a response to auditory stimuli during awakening (MAC_{awake}). The MAC_{awake} for sevoflurane and isoflurane can be estimated below 0.4% and 0.8%, respectively. Below these values the inhalation anesthetic is contributing little to delay in recovery. As these are both low solubility inhalation anesthetic agents, the washout time should be relatively short at approximately 10 or 20 minutes, respectively. However, the inhalation agents are primarily eliminated by exhalation. To prevent delay of washout one must prevent rebreathing of anesthetic agent by flushing the breathing circuit with oxygen or, cautiously, by alternative ventilatory method (e.g., oxygen demand valve, less precise). Indeed, if ventilation is not continued into the recovery period, the inhalation anesthetic will not be eliminated and recovery will be delayed. In addition, hypothermia will increase the effect of the inhalation anesthetic and delay recovery. Given this information, and the knowledge that inhalation anesthetic agents severely depress spontaneous ventilation in cetaceans, there is little reason to deliver any supplemental reversal agents until there is sufficient washout of the inhalation anesthetic agent.

In assessing any delay in the return to spontaneous ventilation, one must consider not only the physiologic condition or disease of the patient, body temperature, and gas anesthetic washout, but also the other sedative, analgesic, and anesthetic drugs used. After addressing the former factors, reversal agents for any other anesthetic drugs may prove necessary to expedient recovery for timely return to normal ventilation. The pharmacokinetics of benzodiazepines, opioids, and their antagonist reversal agents have not been well established in cetacean species. In general, it is anticipated that the sedative and analgesic drugs used to balance anesthesia have a longer half-life in cetaceans than terrestrial mammalian species and will likely be present in the recovery phase at sufficient levels to depress respiration. Benzodiazepine sedative drugs (midazolam and diazepam) may be fully reversed with 1 part flumazenil for every 13 parts of this benzodiazepine (Pawson 2008). Given a degree of metabolism should have taken place, full reversal may not be necessary, but sufficient drug should be on hand for full reversal or repeat dosing should the need arise. In the end, flumazenil is titrated "to effect" based on individual need at the discretion of the attending veterinarian. Opioids will provide analgesia, but contribute significantly to postoperative respiratory depression. The short-acting opioid antagonist, naloxone, can be used to probe and assess the possible causes of any delayed return to spontaneous respiration. Naloxone 0.01 mg/kg IV can be given to fully reverse any opioid-induced respiratory depression, but is best done after elimination or reversal of other agents. One can allow the naloxone to fade over its 20-minute half-life and any residual opioid effect to return for the purpose of analgesia. If respiratory depression remains excessive, naloxone dosing may be repeated. Alternatively, naloxone can be delivered at a lower dosage of <0.005 mg/kg IV to produce only partial reversal of opioid effects both positive and negative, but repeat dosing may be necessary. If analgesia is not necessary or if respiratory control is paramount, the long-acting opioid antagonist naltrexone, lasting approximately 24 hours, can be delivered. Again, any neuromuscular blockade should be reassessed for residual muscle weakness and its influence on return to spontaneous ventilation.

Endotracheal extubation of the dolphin requires the same patient control as intubation. Two assistants again place two soft towels in the mouth, over the mandible and maxilla, in preparation for holding the mouth open for extubation. The anesthetist is ready with injectable anesthetic agent to induce anesthesia IV and regain control of the airway and breathing should it become necessary. Blowhole response to touch and palpebral reflex are continuously monitored during recovery. The palpebral reflex and/or eyelid tone will increase, the blow hole will regain muscular tone and voluntary control, and jaw tone will progressively increase with a washout of anesthetic drug. Purposeful muscular movements or shivering may become evident. Spontaneous ventilation through the endotracheal tube may occur with washout of inhalation anesthetic agent or after delivery of reversal agents. More often, however, dolphins will not spontaneously ventilate with the endotracheal tube in place with full ventilator support. Several dolphins have been observed apparently fully awake and visually tracking the anesthetist but remaining calm and willingly accepting of the endotracheal tube and ventilation for as much as 1–3 hours when maintained on the historical APV (S.H. Ridgway, pers. comm., 2020) and novel AAV (Bailey & Ridgway 2020) modes of ventilation that mimic normal dolphin respiration. With careful monitoring of blood gas data, ventilation may be reduced and $PaCO_2$ allowed to rise, within limits, to promote spontaneous ventilation. Even then, some dolphins will not spontaneously ventilate while intubated. The anesthetist will need to carefully process all of this information and may

simply need to return the larynx to its proper nasopharyngeal location and evaluate the response. As the assistants hold the mouth open with towels, a hand of the anesthetist is inserted into the oropharynx to remove the endotracheal tube and gently grasp the goosebeak to push it back and up into the nasopharynx. The muscular control of the larynx and nasopharynx may be palpated and assessed at that time. The dolphin may move and shake its head in protest at this manipulation if fully awake. Protective arm gear many be desirable for the anesthetist to avoid tooth-raking of the skin. With the larynx now in its proper nasopharyngeal location, stimulation of the patient with percussive thoracic coupage and familiar trainers' voices may promote spontaneous ventilation. If there are not spontaneous efforts to breath, the patient should be reintubated within 2.5–3 minutes, preferably without reinducing anesthesia. It may be necessary to use a smaller endotracheal tube for reintubation. Phenylephrine 0.5–1.0% nasal spray may be sprayed into the nares to trigger vasoconstriction of mucosal blood vessels and reduce any edema developing in the airway during the procedure. This can be done prior to spontaneous ventilation by digital depression of the blowhole or simultaneous to spontaneous inspiratory efforts to breath, or both. If there are efforts to spontaneously ventilate, but stridor or other evidence of obstruction occur that are not responsive to topical phenylephrine or the animal's own efforts to reposition the larynx and breath, then the patient should be reintubated within 2.5–3 minutes. One then must reassess the level of anesthetic and drug reversal, as well as the degree of consciousness and strength of effort to determine if earlier steps should be repeated. Lengthy periods of intubation can lead to significant nasopharyngeal edema and laryngeal muscular weakness. Phenylephrine spray may need to be repeated. Although there is no specific scientific report to support the method, in severe cases topical dimethylsulfoxide and steroids have been used to further reduce inflammation of the airway. In addition, dolphins showing evidence of disease may have some loss of normal pulmonary function and, accordingly, may have difficulty spontaneously ventilating when beached. In one case the dolphin was sufficiently debilitated and distressed when beached that it was not successfully extubated until returned to a neutral buoyant environment (Rosenberg et al. 2017).

Importantly, vagally mediated reflexes will return in the recovery period with anesthetic washout, as evidenced by return of the normal respiratory sinus arrhythmia. Additional vagal reflexes may exaggerate this normal sinus arrhythmia. It is well established that general anesthetics modify the laryngeal reflex, but at light planes of anesthesia, activation of laryngeal vagal reflexes can occur with manipulation of the airway. Triggering of laryngeal or pharyngeal reflexes can lead to an exaggerated sinus arrhythmia with periods of profound bradycardia. As the dolphin attempts to consciously move the larynx while still intubated, or as the anesthetist attempts to extubate and reposition the larynx, extremes of bradycardia may be evident. This exaggeration of the sinus arrhythmia should resolve with extubation, replacement of the larynx into the proper nasopharyngeal location and normal conscious laryngeal control. However, if necessary, these vagally mediated reflexes can be prevented or treated by administration of parasympatholytic drugs, such as atropine.

The anesthetic agents used, the duration of the procedure, and the magnitude of physiologic dysfunction of the disease state primarily determine the duration and quality of recovery. With all contributing factors the same, it may be said that recovery of dolphins is generally slower than that of many terrestrial mammals. A recovery to extubation typically takes from 45 to 60 minutes (Bailey 2016; Ridgway 1968), but has ranged from 20 to 180 minutes with variability in physiologic dysfunction of the subject. Prolonged recovery is usually due to hypothermia or residual benzodiazepines and/or opioids. Reversal agents may need to be repeated for successful extubation, expedient recovery, and timely return to the more appropriate aquatic environment affording neutral buoyancy. Further investigations into recovery directly in a near-neutrally buoyant water recovery tank are underway, but the method is not a current common practice. Once the dolphin is extubated and demonstrates consistent, strong spontaneous respiration and normal physiologic parameters, including an ability to thermoregulate, the electronic monitoring equipment may be removed, the catheter prepared for an aquatic environment if not removed, and the patient moved to a shallow pool for further observation. Multiple experienced animal handlers will now support the dolphin in the shallow water, assessing behaviors as evidence of consciousness, as well as the animal's ability to right itself in the water column. As the dolphin progresses in movement and strength, echolocating as it goes, the trainers may release the subject to test its ability to manage the aquatic environment.

Disease Issues Affecting Anesthesia

Given their anatomy and physiology, cetaceans are particularly susceptible to lung infection and pneumonia is the most commonly diagnosed cause of severe disease in these species. Consequently, since these animals mask disease (Geraci & Sweeney 1986), a high index of suspicion should be maintained. Any animals showing evidence of disease may have some loss of normal pulmonary function and, accordingly, the potential for hypoxemia. With this in

mind, the bronchodilator albuterol has been delivered by inhalation at 2 μg/kg during anesthetic procedures as part of the management of patients demonstrating hypoxemia and suspected of a degree of pulmonary disease (Russell et al. 2021).

Field Techniques and Strategies

Due to limited experience and serious potential complications associated with the use of sedatives in small cetaceans, most fieldwork is accomplished with animals physically, rather than chemically, restrained. There appear to be few peer-reviewed publications describing data for sedation of odontocetes in a field setting. However, there are anecdotal reports, such as Ridgway delivering ketamine at a subanesthetic dosage (2.76 mg/kg IM) by hand-thrown dart in one free-swimming dolphin and observing slow swimming and sufficient behavioral change in this evasive subject to allow for manual restraint (S.H. Ridgway, pers. comm., 2020). Sedations of entangled North Atlantic right whales (*Eubalaena glacialis*) have been achieved by Moore (Moore et al. 2010, 2013). Midazolam, meperidine, and butorphanol were given alone and in combination by cantilevered pole syringe or ballistic dart to two whales. The goal was to achieve sufficient sedation or behavioral modification to reduce boat avoidance to permit safe removal of the entangling fishing gear, while at the same time allowing for proper blowhole functionality, ventilation, and awareness in the water column. The authors concluded that these conservative attempts produced less sedation than perhaps desired, but did ultimately lead to behavioral changes that dramatically improved disentanglement efforts.

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44

Elephants

Jeffery R. Zuba and Khursheed R. Mama

Introduction

To offer the highest standard of healthcare and welfare for managed elephant collections, the zoo and wildlife veterinarian must be prepared to provide safe and effective sedation and anesthesia for a variety of medical and husbandry procedures. A comprehensive review of anesthetic protocols exclusively in managed elephants has not been thoroughly discussed in the literature, therefore the objective of this chapter is to specifically address the unique challenges and protocols necessary for the successful clinical management of anesthesia in elephants under human care.

Although free-ranging elephant anesthesia will not be specifically reviewed in this chapter, the reader is encouraged to study this important information, which can be found in previous editions of this book (Horne & Loomis 2014) and other notable references (Kreeger & Arnemo 2018a; Meyer et al. 2021a; Burroughs et al. 2021). The anesthetic drugs, protocols, and equipment used in free-ranging African elephants are conditionally relevant and valuable for elephants housed in zoological settings. Conversely, the clinical and anesthetic skills of veterinarians who manage elephants in zoological institutions will hopefully contribute to safer anesthesia in free-ranging elephants. A thorough understanding of the fundamentals of domestic and wildlife anesthesia, especially the principles of respiratory and cardiovascular physiology, pharmacology, and clinical support is highly recommended for the benefit of our elephant patients. Since there is a lack of published data on the cardiopulmonary support of the anesthetized elephant, authors have elected to extrapolate from literature related to physiological and anesthetic considerations of domesticated horses (Zuba & Oosterhuis 2012; Greene et al. 2019). This chapter reflects the authors' experiences in free-ranging and managed elephant anesthesia as well as comparative anesthesia and physiology in domestic and wildlife species. We acknowledge our contemporaries and previous authors and pioneers for their dedication and valuable contributions to zoo and wildlife anesthesia, including the elephant. The chapter is written in step-by-step chronological order as if planning and performing an anesthetic procedure in the world's largest land mammal at a managed care facility.

General Information

Taxonomy

All elephants belong to the mammalian order Proboscidae and the family Elephantidae (IUCN 2021; Rees 2021a). The African savannah, or bush, elephant (*Loxodonta africana*) and the African forest elephant (*L. cyclotis*) are the two distinct species found on continental Africa. The African savannah elephant is likely the only species found under human care in the United Staets and Europe. Adult *L. africana* in captivity generally weigh between 3000 and 7000 kg (Horne & Loomis 2014), with males being larger than females. See Table 44.1 for taxonomic, geographical, and anatomical information for elephants.

The taxonomic status of the Asian elephant (*Elephas maximus*) is a bit more complex but the International Union of Conservation of Nature (IUCN), a global authority of animal status, currently recognizes only three subspecies (Shoshani 2006; IUCN 2021; Rees 2021a). They are based on geographical distribution: *E. m. indicus* on mainland Asia, *E. m. maximus* in Sri Lanka, and *E. m. sumatranus* in Sumatra. No reference could be found to determine which species are found under human care so the term Asian elephant (*E. maximus*) will be used in this chapter. Adult *E. maximus* in captivity weigh between 2000 and 5500 kg (Horne & Loomis 2014), with males being larger than females.

It has been observed by the authors and others that Asian and African elephants under human care appear to have

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Table 44.1 Geographic distribution, height, and weight of officially recognized elephant taxa.

Taxonomic Designation	Common Name	Geographic Range	Weight (kg)	Height (m)
Elephas maximus indicus	Mainland or Indian elephant	Indian Subcontinent, Southeast Asia, Peninsular Malaysia	2000–5000	2.5–3.5
Elephas maximus maximus	Sri Lankan elephant	Island of Sri Lanka	2000–5500	2.5–3.5
Elephas maximus sumatranus	Sumatran elephant	Island of Sumatra, Indonesia	2000–4000	2.5–3.2
Loxodonta africana[a]	Savanna or bush elephant	East and South Africa	4000–7000	3.0–4.0
Loxodonta cyclotis[a]	Forest elephant	Central and West Africa	2000–4500	2–3

[a] Ranges may overlap somewhat.
Source: Horne & Loomis (2014).

similar basic awake physiology and vital signs (Honeyman et al. 1992; Mikota 2006). Clinical responses to the drugs and drug dosages used for sedation, anesthesia, and support are also similar (Horne & Loomis 2014; Kreeger & Arnemo 2018b), therefore they will be considered the same in this chapter unless specified.

The basic biology and natural history of elephants under our care is beyond the scope of this chapter and the reader is referred to many fine reviews in the literature (Olson 2004; Association of Zoos and Aquariums 2012; Kolpin et al. 2020; Rees 2021). The Zoological Information Management Software (ZIMS) by Species 360 is a highly recommended and expansive subscription database for zoos, aquariums, and wildlife institutions for animal husbandry and veterinary care. This includes, but is not limited to, valuable information such as body weight for various age groups and species of elephant to assist with the planning for anesthesia.

Population Status

The savanna elephant has recently been reclassified as Endangered and the forest elephant as Critically Endangered. The most recent estimate of free-ranging African elephants is approximately 415,000 for both species and their numbers have plummeted in the past decade (Thouless et al. 2016; Chase et al. 2016; Burroughs et al. 2021). The IUCN also recognizes the free-ranging Asian elephant (*Elephas maximus*) as Endangered (IUCN 2021), with a total population of approximately 50,000 (Williams et al. 2020). It is estimated that 10,000–15,000 Asian elephants are currently under human care in Southeast Asia, which represents approximately one third of the world population (AsERSM 2017; Martinez & Roberts 2019; Rees 2021a). The total number of elephants under human care in North America and Europe is approximately 969 (546 Asian, 423 African), therefore the estimated total worldwide number of potential managed elephants requiring veterinary care, which may require anesthesia, is approximately 16,000 individuals.

Management and Husbandry of Elephants under our Care

Recent publications on managed elephant facilities highlight the importance of husbandry and care in elephant health and welfare (Miller et al. 2016; Greggor et al. 2018; Edwards et al. 2019; Wendler et al. 2019). There are several publications dedicated to the management of captive elephants. They include recommendations on welfare and enrichment, enclosure and environmental requirements, personnel, handling techniques, behavioral training and management, basic health issues, and veterinary care (Olson 2004; Riddle & Stremme 2011; Association of Zoos and Aquariums 2012; Koplin et al. 2020). Key to sedation and anesthesia management is the importance of training elephants specifically for medical procedures.

Protected (vs. free) contact which includes physical separation between personnel and the elephant is the most common and acceptable method of management to ensure human safety (Honeyman et al. 1998; Horne & Loomis 2014; Rees 2021c; Roocroft 2023a,b). Positive reinforcement methods are used for training elephants for many beneficial behaviors to facilitate basic husbandry and care, including medical, dental, and reproductive examinations, foot care, diagnostics (e.g., venipuncture), treatments (e.g., oral or injectable medications), and minor medical procedures (Figs 44.1, 44.2, and 44.3). Standing sedation can also be performed in animals trained to an elephant restraint device (ERD) for more invasive procedures (e.g., wound management).



Figure 44.1 An elephant restraint device is used to gently control a female adult African elephant for transabdominal ultrasound to diagnose and monitor the progress of her pregnancy. Photo of Drs. B. Durrant and M. Clancy courtesy of J.R. Zuba.



Figure 44.2 A training wall is used for protected contact with an adult African elephant to train medical behaviors to safely monitor oral and dental health. Photo courtesy of J.R. Zuba.



Figure 44.3 A well-designed and versatile training wall for elephants with numerous access doors and a protective trunk cage. This device allows for the safe health evaluation of the left and right side of the elephant's body, as well as the oral cavity. Photo courtesy of J.R. Zuba with permission from Dr. Scott Citino.

Preprocedural Planning

The preprocedural planning period is critical to nonemergent anesthesia as it allows delegation of assignments to reduce risk (Fig. 44.4). This may include organizational, facilities-related, personnel, and technical considerations. There is recognition that there are inherent sensitivities associated with this planning and that communication must include administrators, curators, trainers, elephant staff, facilities managers, veterinary staff, and consultants. In situations where the need is more urgent, a predetermined plan can be helpful to ensure a timely and effective response to minimize animal suffering and maximize human and animal safety.

The most common medical considerations in elephants include those of the musculoskeletal, dental, gastrointestinal, and reproductive systems and these have been reviewed elsewhere (Horne & Loomis 2014). Of these four, health represents one of the most frequent medical concerns in zoo elephants (Gage et al. 1997; Lewis et al. 2010; Miller et al. 2016; Edwards et al. 2019; Wendler et al. 2019; Greene & Brenner 2020) and may include osteoarthritis (Siegal-Willot et al. 2021) and nail or sole infections (Ollivet-Courtois et al. 2003; Zuba et al. 2006). Dental issues such as tusk fractures with exposed pulp, malocclusion, molar fractures, and retained molars (Fagan et al. 2009; Steenkamp 2019, 2021) are also a common consideration. Less often gastrointestinal problems, including colic (Greene & Brenner 2020), may necessitate sedation or anesthesia to provide supportive care.



Figure 44.4 The importance of communication, recurring meetings, and open discussions directed by veterinary leadership cannot be overemphasized when preparing for an elephant procedure requiring anesthesia. Due to the inherent complexities involved in an elephant anesthesia, a preparedness plan should be in place in case of emergency and reviewed annually for all institutions with elephants under their care. Photo courtesy of Ken Bohn, San Diego Zoo Wildlife Alliance.

Veterinary Factors to Consider

The experience and leadership skills of the veterinary team are an obvious and fundamental component in the preparation of a safe and effective elephant anesthetic event. The team must have a comprehensive and contemporary understanding of the many unique anesthetic challenges and potential complications in a large species such as the elephant. Furthermore, it is the veterinarian's responsibility to develop a safe and effective anesthetic plan with consideration of the medications, skill level of personnel, and environment they are working in. The veterinary team should also be leaders in coordinating the safety of personnel when working with controlled substances and other potent anesthesia drugs, and should have a plan in case of accidental human exposure (Kreeger & Arnemo 2018c; Zuba & Greenberg 2019; Morkel et al. 2021). Additionally, veterinarians should work with key personnel to minimize challenges relative to the size and disposition of elephants. It should be recognized that even a trained elephant may not respond favorably to commands if unwell or in a unique circumstance.

While each anesthetic event and circumstance is different, teams familiar with anesthetic and logistical considerations working together are likely to be most successful. Often tasks are assigned to members of the team well in advance of administering drugs, with recognition that due to the limited frequency of anesthesia in elephants, there may be a relearning curve each time. While these events can be a great opportunity to train people, the lead veterinarian must be willing to intervene to maximize animal safety.

Patient Factors to Consider

Individual animal history, current health and physical status, temperament, level of behavioral training, and preexisting conditions are important. Laboratory values can also be helpful if they can be obtained prior to anesthesia. The American Society of Anesthesiologists physical status classification has been adapted for veterinary species (Portier & Ida 2018) and may be useful to determine animal risk and communicate the same to stakeholders. Although a sensitive subject, it may be important to discuss the potential for euthanasia and plan for the same if the elephant patient has a poor prognosis. It should be recognized that special arrangements will be necessary to accomplish this in a humane and compassionate manner and that subsequent considerations for disposition of the carcass may need to be considered.

Most facilities can weigh their animals so accurate dosages can be administered, which is an advantage over free-ranging elephants where estimates are made by shoulder height (du Toit 2001a). It is estimated that 74% of elephants under human care in North America are overweight or obese (Morfeld et al. 2016). Additionally, a recent American Association of Zoo Veterinarians survey of 314 managed elephants of both species reported that 45% were considered geriatric and 36% were on their last set of molars (Greene & Brenner 2020). Preexisting conditions such as obesity and geriatric status are just two examples of conditions which may negatively influence patient safety during anesthesia (Johnson et al. 2009; Greene & Brenner 2020). Furthermore, preexisting musculoskeletal disorders may prevent the anesthetized elephant's ability to stand during recovery so arrangements must be made for assisted standing.

Since anesthesia for the management of clinical disorders in captive elephants is an infrequent event, there is a lack of detailed information on the physiologic response and patient support during anesthesia (Horne & Loomis 2014; Kock et al. 2021), especially during prolonged procedures. The authors therefore recommend published physiologic data and protocols of the anesthetized domestic equid to serve as a reference for the acid-base, cardiovascular, and respiratory systems of the anesthetized elephant (Robinson 2009; Schwarzwald et al. 2009).

Generally, more anesthetic events occur in free-ranging African elephants than in zoological institutions due to management procedures such as relocations, disease investigations, and research studies. Published doses of anesthetic drugs and doses (Horne & Loomis 2014; Kreeger & Arnemo 2018a; Kock 2020; Burroughs et al. 2021) may provide guidance when developing a plan for elephants under human care but likely need to be adjusted downward given the circumstances surrounding administration in the two environments. While stressors exist in both circumstances and may influence anesthesia (Wagner 2009; Kreeger & Arnemo 2018d), it is more likely that anxiety can be better managed to avoid activation of the sympathetic nervous system (Kroll & Gassmayr 1998) in the captive animal.

A consideration unique to the male elephant is "musth," which is a mostly seasonal, hormonal activity of the temporal gland characterized by elevated circulating testosterone levels, heightened aggression, and a strong drive to mate (Ganswindt et al. 2010; Kolpin et al. 2020; Burroughs et al. 2021). Animals may be unpredictable and show a lack of compliance for requested trained behaviors during this period. While it is unclear if musth influences the effectiveness or dosage of our sedatives and induction agents (Kock et al. 1984; Firyal & Naureen 2007; Ahmed & Ahmed 2017; Ahmed et al. 2017) it may be wise to avoid elective procedures as at least one report cites the need for increased dosage of sedatives with an excited Asian bull in musth (Firyal & Naureen 2007).

A standardized protocol for withholding food and water in the elephant does not exist due to the many factors that may influence the decision, including patient health, hydration status, environmental temperature, social issues, and preexisting conditions. For example, elephants may become noncompliant with trainers if food and treats are withheld. Conversely, if receiving food or treats, the pharyngeal pouches may need to be manually cleared to prevent aspiration of food debris into the trachea during intubation. Guidance from horses may be extrapolated since both the elephant and horse are hindgut fermenters. Pending diet, an approximately 6–12-hour fasting period was recommended in horses (Robertson & Scicluna 2009; Bettschart-Wolfensberger 2015) and this likely is still appropriate when anticipated recumbency is greater than 90 minutes to 2 hours; fasting duration may need to be even longer for certain procedures (e.g., laparoscopy). However, recent data (Barton et al. 2023) show that for elective orthopedic procedures of short duration, providing grass hay in the perianesthetic period may reduce postoperative ileus.

Anesthetic Risk

The potential for anesthetic-related complications exists in all animals but the elephant poses additional challenges because of their large size, unique anatomy, and physiology. The only description of anesthetic-related morbidity and mortality in managed elephants was reported four decades ago and some of these risks are still relevant today (Fowler 1981). Anesthetic complication rates have been published in small animals (Brodbelt et al. 2015; Matthews et al. 2017), humans (Bainbridge et al. 2012), and horses (Muir & Hubbell 2009; Bidwell 2015; Brodbelt et al. 2015; Dugdale & Taylor 2016; Larenza et al. 2020). The latter demonstrate a higher risk with multifactorial causes including patient characteristics, familiarity of personnel with anesthesia management, analgesic and anesthetic medications or techniques, and tools available for transportation, positioning, physiological monitoring (e.g., direct blood pressure), and support (e.g., oxygen, ventilator).

Patient positioning has been shown to influence outcomes. As with horses, where sternal recumbency was associated with a higher risk of postanesthetic myopathy despite well-maintained respiratory function (Steffey et al. 1990), similar positioning for long duration is believed to be contraindicated and possibly fatal in elephant (Stegmann et al. 2014; Burroughs et al. 2021). In horses increased size is considered a risk factor for development of myopathy or neuropathy (Valberg 2014), which may result in the animal's inability to stand following recumbency. Injuries (e.g., long bone fracture), resulting from the transition to standing are another cause of perianesthetic mortality in horses (Brodbelt et al. 2015). Proper padding, positioning, and blood pressure support can be helpful in alleviating this, but may be challenging when managing a large elephant and can often add significant time to the anesthetic process, which is not desirable. Similarly, drug-induced recumbency is associated with both cardiovascular (e.g., hypotension) and respiratory (e.g., atelectasis and ventilation/perfusion mismatching) compromise. These complications are also known to occur in the anesthetized elephant (Wiedner et al. 2006; Zuba & Oosterhuis 2012; Asquith-Barnes et al. 2017) and early institution of supportive care can be helpful but requires specialized equipment. Recall that it is challenging to successfully perform cardiopulmonary resuscitation in the adult horse and likely impossible in the adult elephant so prevention of life-ending complications is paramount.

Unique Respiratory Anatomy

Elephants have unique respiratory anatomy speculated to be a functional adaptation to gravitational stresses due to the size and weight of the lung (Brown et al. 1997). The elephant thoracic cavity has no true pleural space but has a distensible network of connective tissue which adjoins the parietal surface of the lung to the visceral surface of the thoracic wall (Brown et al. 1997). The connective tissue is not thought to restrict lung movement and it remains unclear if it assists in keeping the large lung inflated during inspiration and expiration (Brown et al. 1997; Stegmann et al. 2014; Rajani et al. 2019). The lung is separated into 1-cm^3 parenchymal units by a system of elastic septa that originates from the lung's thick elastic external capsule or visceral pleura and branch through the lung (Brown et al. 1997). This unique adaptation helps protect dependent alveoli from compression resulting in atelectasis. The diaphragm in the elephant is approximately a 45° angle to the spinal axis, which may minimize compression of the lungs by the intestines in the standing animal (Brown et al. 1997; Stegmann et al. 2014). During recumbency, compression from the intestinal tract my negatively influence breathing (Fowler 1981; Honeyman et al. 1992).

The importance of understanding elephant laryngeal anatomy for intubation and controlled ventilation has been eloquently described by Horne and Loomis (2014). The pharyngeal pouches or saccules are most prominent lateral to the tracheal opening, although a medial ventral saccule has also been described (Rajani et al. 2019). These pouches should be cleared of water or food prior to intubation. A combination of anatomical characteristics makes blind

intubation in the elephant a challenge when compared to the horse. These include a large bulbous tongue, a tracheal opening which is slightly tilted back from the long axis of the oral cavity, and limited dorsiflexion of the head and neck. Hence manual intubation (possibly with a stilette as a guide) is generally recommended. The large inside diameter of the adult elephant trachea necessitates endotracheal tubes (Stegmann et al. 2014) varying in size from 35 to 55 mm inside diameter and 1.6 to 1.8 m in length (In Case of Anesthesia) (see Fig. 44.5). The commercial availability of these specialized tubes has been limited, although a new manufacturer (Mila International Inc.) appears to be dedicated to their production.

Approximately 70–80% of air movement in the awake elephant is through the trunk or nasal passage (Fowler 1981; Isaza 2006; Stegmann et al. 2014; Horne & Loomis 2014), but the elephant can control this and breathe through the mouth if needed. During anesthesia this ability is lost, and the spontaneously breathing elephant is fully dependent on trunk breathing. Hence maintaining the integrity of the trunk during induction of anesthesia and the transition to recumbency is critical. The emergency management were a trunk to become obstructed under the elephant's body must be discussed in advance. Partial obstructions may also occur as the trunk relaxes following drug administration so supporting the same and providing supplemental oxygen during intubation is recommended.



Figure 44.5 A 52 mm inside diameter and 1.8-m long silicone megavertebrate cuffed endotracheal tube specifically manufactured for elephants. Photo of Dr. Julie Sheldon courtesy of J.R. Zuba.

Unique Vascular Anatomy

Vascular access in elephants is readily available from the auricular vessels located on the caudal surface of the ear, although less prominent vessels can also be found on the front of the ear. If ambient temperatures are cold and vessels appear collapsed, the use of warm compresses on the ear will stimulate vasodilation. Since captive elephants can become hypotensive during anesthesia it may be prudent to identify and mark visible veins on the ear and legs with a marker pen before or early after induction in case they become difficult to locate for catheterization. The ear veins are the primary site for rapid intravenous (IV) administration of anesthetic agents (top-ups) during induction or maintenance of anesthesia and may be catheterized. Glue, tape, and sutures or staples are helpful in stabilizing a catheter in case of ear movement during the procedure. Auricular arteries are similarly prominent and may be catheterized to obtain direct blood pressures, arterial blood for analysis of pH, blood gases, and laboratory analytes. Administration of large volumes of fluid requires IV catheters to be placed in the peripheral veins of the limbs. The saphenous vein on the medial surface of the rear leg or the branches of the cephalic veins on the cranial and medial surface of the front leg are typically used. Elephants may also have a moderately sized ventral abdominal vein in a similar location as the milk vein described in the bovid (Pandey et al. 2018), which has been successfully cannulated on several male and a female elephant by one of the authors (J.Z.). The skin overlying the vessels of the leg and abdomen is thick and tough, and will damage the polyurethane sheaths of catheters as they are advanced through the dermis so at least a partial surgical cutdown is recommended, especially if using large-gauge catheters.

Elephant Skin

Since adult elephant skin is thick and tough it is necessary to use long needles (60, 80, or 100 mm in length; DanInject USA) to ensure remote delivery of injectable anesthetic agents deep into a muscle for optimum absorption. These skin characteristics prevent properly placed darts from bouncing out so barbed needles which are difficult to

remove are not required. Ideal dart placement in captive elephants includes the caudal and cranial thigh musculature or the lateral triceps administered perpendicular to the skin. Dart wound treatment is essential and intramammary wet cow preparations have been recommended (Burroughs et al. 2021). Sterile or infected abscesses may occur at the dart site so injection site care should be considered and documented in the medical record for reference.

Procedural Factors

The risks, requirements, and repercussions of the proposed procedure are critically important factors to consider when planning anesthesia in elephants. Medical and anesthetic procedures, for all but very young elephants, will likely need to be performed at the institution's elephant facility away from the familiar comforts of the veterinary hospital. This produces logistical challenges and requires forethought to determine what equipment and supplies need to be relocated to the elephant barn to support the animal and keep those working with the patient safe (Chinnadurai et al. 2016).

Personnel Factors

Since elephant procedures are a "mammoth" undertaking, a successful anesthetic outcome starts with the development and collaboration of many different teams tasked with specific roles. The veterinary team should be experienced with the drugs used for safe and effective anesthesia in elephants, understand the principles of comparative respiratory and cardiovascular physiology during recumbency, and be able to anticipate, interpret, and manage the changing physiologic needs of the anesthetized elephant. Additionally, they should be knowledgeable and willing to guide logistics to favorably influence animal outcome.

The elephant management team should be familiar with the patient's medical issues, individual characteristics, and disposition, and the animal's status within the social dynamics of the herd. They must also be capable of eliciting the trained behaviors necessary for controlled recumbency, skilled in patient rigging and positioning, etc. This team will be relied on greatly to assist in troubleshooting and emergency response.

The facilities and equipment team should be skilled with the operation of the hoist if one is available or additional heavy machinery to move and/or lift an elephant. They should also be trained to use ropes and mechanical advantage equipment and have the tools and experience needed to troubleshoot and repair equipment and facilities. Finally, they should be willing to assist with physical and technical tasks in case an emergency intervention is needed.

Pending the size of the team and availability of skilled and knowledgeable personnel, it is ideal to have an experienced individual assigned to observe the entire process with an eye to keeping personnel safe. A decision-making team of a small number of experienced, ranking individuals from the veterinary, curatorial, and elephant care teams should be identified in advance to help make important and timely patient decisions before, during, and after the procedure. A team meeting prior to the procedure is strongly encouraged so personnel are familiar with everyone and understand individual roles and responsibilities.

Facilities and Equipment Factors

Ideally, elephant facilities should have areas designed specifically to accommodate sedation and anesthesia so that the highest standard of medical care may be administered under protected contact protocols. Climate-controlled enclosures and hospital stalls large enough to move or reposition the patient and safely hold all of the medical and anesthetic equipment, supplies, and personnel are ideal. A training wall to teach medical- and anesthetic-related behaviors where placement of anklets or tethers can be facilitated and with several strategically placed access points for safe movement into and out of the stall in case of emergency is beneficial. Stall modifications for controlled transition to recumbency and an overhead hoist on a mobile gantry if needed for animal movement or assistance to standing as well as a staging area for equipment and personnel close to the procedure stall but out of view and hearing of the patient are also helpful. An essential piece of equipment is an ERD, which allows for the safety of protected contact while allowing behavioral training and minimally invasive husbandry, and reproductive and medical procedures (Rees 2021c; Roocroft 2023a,b). Ideally, an ERD will provide 360° access to the elephant so a variety of diagnostic and treatment practices can be performed, which may reduce the need for sedation and anesthesia for certain medical interventions. The authors recognize that while this describes ideal circumstances, this is likely not available to all those working with elephants and adaptations will be necessary. One author (K.M.) has witnessed the use of other trained elephants to help position the animal being anesthetized. There are also instances where a crane has been brought in to help with animal movement.

The substrate on the floor of the proposed anesthetic enclosure must provide good footing during induction, recovery, and standing while providing optimal padding and support of the patient's body during recumbency. An example is adding 18 inches of sand to the enclosure well in advance of the procedure to acclimatize the patient,

which offers proper footing and conforms to the patient's body for even weight distribution during recumbency. It also will drain fluids if this becomes a concern. Mattresses, thick foam pads, and water beds have been used successfully for anesthetized elephants (Fowler 1981), but getting them to lie on these items is challenging during the transition to recumbency. Prior training such that the animal is positioned appropriately on it while conscious or the ability to move the animal when recumbent so personnel are not compromised can be helpful. Additionally, consideration should be given to supporting upper limbs and head and protecting the eyes. Attention to proper substrate or other support is an important detail that will optimize conditions for standing on reversal and reduce the iatrogenic causes of myopathy and neuropathy.

Ideally, elephant anesthesia and medical interventions are performed in a climatically controlled indoor location of the elephant facility. However, due to need or request, anesthesia may be required outdoors so climatic conditions must be controlled for patient safety. Excessive heat, cold, or precipitation can typically be anticipated so items such as shade/rain structures, fans, heat sources, and water for cooling should be made available.

Developing a Sedation and Anesthetic Induction Plan

The anesthetic plan begins with broad recognition of the needs of the patient, the procedure to be performed, the resources and anesthetic agents available, staff experience, and potential complications. The anesthetic plan is tailored by an experienced anesthesia team for the safety of the patient and success of the procedure. On a larger scale than for other animals, the attending anesthetist will consider three general types of restraint as available for the procedure: physical, behavioral, and chemical. Facilities that have their elephants conditioned for behavioral restraint make these procedures safer and the interested reader is referred to additional information (Riddle & Stremme 2011; Roocroft 2023a; Asquith et al. 2017; Association of Zoos and Aquariums 2018). This section will focus largely on medications used to tranquilize, sedate, and induce anesthesia in elephants. Additional information representing both free-ranging and captive elephant anesthesia may be found in the literature (Lamont & Grimm 2014; Horne & Loomis 2014; Muir 2009; Kreeger & Arnemo 2018a; Meyer et al. 2021a; Mikota & Plumb 2022; Plumb 2022). The selection of medications will depend on other available resources (including facilities and personnel). Delivery options will be discussed subsequently.

Anxiolytics, Tranquilzer, and Sedatives

Please refer to Table 44.2 for additional dosing information and references.

Anxiolytics

Anxiolytics, such as *midazolam*, although available in a concentrated formulation (50 mg/mL injectable formulation; Midazolam HCl, Zoo Pharm), are not used as commonly in elephants under human care as they are in other megavertebrates, such as the white rhinoceros (Jeon et al. 2017). However, one of the authors (J.Z.) has used oral alprazolam in elephants for anxiolysis based on an equine dose developed for an anxious mare during separation from its foal (Wong et al. 2015). Other examples of the successful use of benzodiazepines include oral alprazolam (30 μg/kg) in an anxious adult Asian elephant who was reluctant and fearful of moving into an ERD for an upcoming minor medical procedure (D. Brenner, pers. comm.), an Asian elephant for preinduction anxiolysis prior to placement of rigging equipment in preparation for general anesthesia (D. Brenner, pers. comm.), and an adult female African elephant for temporary separation from its calf who required a minor medical procedure (A. Roth, pers. comm.).

Tranquilizers

Tranquilizers relieve anxiety and tension generally without significantly affecting consciousness, in contrast to sedatives, which may also relieve anxiety but in general cause more whole-body effects such as sleep, muscle relaxation, and analgesia. *Azaperone* is a short-acting and commonly used tranquilizer in free-ranging African elephants for short-duration relocations for management purposes (Coetzee 1996; du Toit 2001b; Grobler et al. 2008; Burroughs et al. 2021; Kreeger & Arnemo 2018b; Rees 2021). In captive elephants, it has been used alone or in combination with sedatives for standing tranquilization for minor medical procedures (Ramsay 2000; Mikota & Plumb 2022) and as a preinduction calming agent prior to etorphine anesthesia (Thongtip et al. 2015; Wenger et al. 2015). It is also a component of BAM™ (Zoo Pharm), a commercially available combination of butorphanol, azaperone, and medetomidine. Azaperone is commonly used with ultrapotent opioids (UPOs) in free-ranging African elephants as it is known to decrease blood pressure and is thought to benefit these animals, which often demonstrate "pink foam syndrome" (Raath 1993; Hattingh et al. 1994a; Still et al. 1996; Plumb 2018; Burroughs et al. 2021), presumed to result from hypertension resulting in pulmonary edema. Elephants in captivity do not seem to develop this side effect with UPOs so azaperone is not typically considered necessary.

Table 44.2 Sedative, anxiolytics, and tranquilizers used in elephants under human care.

Sedative Drugs Used in Elephants

Drug	Dose (mg/kg)	Species	Captive or Wild	Route of Administration	Additional Drugs (mg/kg)	Intent of Additional Drugs	Reference
Azaperone	0.08–0.09	Loxodonta	Captive	IM			Ramsay (2000)
Azaperone	0.017–0.046	Elephas	Captive	IM			Schmitt et al. (1996)
Azaperone	0.060–0.150	Loxodonta		IM			Page (1994)
Azaperone	0.067	Loxodonta	Wild	IM			Raath (1993)
Azaperone	0.04–0.08	Loxodonta	Wild	IM			du Toit (2001a)
Azaperone	0.027	Elephas	Captive	IM			Thongtip et al. (2015)
Azaperone	0.044	Loxodonta	Captive	IM	Detomidine (0.02)	Sedation	Wenger et al. (2015)
	0.048				Detomidine (0.024)	Sedation	
Azaperone	50–90 mg (juvenile)	Loxodonta	Wild	IM	Etorphine (4–8 mg), carfentanil (4–8 mg) (juvenile)	Recumbency	Hattingh (1994b)
Azaperone	80–120 mg (adult), 60–80 mg (subadult)	Loxodonta	Wild	IM		Sedation	Burroughs et al. (2021)
Azaperone	0.04–0.13	Loxodonta	Wild	IM	Etorphine (0.004–0.013)	Recumbency	Still et al. (1996)
Haloperidol	20–30 mg (adults)	Loxodonta	Wild	IM		Sedation	Burroughs et al. (2021)
Haloperidol	0.05	Loxodonta	Wild	IM			du Toit (2001a)
Haloperidol	120 mg (adult)	Loxodonta	Captive	Oral			Papp et al. (2016)
Haloperidol	Variable	Loxodonta	Wild	IM			Raath (1993)
Xylazine	0.2–0.3	Loxodonta	Captive	IM			Ramsay (2000)
Xylazine	0.08–0.15	Elephas		IM			Schmidt (2003)
Xylazine	0.11–0.55	Loxodonta		IM			Schmidt (2003)
Xylazine	0.04	Elephas	Captive	IV			Thongtip et al. (2009)
Xylazine	0.044	Elephas	Captive	IV			Schaftenaar (2013)
Xylazine	0.1	Loxodonta	Captive	IM	Ketamine (0.6)	Standing sedation	Heard et al. (1988)
Xylazine	0.1	Elephas	Captive	IM	Ketamine (0.8)	Standing sedation	Amhed et al. (2017)
Xylazine	0.1	Elephas	Wild	IM		Profound sedation	Kreeger & Arnemo (2018e)
Xylazine	200 mg (adult)	Loxodonta	Wild	IM		Sedation	Burroughs et al. (2021)
Xylazine	0.04–0.08	Loxodonta/Elephas	Captive	IM, IV	Acetylpromazine (0.03–0.07)	Sedation	Fowler (1981)

(*Continued*)

Table 44.2 (Continued)

Sedative Drugs Used in Elephants

Drug	Dose (mg/kg)	Species	Captive or Wild	Route of Administration	Additional Drugs (mg/kg)	Intent of Additional Drugs	Reference
Medetomidine	0.005	Elephas		IM			Sarma et al. (2002)
Medetomidine	0.009	Loxodonta	Captive	IM	Butorphanol (0.03)	Standing sedation	Luders et al. (2016)
Medetomidine	0.005	Elephas	Wild	IM		Profound sedation	Kreeger & Arnemo (2018e)
Medetomidine	0.006	Loxodonta	Captive	IM	Azaperone (0.0008), butorphanol (0.016)	Standing sedation	Laubscher et al. (2021)
Detomidine	0.0055	Elephas		IM			De Silva & Kuruwita (1994)
Detomidine	0.0147–0.0162	Loxodonta	Captive	IM	Butorphanol (0.0147–0.0162)	Standing sedation	Neiffer et al. (2005)
Detomidine	0.018	Elephas	Captive	IM	Butorphanol (0.018)	Standing sedation	Bouts et al. (2017)
Detomidine	0.012–0.025	Elephas	Captive	Transmucosal			C. Bradford (pers. comm.)
Detomidine	0.018	Elephas	Captive	Oral gel			J.R. Zuba & C. Bradford (pers. comm.)
Detomidine	0.012	Elephas	Captive	IM	Azaperone (0.012), butorphanol (0.012)	Sedation	Siegal Willot et al. (2021)
Butorphanol	0.12	Loxodonta	Captive	IM			Ramsay (2000)
Butorphanol	0.01–0.03	Loxodonta	Captive	IV			Ramsay (2000)
Perphenazine enanthate	200–300 mg (adults)	Loxodonta	Wild	IM		Sedation	Burroughs et al. (2021)
Perphenzine hydrochloride	50–200 mg (adult bulls)	Loxodonta	Wild	IM		Sedation	Burroughs et al. (2021)
Zuclopenthixol acetate	100 mg (adults)	Loxodonta	Wild	IM		Sedation	Burroughs et al. (2021)
Dexmedetomidine	0.002	Elephas	Captive	IM			Buranapim et al. (2022)

IM, intramuscular; IV, intravenous.

Haloperidol is a butyrophenone tranquilizer with both oral and injectable forms (Kreeger & Arnemo 2018c; Burroughs et al. 2021). Its intramuscular use is reported for transportation-related tranquilization following immobilization in numerous free-ranging elephants (Coetzee 1996; du Toit 2001b). Successful long-term use of oral haloperidol to treat social disorder and self-destructive behavior in an elephant under human care following relocation to another facility has also been described (Papp et al. 2016).

Sedatives

These can be given to facilitate standing procedures prior to or in combination with other medications, including anesthetic induction agents, as the situation warrants. As mentioned previously they cause a relaxed, sleep-like state that is often accompanied by muscle relaxation or ataxia, and some have analgesic benefits. The most common class of drugs in this category are the *alpha-2 adrenoreceptor agonists*, with many available to choose from. While this class of drugs provides effective sedation and analgesia, cardiovascular side effects, including an initial hypertensive phase that is accompanied by baroreceptor mediated bradycardia, are common. This is usually followed by a hypotensive period. The duration of these effects varies with species, drug, dose, and route of administration.

Xylazine, which was popular historically, has been used successfully for standing sedation in both species of elephants (Ramsay 2000; Thongtip et al. 2009; Schaftenaar 2013). It has also been used in combination with ketamine for transport of African elephants (Heard et al. 1988) and for standing sedation in Asian elephants (Ahmed & Ahmed 2017). It has largely been replaced by detomidine and medetomidine. *Detomidine* is a more potent alpha-2 agonist drug used in elephants for sedation and is frequently combined with butorphanol to facilitate minor medical procedures (Neiffer et al. 2005; Bouts et al. 2017). The transmucosal formulation of detomidine intended for use in horses (7.6 mg/mL; Dormosedan® Gel, Zoetis Inc.) has been effective for repeated standing sedation to facilitate blood collection and treatment in both juvenile and adult Asian elephants during an elephant endotheliotropic herpesvirus outbreak (C. Bradford, pers. comm.). The effective dose was somewhat variable (12–25 μg/kg) but was less than the recommended equine dose of 40 μg/kg. Elephants were trained to accept administration of gel to ensure sublingual mucosal contact as per label instructions, which was particularly useful in animals with an aversion to needles. Oral detomidine gel (18 μg/kg) was administered to a trained adult female Asian elephant as a preinduction sedative, who then complied with a request to lie down in lateral recumbency for IV thiafentanil induction for a prolonged surgical procedure (J.R. Zuba & C. Bradford, pers. comm.).

Medetomidine, a highly selective alpha-2 agonist, has been used in a number of species (Plumb 2022) and is available in a concentrated injectable form of 40 mg/mL (Medetomidine HCl, ZooPharm and NexGen Pharmaceuticals) that allows its inclusion in darts for remote delivery. Medetomidine administered intramuscularly at 5 μg/kg in Asian elephants produced effective standing sedation and analgesia for minor surgery for 1–2 hours without significant bradycardia (Sarma et al. 2002). It has also been combined with butorphanol (Luders et al. 2016) or with butorphanol and azaperone, as BAM® (Laubscher et al. 2021) to provide standing sedation in elephants. The authors and others (Buranapim et al. 2019) have used medetomidine with etorphine or thiafentanil successfully as an adjunct to improve the quality of anesthesia induction for major procedures. *Dexmedetomidine* is the dextrorotary enantiomer of medetomidine and has similar sedative characteristics (Plumb 2022). The first documented use of dexmedetomidine (Dexdormitor®, Zoetis Inc.) in adult bull Asian elephants was recently reported with promising results (Buranapim et al. 2022). When given at 2 μg/kg intramuscularly, dexmedetomidine provided moderate to heavy standing sedation for an average duration of 70 minutes with minimal side effects. Dexmedetomidine is not available in a concentrated formulation at this time.

Alpha-2 adrenoreceptor agonists may be reversed as will be discussed later. BAM™ has been used successfully for standing sedation in semicaptive African elephants with good results (Laubscher et al. 2021). The butorphanol and medetomidine were reversed using naltrexone and atipamezole, respectively, with excellent results. It has been used in zoo and wildlife sedation and anesthesia for years as a replacement for potent opioids in some ungulate species (Burroughs et al. 2021; NexGen Pharmaceuticals 2021). In the near future a more concentrated version of this combination may become available for full immobilization of elephants and other megavertebrates.

Butorphanol is an opioid agonist–antagonist with mild to moderate analgesic and sedative effects in elephants, as with other zoo and wildlife species (Tana et al. 2010). It can be combined with sedatives or tranquilizers for standing sedation in elephants (Neiffer et al. 2005; Luders et al. 2016; Bouts et al. 2017; Laubscher et al. 2021) and is a component of BAM™, as mentioned previously. Butorphanol is available in standard veterinary formulations or in a 50 mg/mL concentrated form (Zoo Pharm). It may be reversed with naloxone or naltrexone, as mentioned later.

Anesthetic Induction Agents

Please refer to Table 44.3 for additional dosing and reference information.

Table 44.3 Anesthetic induction agents used in elephants under human care.

Drug	Dose (mg/kg)	Species	Captive or Wild	Route of Administration	Additional Drugs Given (mg/kg)	Reference
Etorphine	0.001–0.002	Loxodonta		IM	Acetylpromazine (0.002–0.009)	Wallach & Anderson (1968)
Etorphine	5–6 mg	Elephas		IM		Fowler & Hart (1973)
Etorphine	5–9 mg (in calves)	Loxodonta	Wild	IM	Carfentanil (3–7 mg in calves, 10–12 mg in adults), azaperone (40–70 mg)	Raath (1993)
	12–16 mg (in adults)					
Etorphine	4–8 mg (juvenile)	Loxodonta	Wild	IM	Azaperone (40–90 mg)	Hattingh et al. (1994a)
Etorphine	0.003	Loxodonta/Elephas	Wild	IM		Horne & Loomis (2014)
Etorphine	0.002–0.004	Loxodonta/Elephas	Captive			Zuba & Oosterhuis (2012)
Etorphine	0.001	Elephas	Captive	IV		Gage et al. (1997)
Etorphine	0.00066–0.001	Elephas	Captive		Azaperone (0.0266)	Thongtip et al. (2015)
Etorphine	0.0017	Loxodonta	Captive	IM	Acepromazine (0.008)	Wenger et al. (2015)
	0.002				Acepromazine (0.009)	
Etorphine	0.0019	Loxodonta	Captive	IV, IM		Heard et al. (1988)
Etorphine	0.003	Loxodonta/Elephas	Wild	IM		Kreeger & Arnemo (2018e)
Etorphine	14–20 mg (adult male), 10–12 mg (adult female), 2–9 mg (subadult)	Loxodonta	Wild	IM	Azaperone 40–60 mg (adult), 20–40 mg (subadult)	Burroughs et al. (2021)
Etorphine	0.0015	Loxodonta	Captive	IV		Cerreta et al. (2019)
Thiafentanil	12–15 mg (adult)	Loxodonta	Wild	IM		Lance & Kenny (2012)
Thiafentanil	0.003	Loxodonta	Wild	IM		Horne & Loomis (2014)
Thiafentanil	0.0018	Loxodonta	Captive	IV		Cerreta et al. (2019)
Thiafentanil	0.003	Loxodonta	Wild	IM		Kreeger & Arnemo (2018e)
Thiafentanil	9–15 mg (varies by size/age)	Loxodonta	Wild	IM	Azaperone (40–60 mg) (varies by size/age)	Branco & Long (2018)
Thiafentanil	12–15 mg (adult), 2–9 mg (subadult)	Loxodonta	Wild	IM	Azaperone 40–60 mg (adult), 20–40 mg (subadult)	Burroughs et al. (2021)
Ketamine	1.14	Loxodonta	Wild	IM	Xylazine (0.14)	Kreeger & Arnemo (2018e)
Carfentanil	0.0021	Loxodonta	Wild	IM		Kreeger & Arnemo (2018e)
BAM	30 mg, 12 mg, 12 mg (adult)	Loxodonta	Captive	IM		Burroughs et al. (2021)

IM, intramuscular; IV, intravenous.

Ultrapotent Opioids

These have revolutionized zoo and wildlife anesthesia as primary injectable induction agents due to their concentrated formulation and suitability for remote delivery. Other qualities include rapid reversibility and analgesia. Muscle relaxation and cardiopulmonary side effects may be modulated with other drugs and the dose administered. In general, these drugs have a high therapeutic index if respiratory depression can be controlled. They are believed to produce a catatonic state more consistent with immobilization but possibly not true surgical anesthesia, although they are considered analgesic drugs (Kreeger & Arnemo 2018a; Meyer et al. 2021a). The potency of drugs classified in this manner is reported in the literature to be 500 to 10,000 times that of morphine (Haigh 1990; Kreeger & Arnemo 2018d; Meyer et al. 2021a). Additionally, they are highly lipophilic, allowing for rapid passage across the blood–brain barrier. Renarcotization following reversal of potent opioids is described and may manifest as sedation or excitement (Allen 1989). This can be life-threatening if not addressed and is theorized to be due to enterohepatic circulation or redistribution from adipose depots with parent drug outlasting the reversal agents (Lance & Kenny 2012; Kreeger & Arnemo 2018a; Wildlife Pharmaceuticals Ltd. 2022a). Fortunately, while common in ungulate species, documented cases of renarcotization in an elephant could not be found in the literature or in discussion with zoo and wildlife veterinarians experienced in elephant anesthesia.

The UPOs currently available in the United States are *etorphine* and *thiafentanil* (individually discussed below), which require a Schedule II controlled substance license for their use. Clinically they appear to be equipotent in immobilizing healthy captive African and Asian elephants and doses are similar to those used in free-ranging elephants (Horne & Loomis 2014; Kreeger & Arnemo 2018a; Meyer et al. 2021; Mikota & Plumb 2022; D. Grobler, pers. comm.; J.R. Zuba, pers. comm.). Because of their potential danger to humans, some organizations prefer not to utilize these drugs and alternate anesthetic induction agents such as ketamine may need to be considered. Regardless, they must be used with care and accidental exposure protocols should be established and thoroughly reviewed with all personnel before each use (Caulkett & Shury 2014; Zuba & Greenberg 2019; Kreeger & Arnemo 2018d; Morkel et al. 2021). Sedatives or tranquilizers can be used in UPO combinations to reduce the amount of primary induction agent and improve the quality of anesthesia induction. In some circumstances, butorphanol is combined with potent opioids to alleviate the respiratory depression observed with the potent opioids.

Etorphine is the most commonly used UPO in captive and free-ranging elephants due to its long-proven history of anesthetic safety and effectiveness. Etorphine is a thebaine derivative estimated to be 6000 times more potent than morphine (Haigh 1990; Meyer et al. 2021; Wildlife Pharmaceuticals Ltd. 2022b) and has been used in elephants for over 55 years (Wallach & Anderson 1968). It was first synthesized by Bentley and introduced to wildlife anesthesia in the 1960s (Haigh 1990; Horne & Loomis 2014; Kreeger & Arnemo 2018d), with the first report in a captive elephant in 1973, where it was used as an intravenous induction and maintenance agent for the prolonged anesthesia and castration of an Asian elephant (Fowler & Hart 1973). Even 50 years ago, the clinical courage, wisdom, knowledge, and foresight of Dr. Fowler is to be applauded! In the United States, etorphine is available as a 10 mg/mL formulation (Zoo Pharm) or internationally as a 9.8 mg/mL formulation (Captivon 98®, Wildlife Pharmaceuticals Ltd.).

As briefly mentioned earlier, in free-ranging elephants, etorphine is known to cause pulmonary edema and capillary bleeding presumed to be related to the associated hypertension. This has been termed "pink foam syndrome" due to the appearance of pink froth emanating from the trunk (Raath 1993; Hattingh et al. 1994a,b; Horne & Loomis 2014; Burroughs et al. 2021). Interestingly, there are no reports of this syndrome and presumed associated hypertensive episodes in etorphine-anesthetized captive elephants. Some captive elephants are reported to become hypotensive during long anesthetic procedures when etorphine is used as the primary induction agent (Zuba & Oosterhuis 2012; J.R. Zuba, pers. comm.).

Typically, intramuscular etorphine alone or combined with a sedative/tranquillizer can be used to induce anesthesia of an adult male or female elephant under human care within 10–20 minutes depending on dose and other factors. Induction with IV etorphine has also been reported (Fowler & Hart 1973, 1981; Gage et al. 1997; Thongtip et al. 2015; Cerreta et al. 2019). Induction doses generally provide adequate immobilization for most medical procedures for approximately 50–60 minutes and then a method of supplementation or maintenance of anesthesia may be needed. There are also several reports of the successful use of etorphine by constant rate infusion in the captive elephant literature (Fowler & Hart 1973; Zuba & Oosterhuis 2012; Cerreta et al. 2019) and it has been used safely for prolonged maintenance of anesthesia for up to 4 hours in numerous free-ranging and captive elephants (J.R. Zuba & D. Grobler, pers. comm.).

Thiafentanil, an analog of fentanyl, is the newest of the highly potent opioids for use in zoo and wildlife anesthesia and is considered to be equipotent to etorphine in elephants

but with a shorter half-life (Lance & Kenny 2012; Horne & Loomis 2014; Kreeger & Arnemo 2018a; Kock 2020; Burroughs et al. 2021; Meyer et al. 2021a; Wildlife Pharmaceuticals Ltd. 2022a). It became commercially available in 2016 and is available as Thianil® in the United States (10 mg/mL; ZooPharm) and internationally (10 mg/mL; Wildlife Pharmaceuticals Ltd.). Thiafentanil is fully reversed by naltrexone hydrochloride, which competitively binds and displaces thiafentanil from opioid receptors (Wildlife Pharmaceuticals Ltd. 2022c). The shorter half-life of thiafentanil makes renarcotization less likely when reversal agents are appropriately dosed. Due to equipotency with etorphine, thiafentanil can be used for similar clinical indications, including anesthesia induction, supplementation, and by constant rate infusion (CRI) with similar doses. Although there are limited reports of thiafentanil anesthesia of captive elephants in the literature, its use is increasing in both species of elephants with positive clinical results (Cerreta et al. 2019; J. Barnes & J.R. Zuba, pers. comm.; C. Bradford & J.R. Zuba, pers. comm.). In free-ranging African elephants, thiafentanil produces a favorable anesthetic quality with quicker induction times so may become the drug of choice in this species (Branco & Long 2018; Kock 2020; Burroughs et al. 2021; Laubscher 2022; D. Grobler, pers. comm.).

Both etorphine and thiafentanil can be used to provide safe, predictable, and titratable maintenance of IV anesthesia by constant rate infusion in elephants (Zuba & Oosterhuis 2012; Cerreta et al. 2019; Burroughs et al. 2021). This may be desirable due to the ability to rapidly reverse the patient in an emergency. The clinical use of UPOs specifically for maintenance of anesthesia in captive elephants is discussed later in this chapter in the section on the maintenance of anesthesia.

Dissociatives

Ketamine has been used for anesthetic induction of elephants generally in combination with an alpha-2 agent, most commonly xylazine. In one report (Nath et al. 2010), an aggressive adult Asian elephant was administered intramuscular (IM) ketamine (0.1 mg/kg) in combination with xylazine (0.17 mg/kg), which facilitated heavy standing sedation to facilitate translocation. In another report (Jacobsen et al. 1985), 22 juvenile African elephants received IM xylazine (0.14 mg/kg) with ketamine (1.14 mg/kg), which facilitated sedation. IM or IV supplementation of both drugs resulted in recumbency. Reversal of xylazine was accomplished using yohimbine. Allen (1986) describes recumbency in about 14 minutes following xylazine (0.2 mg/kg) and ketamine (1–1.5 mg/kg) IM in African elephants.

Considerations for Induction of Anesthesia and Instrumentation

In this section we will assume the following: the preprocedural planning has been accomplished, experienced subject matter experts will be available as needed, a safe and effective anesthetic plan has been finalized, the patient has been trained to comply at some level of acceptance of rigging equipment for ideal positioning on an appropriate substrate while following protected contact protocols for safety, duties and tasks have been assigned, and all personnel, facilities, and equipment are ready. It's time for induction.

Induction of Anesthesia

Drug Delivery and Route of Administration

Administration of induction drugs is dependent on several factors, including veterinarian experience, drug type and concentration, facility, equipment, and patient compliance. Some animals may be conditioned for IM or IV hand injections at a training wall or ERD, but this requires skill to perform safely with UPOs, which are the most commonly used induction agent. Hand-injection challenges include the risks of accidental exposure as a result of a potentially noncompliant anxious elephant and the technical difficulties of introducing a needle through an elephant's tough skin. Both the hindlimb and triceps musculature are possible hand-injection sites; it is important to be mindful of the elephant's trunk when performing this technique on the front limb. The use of a pole syringe with specialized needles of appropriate length may be less dangerous if the veterinarian has this available and is experienced with its use.

An alternative, safe, accurate, and reliable route for IM administration is through use of remote delivery systems. This can be especially useful in situationally noncompliant or unapproachable patients. Remote delivery systems include projectors, darts, needles, and accessories and have been thoroughly reviewed by others (Horne & Loomis 2014; Isaza 2014; Kreeger & Arnemo 2018e; Kock et al. 2021). Due to the tough, thick skin of the elephant, the dart is equipped with a long needle (60, 80 or 100 mm in length; DanInject) and must make contact perpendicular to the surface to facilitate deep IM injection. Figs 44.6 and 44.7 illustrate recommended dart sites in elephants. Darting from a safe distance and out of view from the elephant with all personnel clear of the dart's trajectory is essential. Once able, the dart should be safely recovered and the injection site rinsed to prevent human exposure to induction agents. It is then cleaned and disinfected thoroughly. All personnel

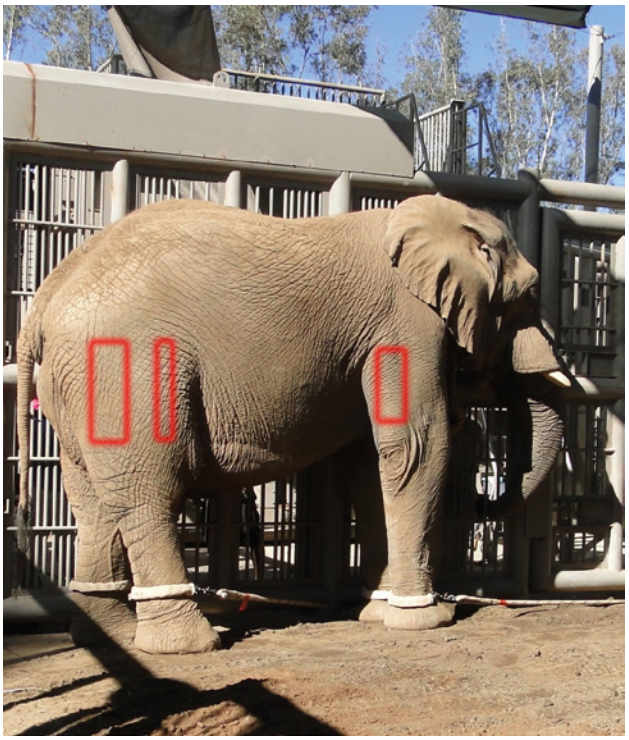


Figure 44.6 Recommended lateral dart sites (red rectangles) for injection of intramuscular anesthetic agents in adult elephants. Long needles (60–100 mm in length) must be used for deep injections and should impact the skin perpendicular to the surface. If darted in the triceps of the front leg, an elephant may be capable of grabbing the dart with its trunk, making it less safe than darting in the rear leg. Photo courtesy of J.R. Zuba.

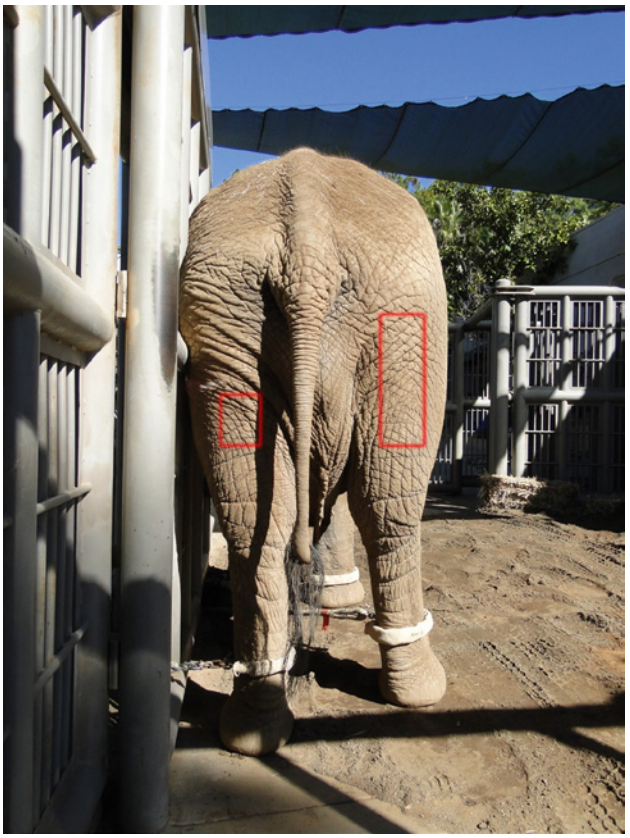


Figure 44.7 When darting an adult elephant from behind and into the caudal thigh muscles, the prominent skin folds must be avoided. Note the skin folds produced due to the position of the left leg, which greatly reduces the area available for proper darting (red rectangles) when compared with the right. Photo courtesy of J.R. Zuba.

should be wearing protective gloves, especially if working around the dart site.

IV administration has been used effectively for induction by several authors (Fowler 1981; Welsch et al. 1989; Gage et al. 1997; Thongtip et al. 2015; Cerreta et al. 2019) but may also include some of the same inherent dangers. For the standing trained elephant, the ear is presented at an access point in the ERD or training wall for IV injection and must be held firmly to avoid unpredictable ear movement when administering potentially dangerous induction agents. Certain elephants can be trained to lie down next to a training wall for IV or IM administration of induction drugs (Fowler & Hart 1973, 1981; Dunlop et al. 1985; Heard et al. 1988; Welsch et al. 1989; Gage et al. 1997; Isaza 2014; Thongtip et al. 2015; Asquith-Barnes et al. 2017; Ceretta 2019). If it is necessary for the patient to be in a specific lateral position for the procedure, it must be trained to stay recumbent for several minutes to mimic the induction period to avoid walking away and becoming recumbent on the incorrect side and in an improper location to perform the medical procedure. Induction by IV administration may only take 1–2 minutes so all team members must be ready to quickly manage the patient if necessary.

Opioid induction dosages are shown in Table 44.3. In general, the higher dosages should provide a smoother transition to recumbency and a deeper plane of anesthesia. Lower doses will provide the expected slower induction but may require the need for supplemental anesthetic agents sooner following recumbency. If rigging for controlled recumbency cannot be finalized prior to induction, an adjusted drug protocol may be necessary to complete the safe placement of the required equipment. This may include a two-dart protocol with a sedative dart to allow rigging followed by the UPO induction dart for recumbency prior to the dart containing the induction agent. Alternatively, a single dart with a lower drug dose may be used to provide a delayed induction so rigging can be completed. In general, the use of standard elephant induction doses (Table 44.3) will provide approximately 45–60 minutes of a safe level of anesthesia before supplemental top-ups or maintenance

anesthetic drugs are necessary (see the section on maintenance of anesthesia). It is advised that the anesthetist have predetermined top-up or maintenance drugs ready to be given in case of unexpected arousal.

Incomplete induction and failed recumbency can occur due to underdosing or dart mishaps (i.e., partial injections, poor dart placement) and present the anesthetic team with a challenging situation. In the author's experience with elephant and other zoo and wildlife species, underdosing a partially anesthetized animal will cause further problems, so a minimum amount of supplement is recommended. The amount of additional drug should be based on the disposition of the partially anesthetized elephant. Broadly, authors suggest allowing 15–20 minutes following the initial dart prior to re-dosing and suggest no less than 50% of the initial UPO dose is given to reduce the potential for underdosing. If only mild or subtle signs are observed, one could consider readministering the same dose as initially administered. As a simple clinical guideline, if the patient is showing only 10% of the expected signs, consider using 90% of original dose; if only showing 30% of expected signs, consider no less than 70% of the original dose and always no less than 50% of the original induction dose in any standing elephant. Since these are guidelines based on clinical experience, it is important to have oxygen available, and be ready to intubate and ventilate the animal. Administration of respiratory stimulants or antagonists to abort the procedure should be considered if the animal is not breathing and therapies cannot be instituted. If problems have escalated due to the partial injection and the safety of the patient and personnel are in question, consider providing reversal agents and reschedule the procedure.

Induction Characteristics and Timing

The timing of induction will be dependent on many factors, including the type and amount of induction agents used, the patient's physical status and general health, type and completeness of administration, and the patient's training and disposition. The expected range of induction characteristics should be reviewed thoroughly with staff members so they can contribute to the elephant's safety and the smoothness of the induction. During induction it is extremely important to keep everything as normal as possible, which includes limiting conversation and loud noises, minimizing elephant exposure to unfamiliar personnel, and keeping activities around the enclosure to a minimum.

Immediately after injection of the induction agent, a favorite trainer may attempt to provide reassurance and minimize apprehension or anxiety. Trainers should be aware that the disposition of a darted or drugged elephant will change, and caution should be used. All personnel should be instructed to keep clear of the administration site on the animal. Dart retrieval should be performed only by an experienced veterinarian following protected contact and safe dart retrieval protocols, including depressurization of the dart prior to removal. As stated previously the UPO dart site should be cleaned, marked, and the area restricted to only experienced personnel wearing gloves.

The following is a common progression of clinical signs in an elephant during induction with UPOs but note that times are estimates and could vary.

- 0–2 minutes post administration: The elephant may be anxious due to intramuscular dart placement.
- 2–3 minutes post administration: Initial signs will be subtle and may include slight behavior changes such as ear flapping, lack of focus, shifting weight, and mild anxiety as the patient experiences the initial drug effect.
- 3–7 minutes post administration: Eyes may become dull and unfocused, ear and tail movement decrease, but the patient still has interest in treats if offered by its trainer.
- 7–10 minutes post administration: The elephant's trunk will become relaxed and it is less successful in finding treats, less responsive to behavioral requests and interactions, penis protrusion may occur in males, patient may assume a base wide stance for stability and possibly lean against nearby bollards or barriers.
- 10–14 minutes post administration: The trunk and nares become progressively more relaxed and flaccid, and the end of the trunk rests on the ground, there is no response to trainer requests and the animal will not eat treats if offered, and the legs may be shaking. This period when the elephant is unresponsive but steady on its feet is a critical time when the experienced support and positioning team may need to enter the procedure arena to place padding in the predicted area of recumbency (if needed) or complete final rigging for controlled recumbency and repositioning. Two belly bands should be in place under the elephant's abdomen and axillary area. If casting the elephant into position with mechanical advantage equipment is planned, slight tension is now placed on the casting ropes.
- 14–20 minutes post administration: The patient becomes increasingly ataxic with minor buckling of legs; personnel must be attentive and keep a safe distance from the patient at this stage as recumbency may be rapid and unpredictable. If using casting ropes, increased tension is placed to guide the patient into lateral recumbency. The induction area should be quiet and calm as the elephant adjusts to being in a recumbent position.

Controlled Recumbency and Initial Patient Positioning

This is a critically important aspect of the elephant anesthetic procedure and, if planned, practiced, and performed properly, can decrease anesthesia time significantly. It is

highly recommended to consult with someone experienced with controlled elephant recumbency and repositioning. Depending on facility, equipment, and personnel it is not unusual for repositioning to take 30 minutes or more. Ideally, the elephant has been trained to accept the placement of anklets, tethers, straps, and stationing prior to induction to assist in controlled recumbency to the best location for the medical procedure.

The process of casting an elephant to recumbency involves behavioral, physical, and chemical restraint and requires an experienced team with specialized equipment, facilities, and training (see Fig. 44.8 for casting an elephant) (Fowler 1981, 1995; Zuba & Oosterhuis 2012; Roocroft 2023a). A coordinated effort is a must. Options for managing elephant movement during induction and subsequently include heavy machinery such as a front-end loader, tractor or reach forklift and mechanical advantage equipment such as block and tackle pulley systems, snatch blocks, come-alongs, winches, and hoists. Several ground-level anchor points equipped with snatch blocks within the induction area are essential for redirecting pulling forces with ropes if the elephant needs to be moved in an unexpected direction. Once recumbent, the elephant should immediately be moved to the ideal location for the proposed procedure. It is also important that this location is appropriate for reversal and standing in case there is an unexpected need for a rapid recovery. For repositioning, a variety of straps of different widths and lengths (4–10 inches wide, 20–40 feet in length) are placed on the elephant and connected to heavy machinery by ropes or chains. Straps are necessary when moving an elephant to evenly distribute tension on contact points of the ankles, legs, abdomen, thorax, neck, or other body parts.

Initial Patient Care and Assessment of Depth of Anesthesia

Just as in all anesthetized patients, the elephant is vulnerable during anesthesia and requires special attention and care. Once recumbent and safe to approach, the anesthesia team should immediately assess the elephant patient for depth of anesthesia, obtain an initial heart rate, respiratory rate and depth, and temperature and, if possible, obtain a blood sample for pH and blood gas analysis. Physical signs of depth of anesthesia following induction include movement of ears, limbs, or trunk, jaw tone, palpebral and swallowing reflexes, response to noxious stimuli, and changes in respiratory rate and rhythm. Since the elephant appears to be an obligate nasal breather during anesthesia the trunk is extended, nares are held open to improve respiratory flow, and supplemental oxygen is provided until intubation. Since repositioning such a large patient can become loud



Figure 44.8 (a) An adult African elephant darted with etorphine is equipped with ropes, pulleys, and mechanical advantage equipment to cast the patient into left lateral recumbency for the intended procedure. The rigging needs to be placed quickly and safely before the bull progresses to full recumbency. Photo courtesy of J.R. Zuba. (b) Traction is applied to the casting ropes by trained personnel to guide the patient to sternal recumbency and while preventing falling on to its right side. Photo courtesy of J.R. Zuba. (c) The recumbent patient is now pulled into left lateral position for the procedure once the depth of anesthesia is adequate. Sometimes heavy machinery such as a tractor, front end loader, or similar is necessary to pull larger patients into the preferred lateral position. Photo courtesy of J.R. Zuba.

and distracting, it is recommended to intubate to establish an airway and ventilate the animal as needed prior to and during the repositioning.

As previously noted, the tip of the trunk/nares may get pinned under the elephant's head or body, causing an obstruction, so a designated team should be ready for emergency intervention. The head of larger elephants may also need to be repositioned for intubation or dental/tusk procedures so straps of appropriate length and strength are attached to an overhead hoist or front-end loader to make quick adjustments. Anesthetized elephants should be maintained in a comfortable thermoneutral environment with equipment to control heat loss or dissipation (i.e., heaters, blankets, fans, shade structures, rain protection, etc.). Eyes must be covered with towels to protect from exposure to the elements and visual stimulation. The eyes are also treated with eyewash and lubricating ointments before attempting to close the eyelids with tape or binder clips on eyelashes if warranted. The downside eye may be difficult to access but should not be overlooked. Ear plugs can be made of various materials to decrease auditory stimulation. Long tags made of tape or rope should be attached to all accessories such as ear plugs so they are obvious and not forgotten at reversal. The downside ear and its auricular cartilage can be damaged during recumbency if it is pinned under the elephant's head in an abnormal position. This is especially true in the African elephant; the ideal position is flat against the downside neck. This ear can then also be more readily used for catheter placement and blood collection. The upper ear can be folded cranially for access to the prominent vasculature on the back of the ear and should be secured in place using sandbags or similar since ear flapping may occur unexpectedly during anesthesia. Legs must be kept in the proper position with the dependent forelimb leg stretched forward and the rear leg perpendicular to the body. Both upper limbs should be supported just as in the horse to decrease the potential for muscle and nerve damage. Hay bales or similar may be used to support the length of each independent leg in a normal anatomic position to avoid impingement of inguinal and axillary nerves and vessels. Occasional massage and physical therapy of the legs of the recumbent elephant should be considered if it can be done safely, especially during prolonged procedures. Any observers without a task should stand at least 10 feet from the patient to allow 360° access for essential personnel and for safety.

Instrumentation

Controlling the Airway, Intubation, and Breathing

The fundamental need for intubation is to establish an airway in anesthetized veterinary species. According to the literature, elephants are estimated to be 70–80% nasal breathers (Fowler 1995; Isaza 2006; Stegmann et al. 2014; Horne & Loomis 2014) when awake and this approaches 100% during drug-induced recumbency. However, the elephant also loses control of the musculature of the trunk and the nares may collapse, which can obstruct nasal breathing. The additional respiratory depression associated with some drugs may further impact breathing, therefore the trunk should be fully extended away from the head and the nares should be propped open. It is recommended that supplemental oxygen be provided through the nares until the elephant is intubated.

The oral cavity of an elephant is unique due to a small mouth for the size of animal and the following considerations: limited articulation in the temporal mandibular joint (which can result in crossing of the dental arcades), large, fleshy, mobile tongue, narrow dental arcade, and redundant cheek tissue. These features obscure visual access except with an endoscope and can make manual access to the caudal oropharynx and the trachea challenging. The position of the larynx, epiglottis, and glottis opening is tilted back at an angle dorsally, which adds to the difficulty in attempts for blind intubation. The vocal folds are robust, rigid, and between breaths, or during apneic episodes, are positioned in a near-closed position thereby producing a narrow and oblong opening to the trachea. This creates a difficult pathway for the endotracheal tube and may hinder the placement of an appropriately sized tube. Additionally, elephants have muscular pharyngeal pouches located in the caudal oropharynx between base of tongue and epiglottis, which may store water and food (Shoshani et al. 1997) and therefore may need to be cleared for safe intubation.

Specialized endotracheal tubes of appropriate material, diameter, length, flexibility, durability, and durometry are necessary for intubation in our larger elephants. The elephant has an acute angle between the long axis of the oral cavity in relation to the trachea, which appears to be greater than other animals. This necessitates using flexible tubes which do not kink under this condition. The commercial availability of variable-sized specialized elephant tubes (35, 45, and 52 mm inside diameter and 1.6–1.8 m in length; In Case of Anesthesia and JZ PICTURE) is limited. However, at this writing, manufacture of these tubes may become available soon (Mila International Inc.). Smaller elephants can be intubated with commercially available endotracheal tubes.

Intubation Protocol

The options for intubating a recumbent elephant will depend on the size of the patient, experience, and equipment. While blind intubation has been described (Thongtip et al. 2015), unlike the horse in which dorsiflexion helps

align the larynx with the oral cavity (Bednarski 2009), this is not easily possible in the elephant. Hand-assisted placement of the endotracheal tube directly into the glottis is possible but requires angling the flexible tip of the tube manually over the fleshy tongue and through the vocal cords (Horne & Loomis 2014). During hand-assisted intubation, the soft palate, which is firmly positioned under the rim of the epiglottis to allow nasal breathing, must first be elevated by the anesthetist's hand, which now will allow breathing through the oral cavity and intubation to proceed. The stylet technique (Bush 1996; Zuba & Oosterhuis 2012) may be used as an alternative and is preferred by many as it tends to be the most efficient technique (Fig. 44.9).

Step-by-Step Guide to Intubation

Multiple people are necessary to intubate an elephant safely and effectively. To gain proper access to the oral cavity, a 2-inch nylon mouth strap with looped ends (or similar), attached to a 12-foot long rope, is placed across the lower jaw (Fig. 44.10). The free end of the rope is then directed through the front legs and grasped by two able-bodied personnel to pull the jaw ventrally to fully open the mouth for proper alignment and access for the anesthetist's arm. The person intubating reaches in with a gloved arm to clean the mouth and pharyngeal pouches of food debris. The caudal edge of the soft palate, which rests under the epiglottis during nasal breathing, is elevated by the intubator's hand to provide direct access to the glottis and tracheal opening. A 2-m long, 8–10-mm diameter stylet, made of acetron, polycarbonate, or PVC (Piedmont Plastics), is cupped in the hand of the intubator, who then reaches into the oral cavity, guiding it through the vocal cords and advancing it approximately 15–20 cm into the trachea. The intubator's arm is removed while maintaining the stylet in place. The external/free end of the stylet is placed through the Murphy eye of the endotracheal tube, which will then guide the endotracheal tube into the trachea. Care is taken to introduce the tube along the midline of the oral cavity to avoid the sharp edges of the molars, which can easily damage the balloon cuff. Once the tube reaches the level of the glottis, it may need to be rotated so the bevel of the tube lines up with the oblong opening of the vocal cords for passage into the trachea. The most practical method of verifying intubation is by movement of air or the presence of breath sounds through the end of the tube during a spontaneous breath. Alternatively, a forced breath from chest compression can be used but this may be difficult in larger elephants. The balloon cuff is pressurized to check for leaks and to confirm there is no air flow through the nares during breathing or ventilation. The endotracheal tube can be secured to a tusk or the trunk by ropes to



Figure 44.9 (a) Stylet technique for intubation of an adult African elephant. The mouth is opened, the anesthetist reaches in with a gloved arm, cleans the oral cavity including the pharyngeal pouches, elevates the soft palate from the epiglottis, places two or three digits in the glottis, then manually advances the tip of the long stylet into the trachea approximately 20 cm. Photo courtesy of Ken Bohn, San Diego Zoo Wildlife Alliance. (b) The free end of the stylet is placed through the Murphy eye of the megavertebrate endotracheal tube (45 mm internal diameter in this 4500-kg patient) and then used as a guide to advance the tube into the trachea. Photo courtesy of Ken Bohn, San Diego Zoo Wildlife Alliance. (c) The beveled distal end of the tube is rotated slightly to assist in entering the trachea through the strong vocal folds for successful intubation. The stylet is removed and the endotracheal tube is stabilized to the patient with ropes. Photo courtesy of Ken Bohn, San Diego Zoo Wildlife Alliance.



Figure 44.10 To intubate, a 2-inch nylon strap with looped ends, attached to a 4-m long rope, is placed around the lower jaw. The free end of the rope is passed through the front legs of the laterally recumbent patient and is firmly pulled caudally by two or three physically capable personnel standing between the front and rear legs to open the mouth. Photo courtesy of J.R. Zuba.

guard against accidental movement during the procedure. During recumbency the mandible should be kept in alignment with the maxilla for the length of the procedure using a support under the lower jaw (e.g., lightweight athletic foam roll, feed bag or pad) (Fig. 44.11).

Vascular Access

When the patient is safely recumbent, the upper ear is folded forward over its eye and stabilized in case of unexpected ear movement. This is easier in the African elephant due to its larger ear size compared to the Asian. Following aseptic preparation, an IV catheter should be placed in one of the many veins on the caudal (and more prominent) surface of the elephant's ear to facilitate drug administration. If a significant duration of recumbency is anticipated, an intra-arterial catheter should also be placed in an auricular artery to facilitate direct blood pressure measurements and sampling of blood for pH, blood gas, and analyte analysis. All auricular catheters (18- or 20-gauge and ideally at least 5 cm in length of a preferred brand) should be stabilized to the ear.

For administration of large volumes of maintenance fluids, the more sizeable veins of the legs are preferred (Fig. 44.12). The medial saphenous vein on the medial surface of the rear leg is accessible in the recumbent elephant, as is the cephalic vein on the craniomedial aspect of the front leg. In larger elephant patients, the length of these vessels will allow multiple large-bore catheters (10, 12 or 14 gauge; Mila International Inc.) to be placed to meet fluid needs for maintenance (Fig. 44.13). To avoid



Figure 44.11 An opioid anesthetized African elephant bull with a managed airway, properly positioned on a thick bed of soft sand to evenly distribute its great weight to avoid muscle and nerve damage. The blue foam roll is used to support the lower jaw in normal alignment which decreases the possibility of kinking of the endotracheal tube and ease of extubation. Photo courtesy of J.R. Zuba.



Figure 44.12 Administration of maintenance intravenous fluids in the rear legs of an opioid anesthetized adult African elephant. Photo courtesy of J.R. Zuba.



Figure 44.13 Three intravenous catheters placed serially in the right medial saphenous vein of an anesthetized elephant for fluid maintenance. Photo courtesy of J.R. Zuba.

damage to pliable catheters, a surgical cut down through the thick, tough skin is typically necessary. It may be advisable to use a permanent marker to identify the course of these veins prior to induction or immediately on recumbency in case of developing hypotension and loss of vessel distention. Several team members may be needed to maintain the patency of these catheters during the procedure due to the finnicky nature of elephant leg vessels. Although more prominent in the female elephant, both sexes of elephants have bilateral subcutaneous abdominal veins, which appear to be similar to the milk vein, which drains the mammary gland in the dairy cow (Pandey et al. 2018). No anatomic description could be found but this vein has been used successfully for blood sampling and fluid administration in recumbent elephants on several occasions (J.R. Zuba & C. Cramer, pers. comm.). The jugular vein and carotid artery have been identified by the author (J.R.Z.) using ultrasound in adult female African elephants, but although catheterization was not attempted, it should be possible using 6-, 8-, or 10-inch long 18-gauge spinal needles (Mila International Inc.).

Drugs, Support, and Monitoring during Maintenance of Anesthesia

The choice of anesthetic and analgesic agents for maintenance is influenced by the patient, drug availability, type and length of the medical procedure, veterinarian experience, equipment, facilities, and personnel. The goal is to keep the elephant at a safe and effective depth of anesthesia and provide suitable analgesia to facilitate the procedure. Additionally, clinical monitoring, interpretation, management, and reassessment are necessary to minimize physiologic complications.

Injectable Drugs used for Maintenance of Anesthesia

As mentioned in the section on anesthetic planning, etorphine and thiafentanil appear to be equipotent in immobilizing healthy captive African and Asian elephants, and doses are similar to those used in free-ranging elephants (Horne & Loomis 2014; Kreeger & Arnemo 2018b; Burroughs et al. 2021; Meyer et al. 2021a; Mikota & Plumb 2022; D. Grobler, pers. comm.; J.R. Zuba, pers. comm.). Both of these UPOs can also be used in the maintenance phase of anesthesia to provide safe, predictable, and titratable maintenance of IV anesthesia by CRI using a syringe pump or by adding drugs to IV fluids set at an intentional rate (Fig. 44.14) (Zuba & Oosterhuis 2012; Horne & Loomis 2014; Cerreta et al. 2019; Burroughs et al. 2021). Etorphine and thiafentanil may alternatively be delivered incrementally intravenously at approximately 10–20% of the UPO induction to maintain the level of anesthesia or add to it in case of unexpected movement (Fig. 44.15) (Fowler et al. 2000; Zuba & Oosterhuis 2012; Thongtip et al. 2015). Ketamine may be used similarly, but has the disadvantage of not being reversible.

Although several factors should be considered, a suggested initial rate for IV etorphine or thiafentanil CRI for maintenance is 0.6 μg/kg/h (Zuba & Oosterhuis 2012) or 2–3 mg/h for adult African elephants (Burroughs et al. 2021). For safety, the attending anesthetist should consider initiating the CRI of an UPO at approximately 60 minutes after induction, which seems to be the time that induction doses lose some effectiveness in providing safe anesthetic depth. The final reversal dose of naltrexone or other antagonists for UPOs is based on the total amount used for induction, maintenance, and supplementation.

Inhalation Anesthesia

Choices for inhaled agents in the elephant are similar to those used in large domestic animals. Isoflurane and sevoflurane are currently the most popular inhaled anesthetics



Figure 44.14 Intravenous and intraarterial catheters placed in the ear of an adult anesthetized African elephant undergoing a prolonged procedure. The anesthetist is actively managing and interpreting direct blood pressure values and collecting arterial samples for blood gas analysis. A constant rate infusion pump provides the intravenous administration of etorphine for maintenance of anesthesia. Photo of Dr. Sathya Chinnadurai courtesy of J.R. Zuba.



Figure 44.15 An etorphine recumbent and immobile African elephant is administered an intravenous supplement of etorphine to ensure proper depth of anesthesia for the procedure. Photo courtesy of J.R. Zuba.

for maintenance of anesthesia in the horse (K. Mama, pers. comm.). While desflurane is available and has benefits in specific circumstances (Brosnan 2013), concerns relative to environmental impacts have resulted in its widespread use being questioned. Both the historic drug halothane (Dunlop et al. 1985; Heard et al. 1988; Welsch et al. 1989; Stegmann 1999) and isoflurane (Dunlop et al. 1994; Gage et al. 1997; Fowler et al. 2000; Thongtip et al. 2015; Wenger et al. 2015; Asquith-Barnes et al. 2017; Buranapim et al. 2019) have been used successfully for maintenance of anesthesia in elephants under human care. While the isoflurane requirement for an elephant is presumed to be similar to that for horses (Dunlop et al. 1994), inhaled anesthetic agents are known to cause myocardial depression and varying degrees of vasodilation, which can result in hypotension and subsequent myopathy (Steffey 2009; Brosnan 2013; Lamont & Grimm 2014; Valberg 2014). Additionally, while dose can be adjusted, it is not possible to immediately able to reverse drug effects in case of emergency and there is the potential for prolonged recovery and difficulty standing (Fowler 1981; Wenger et al. 2015). Hence, thoughtful weaning of the inhaled agent at the end of the procedure is recommended, especially if the injectable agents are to be reversed at the end of the procedure.

Analgesic Drugs

A combination of inhalation and injectable agents may be used to minimize side effects and improve the anesthesia and recovery quality. Alpha-2 agonist drugs and UPOs are not only effective for sedation/induction and maintenance of anesthesia, but are also effective analgesics. Additional perianesthetic and long-term analgesics used in zoological elephants have been reviewed (Bechert & Christensen 2007; Bechert et al. 2008; Kottwitz et al. 2016; Greene & Brenner 2020; Siegal-Willot et al. 2021; Mikota & Plumb 2022) and are summarized in Table 44.4. Experience suggests that elephants may be selective and noncompliant with the intake of oral analgesics so creative strategies are needed when this route is selected, especially for long-term administration. Trainers can be resourced to help with this.

In addition to systemic analgesics, the use of local anesthetics should be considered, as in other species. Not much is known relative to specific nerve blocks, but infiltration, if appropriate, may be utilized. For example, one of the authors (J.R.Z.) has used infiltrative analgesia on five or six cases presenting for tusk removal. While toxic doses are unknown, given their large size it seems unlikely that one could administer a toxic dose/volume for focused procedures. In the example of tusk removal, the total dose used ranged between 0.15 and 0.3 mg/kg. Other examples of the

Table 44.4 Analgesics used in elephants under human care.

Analgesic Drugs Used in Elephants					
Drug	**Dose (mg/kg)**	**Species**	**Captive or Wild**	**Route of Administration**	**Reference**
Flunixin	1		Captive	PO	Mortenson (2001)
Ibuprofen	0.5–4		Captive	PO	Mortenson (2001)
Phenylbutazone	1–2		Captive	PO	Mortenson (2001)
Butorphanol	0.015	Elephas	Captive	IV or IM	Tana et al. (2010)
Iburpofen	4–6	Elephas and Loxodonta	Captive	Oral	Bechert & Christensen (2007)
phenylbutazone	2–4	Elephas and Loxodonta	Captive	Oral	Bechert et al. (2008)
Phenylbutazone	0.25–6	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
Flunixin	0.28–1.1	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
	0.4–1	Elephas and Loxodonta	Captive	IV	Kottwitz et al. (2016)
	0.28–1.1	Elephas and Loxodonta	Captive	IM	Kottwitz et al. (2016)
Iburpofen	1–6	Elephas	Captive	PO, rectal	Kottwitz et al. (2016)
	1–7	Loxodonta			
Ketoprofen	1–2	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
	1–2	Elephas	Captive	IV	Kottwitz et al. (2016)
	0.963	Loxodonta	Captive	IM	Kottwitz et al. (2016)
Firocoxib	0.1	Loxodonta	Captive	PO	Kottwitz et al. (2016)
Xarprofen	0.2–0.3	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
Meloxicam	0.2	Loxodonta	Captive	PO	Kottwitz et al. (2016)
Acetaminophen	0.5–1.5	Loxodonta	Captive	PO	Kottwitz et al. (2016)
Vedaprofen	0.45–0.7	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
	0.5–1			Rectal	
Etodolac	2–2.7	Elephas	Captive	PO	Kottwitz et al. (2016)
Aspirin	62.5 mg	Elephas	Captive	PO	Kottwitz et al. (2016)
Tramadol	0.5–3	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
Butorphanol	0.01–0.08	Elephas	Captive	IM	Kottwitz et al. (2016)
Fentanyl	0.078 μg/kg	Elephas and Loxodonta	Captive	Transdermal patch	Kottwitz et al. (2016)

(*Continued*)

Table 44.4 (Continued)

Analgesic Drugs Used in Elephants

Drug	Dose (mg/kg)	Species	Captive or Wild	Route of Administration	Reference
Glucosamine and chondroitin sulfate	1.1–1.5	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
Gabapentin	0.4–6	Elephas and Loxodonta	Captive	PO	Kottwitz et al. (2016)
	1	Elephas and Loxodonta	Captive	Rectal	Kottwitz et al. (2016)
Prednisolone	up to 1	Loxodonta	Captive	PO	Kottwitz et al. (2016)
Dexmethasone	0.05	Loxodonta	Captive	PO, IV	Kottwitz et al. (2016)
Lidocaine to effect	10–30 mL 1%	Elephas and Loxodonta	Captive	SQ	Kottwitz et al. (2016)
Polysulfated glycosminoglycans		Loxodonta	Captive	IM	Kottwitz et al. (2016)
Pentosan polysulfate	3	Elephas	Captive	IM	Kottwitz et al. (2016)
Flunixin meglumine	0.3–1		Captive	PO, IM	Greene & Brenner (2020)
Ibuprofen	6		Captive	PO	Greene & Brenner (2020)
	5–10		Captive	PO	Greene & Brenner (2020)
	3.5		Captive	PO	Greene & Brenner (2020)
Ketoprofen	1–2		Captive	PO	Greene & Brenner (2020)
Meloxicam	0.5–1		Captive	PO	Greene & Brenner (2020)
	0.1		Captive	PO	Greene & Brenner (2020)
Previcox	57–750 mg		Captive	PO	Greene & Brenner (2020)
Phenylbutazone	1–2		Captive	PO	Greene & Brenner (2020)
Butorphanol	5 mg		Captive	PO	Greene & Brenner (2020)
Gabapentin	1–3		Captive	PO	Greene & Brenner (2020)
	2.5–10		Captive	PO	Greene & Brenner (2020)
	2–5		Captive	PO	Greene & Brenner (2020)
Adequan	?		Captive	IM	Greene & Brenner (2020)
Cosequin	?		Captive	PO	Greene & Brenner (2020)

Emcelle tocopheron	2.5–6.6 IU/kg		Captive	PO	Greene & Brenner (2020)
Ibuprofen	3.2	Elephas	Captive	PO	Siegal-Willot et al. (2021)
Cosequin	8	Elephas	Captive	PO	Siegal-Willot et al. (2021)
Gabapentin	0.2	Elephas	Captive	PO	Siegal-Willot et al. (2021)
Hyauluronic acid	0.077	Elephas	Captive	IV	Siegal-Willot et al. (2021)
Polysulfate glycosaminoglycans	0.13	Elephas	Captive	IM	Siegal-Willot et al. (2021)
IRAP	12–15 mL per site	Elephas	Captive	IA	Siegal-Willot et al. (2021)
Buprenorphine	0.0008	Loxodonta	Captive	IM	Wenger et al. (2015)
Meloxicam	0.12	Loxodonta	Captive	SQ	Wenger et al. (2015)

IA, Intraarterial; IM, intramuscular; IV, intravenous; PO, orally; SQ, subcutaneous.

use of local anesthetic techniques include a modified retrobulbar block using mepivacaine for bilateral cataract removal (Cerreta et al. 2019) and bupivacaine for eye enucleation (Bliss et al. 2023). Information from the dissection of the infraorbital nerve of a postmortem African elephant has been used to guide the infiltration of 100 mL of a 50:50 mix of 0.5% bupivacaine and 2% lidocaine in an attempt to desensitize this nerve in several opioid-anesthetized adult African elephants for dental and tusk procedures (A. Woody and J.R. Zuba, pers. comm.). Protocols used in the horse have been suggested for elephants.

Support During Anesthesia

In addition to appropriate positioning and padding as previously discussed, ocular protection is important. On recumbency each eye should be flushed and treated with an eye lubricant, and this should ideally be repeated at necessary intervals. This can be challenging with the lower eye, so after initial cleansing and lubrication the eyelids may be shut with binder clips across the eyelashes or with tape or transparent film dressing (Tegaderm Film, 3M Healthcare) placed over the eye. At a minimum a towel should be placed on the ground under the head to protect the eye from dust and debris.

Cardiovascular Support

Fluid Therapy

Maintenance fluid requirements during anesthesia in elephants are not established but it is reasonable to use 3–5 mL/kg/h, which is commonly used in the domestic equid (Crabtree & Epstein 2021; Nolan-Walston 2012). Others suggest 3–5 mL/kg/h plus colloids at 4–5 mL/kg/h in the equine patient, which may maintain hemodynamics better than crystalloids alone (Hardy 2009) but this technique is not broadly used. A 12-gauge short-term catheter properly placed in anesthetized domestic horses can deliver 7 L per hour with the fluid bag elevated 2.5 feet above the patient (Munsterman 2020). Furthermore, fluid flow rates can be increased by using wider bore catheters and increasing the height of the fluid bag (Lord et al. 2021) or by using specialized administration tools. To meet the maintenance fluid requirements of adult elephants, administration of volumes of 15–30 L of fluid per hour can be achieved by using multiple large-bore (12–14 gauge) catheters in leg veins with fluid bags elevated 5–8 feet above the patient. Fluid pumps may also be used. Rectal fluids using gravity flow might be considered if fluid needs were not met during the procedure or if the animal is debilitated and not expected to drink following full recovery.

Additional Cardiovascular Support

While not much is known about inotropes and vasopressors in elephants, it has been suggested that doses used in horses are a good starting point. One option is ephedrine, which has mixed alpha and beta effects (0.05–0.1 mg/kg IV) and may be administered by bolus for treatment of hypotension. Alternatively, dobutamine (0.5–2 μg/kg/min IV CRI), which has largely inotropic actions, or norepinephrine (0.05–0.1 μg/kg/min IV CRI), which has both alpha and beta actions, or phenylephrine (1–2 μg/kg IV as bolus or by CRI at 0.3–0.5 μg/kg/min IV), which is an alpha-1 agonist, may be used pending the suspected cause of hypotension. If an animal exhibits hypertension, the depth of anesthesia should be evaluated prior to administration of vasodilating drugs.

Respiratory Support

Ventilation

Drug-induced recumbency is known to influence respiratory function in horses (Muir 2009) and author experience suggests that especially when using an opioid and/or inhalation agent-based protocol, hypoventilation is likely and ventilatory support may be needed (Moreno-Martinez & Mosing 2021; Moreno-Martinez et al. 2021).

Options for ventilation of adult elephants include using a large animal anesthesia machine or two joined together (Dunlop et al. 1994; Fowler et al. 2000), a homemade double-demand valve ventilator (Horne et al. 2001), a custom elephant anesthesia machine made by Mallard Medical with 100-L tidal volume capabilities, a portable equine demand valve (JD Medical Equine Demand Valve, JD Medical), and a portable, adjustable, megavertebrate demand ventilator designed for elephants from 1500 to 7200 kg (In Case of Anesthesia) (Fig. 44.16). This device was also reported to be effective in ventilating several UPO-anesthetized adult Southern white rhinoceroses (*Ceratotherium simum*), which are known to have respiratory complications during opioid anesthesia (Jeon et al. 2017). Since anesthetic events in captive elephants are performed away from the hospital, large medical oxygen tanks with regulators capable of delivering high flow rates are needed to supply the power and volumes of oxygen necessary for ventilatory support. The approximate tidal volume for an adult elephant weighing 3000–5500 kg at 10 mL/kg is 30–55 L.

When ventilation is not possible, insufflation of oxygen is recommended to offset the hypoxemia that may develop with hypoventilation and recumbency in room air-breathing animals.



Figure 44.16 A portable, compressed oxygen powered, venturi enhanced, megavertebrate ventilator (made by In Case of Anesthesia) is used by the anesthetist to control respirations in an intubated adult elephant undergoing a prolonged anesthetic procedure. Photo courtesy of J.R. Zuba.

Respiratory Stimulants

Doxapram is a central nervous system respiratory stimulant used in nonventilated anesthetized animals experiencing apnea or hypoventilation (Kreeger & Arnemo 2018a; Meyer et al. 2021a; Plumb 2022). It has been used successfully in the anesthetized African elephant (Jacobson et al. 1988) and in the author's practice. Doxapram is not a substitute for mechanical ventilatory support but may be considered in a respiratory emergency when intubation and ventilation was not intended or is unavailable, such as following extubation of an anesthetized elephant. Since it is considered a central nervous system stimulant, arousal is possible and this potential should be considered relative to animal and personnel safety. It is generally believed to work best when the animal is supplemented with oxygen and not hypoxemic.

Monitoring During Anesthesia

Anesthetic Depth

Physiological and physical or behavioral parameters may be used to monitor anesthesia depth. Published physiologic parameters for awake (Honeyman et al. 1992; Mikota 2006; Horne & Loomis 2014) and anesthetized (Dunlop et al. 1994) elephants are available for reference. While movement is an obvious sign of an animal exhibiting a lighter plane of anesthesia, the goal would be to identify this circumstance prior to this. Increasing trunk tone or ear movement might be early signs of a lightning plane of anesthesia and should be considered in the face of drugs given and time elapsed since administration. Palpebral reflexes, response to noxious stimuli etc. may also have value.

Cardiovascular Monitoring

Clinical monitors for the cardiovascular system are similar to those used in other species and include the electrocardiogram (ECG) and direct and indirect blood pressure. Many anesthetic monitoring models are available, which should have battery options and be capable of withstanding the field-like conditions of captive elephant anesthetic procedures. The ECG is an important monitor in the elephant since direct auscultation of the heart for rate and character can be inconsistent and unrewarding due to chest size, thickness of skin, and background noise during procedures. However, it is important to also remember that the ECG only provides information related to electrical activity so mechanical activity should be assessed using other tools. Six-lead ECG parameters were documented in 27 unsedated Asian elephants and provide reference information (Bartlet et al. 2009). While in clinical practice a three-lead ECG is viable, longer leads and special attachments may be necessary. Portable handheld monitors (e.g., Vetcorder™ PRO, Sentier) are useful both initially prior to equipment set up and at the end of a procedure when most personnel and equipment must be cleared from the immediate area.

Direct blood pressure is ideal when possible since both hypertension (Jacobson et al. 1987; Dunlop et al. 1994) and hypotension during prolonged procedures (Zuba & Oosterhuis 2012; J.R. Zuba, pers. comm.) have been reported. The arteries of the ear are readily catheterized and attached via tubing to a transducer for continuous pressure measurements. This also facilitates sampling of arterial blood for pH, blood gas, and laboratory analytes. The use of indirect blood pressure monitoring with a cuff on the tail of an elephant has provided inconsistent results in the author's experience; similar discrepancies with oscillometric monitors have been reported in the equine literature (Radhakrishnan et al. 2021). As in other species, additional qualitative assessment of cardiovascular function includes mucous membrane color, capillary refill time, vessel distention, and digital palpation of the auricular vessels for pulse strength.

Respiratory Monitoring

As in human beings and other species, indirect (e.g., pulse oximetry, capnography) and direct techniques (e.g., blood gas analysis) may be used to assess function. While the equipment has not been assessed for accuracy in elephants, it does provide trends over time, which can be useful in alerting the anesthesia team to respiratory problems. In equine and other large animal species, drug- and recumbency-associated hypoventilation and ventilation-perfusion mismatching are common and may lead to hypoxemia (Auckburally & Nyman 2017; Larenza et al. 2020). The qualitative properties of respiration, including depth and character, are also important and should be continuously monitored during the procedure.

Pulse oximetry estimates the percentage oxygen saturation of the blood and is a standard tool in indirectly monitoring oxygenation in veterinary species (Haskins 2015), but can be inconsistent in elephants due to anatomy and lack of ideal probe locations. A transmittance probe is intended for use across skin surfaces, but due to the thickness, rough surface, and pigmentation of elephant skin it is sometimes unobtainable or may need frequent attention. The outer edge of the ear can be used but will require thorough cleaning and scraping of surface debris with the edge of a scalpel blade or similar. Any pink unpigmented mucosa such as inside the tip of the trunk, roof of mouth, vulva, prepuce, or sulcus of tusk can be considered. A more reliable method in the elephant is the use of a lightly lubricated reflectance probe carefully placed over the mucosa of the medial canthus of the eye, avoiding contact with the cornea.

Capnography in the intubated elephant provides a breath-by-breath estimate of ventilatory status with continuous readout of end-tidal carbon dioxide ($ETCO_2$) tensions. While the accuracy of this technology is not verified in large mammals such as the elephant, values provide estimations that can be compared with the $PaCO_2$ from arterial blood gas analysis (which is only sampled intermittently) to provide information relative to ventilation and dead space (Rainger et al. 2010).

Monitoring acid-base status with a benchtop or, in its absence, portable point-of-care blood analyzer (e.g., iSTAT, Abbott Laboratories) throughout anesthesia is another valuable method for the early detection and management of emerging complications. Since portable blood gas monitors and associated cartridges are not designed for use in the temperature extremes and unpredictable conditions of an elephant barn or outside enclosure, the analyzer will need a thermal-neutral environment to match manufacturer's recommendations to ensure consistent results.

Monitoring and Management of Other Body Systems

As has been previously mentioned, myopathy and neuropathy are possible in large recumbent mammals such as the elephant. Hence time must be spent in appropriately positioning and padding the animal's body and limbs. Minimizing recumbency time is also helpful as is providing support if blood pressure (and presumably perfusion) is below ideal limits.

Monitoring of the gastrointestinal system of the elephant during anesthesia is similar to that in the horse (Greene et al. 2019). Abdominal distention can occur due to hindgut bloat and may cause discomfort and progressive pressure on the diaphragm, resulting in reduced tidal volume and changes in breathing, especially in lengthy procedures. Since management is difficult once developed, early recognition is important so a decision can be made to abort the procedure if intestinal bloat becomes clinically significant.

Prevention and Management of Complications

Cardiovascular Complications

Both hypertension and hypotension have been reported in captive African and Asian elephants during UPO anesthesia. During prolonged anesthesia and recumbency in elephants, hypotension is perhaps the most clinically significant cardiovascular perturbation, necessitating early recognition and management. Isoflurane-induced hypotension in an opioid anesthetized African elephant has been reported (Wenger et al. 2015) and has been observed by the authors, again highlighting the importance of monitoring blood pressure and having tools available to treat this. A decrease in arterial blood pressure during general anesthesia in horses has been associated with postanesthetic myopathy and poor outcomes (Grandy et al. 1987; Valberg 2014; Rowland 2019). It is reasonable to assume similar conditions are likely in elephants and deserve attention. The clinical definitions of hyper- or hypotension during anesthesia and when to intervene are not well defined in the elephant. Even in human medicine they are not entirely agreed on, but hypertension and hypotension are often defined as 20% above or below the patient's normal arterial pressure, respectively (Lonjaret et al. 2014; Li et al. 2017; London 2021; Saugel & Sessler 2021).

Despite the lack of published information on blood pressure regulation in the elephant, it is still clinically important to intervene using extrapolations from the effective management protocols of the domestic equine. A published mean arterial pressure (MAP) for captive awake standing African and Asian elephants is approximately 144 mmHg (Honeyman et al. 1992) and this has been used by the authors as the target MAP in numerous captive elephant anesthetic procedures. This value is also used to establish an acceptable range for blood pressure

using the human recommendation of 20% above or below the normal value. Hence hypotension may be considered when the MAP is less than 115 mmHg and hypertension when the MAP is greater than 175 mmHg. When values fall outside this range, the cause should be investigated and addressed. This is especially true for hypotension due to the concern for adequate perfusion of muscles, especially those necessary for a return to the standing position on reversal.

Myopathy and Neuropathy

While myopathy and neuropathy are challenging to treat in the horse, the elephant poses a magnitude of challenges beyond them so the impact on outcome can be very significant. Hence, as noted previously, it is recommended that treatment is initiated if the MAP decreases toward 110 mmHg. Since fluid volume is hard to administer rapidly and anesthetic depth adjustments may not be possible in keeping with personnel and elephant safety, management includes the use of inotropes and vasopressors commonly used in domestic horses (Hardy 2009; Muir 2009; Crabtree & Epstein 2021; J.R. Zuba, pers. comm.; Zuba & Oosterhuis 2012). See the section on cardiovascular support for drug and dose information.

If hypertension is noted, patient depth and response to analgesic or anesthetic medications should be evaluated. Hypertension may be a physiological response to poor perfusion in other areas of the body and this hypertension may indicate potential issues that may need to be recognized and treated. Hydralazine may be considered as a nonspecific treatment of hypertension.

Respiratory Complications

Respiratory complications, including hypercapnia or hypoventilation and resulting respiratory acidemia, can occur during anesthetic drug-induced recumbency. The use of potent opioids as induction and maintenance agents, and the use of inhaled anesthetics for maintenance both contribute (Schumacher et al. 1995; Horne & Loomis 2014). If lightening the plane of anesthesia or partially reversing drugs that cause respiratory depression are not options, ventilation of the elephant may become necessary. Options for managing this circumstance were previously noted.

Ventilation perfusion abnormalities or mismatching may also occur during drug-induced recumbency, an effect that seems to be magnified in larger species such as the horse. This (along with hypoventilation in room air-breathing animals) can result in hypoxemia (Steffey et al. 1977; Stegmann 1986; Day et al. 1995). While differences in elephant anatomy including dense connective tissue and elastic connections to the pleural surface (Brown et al. 1997) may reduce hypoxemia resulting from atelectasis, the partial pressure of arterial oxygen (PaO_2) was shown to significantly decrease over time in nonmedicated laterally recumbent elephants of both species (Honeyman et al. 1992). This was speculated to be due to shunting (of blood away from ventilated alveoli) and not hypoventilation since a rise in $PaCO_2$ was not seen. It is not known if anesthetic drugs contribute further to this, but reports suggest that this decrease in PaO_2 over time is evident in anesthetized elephants, for example a significant decline in PaO_2 was found over time in juvenile African elephants anesthetized with UPOs (Schumacher et al. 1995). The author's experience suggests that oxygen tensions decrease over time despite early ventilation using pressures that would be considered high for a domestic horse of approximately 40–50 cmH_2O. Since this pressure is usually measured on a gauge external to the animal, the pressure and compliance dependent volume being delivered to the lung are not known and it is possible that uniform lung expansion is not being achieved. The equipment available to provide ventilatory support is often not designed for such a large mammal and might also be a factor. Supportive mechanisms such as the use of positive end expiratory pressure or bronchodilators have not been evaluated in the elephant.

Aside from being aware of this potential and trying to minimize recumbency duration, there is concern that hypoventilation and hypoxemia may continue into the recovery phase at a time when oxygen and ventilatory support are being tapered or discontinued. Data from horses support that the sternal or standing position is better for pulmonary function than lateral recumbency (Francois et al. 2014; Stegmann 1986) so if it is possible to maneuver the recovering elephant into sternal recumbency there may be benefit to the animal. There is, however, limited data from elephants to endorse this approach uniformly and other negative effects of sternal positioning may need to be considered. Another approach is therefore to safely reverse UPO and alpha-2 agonist drugs while providing oxygen by insufflation initially through the endotracheal tube and subsequently through the trunk.

Reversal and Recovery

Recovery from anesthesia is a critical phase, especially in large mammals such as elephants. This phase of anesthesia has inherent risks as the ability to monitor and manage the patient is diminished. Ideally the elephant should be positioned in a location that facilitates a safe recovery following the induction of anesthesia, but this may not be possible and the animal may need to be moved again or repositioned during recovery. Similar tools and processes as described

during induction with skilled personnel and appropriate equipment to maximize efficiency are recommended. Basic principles such as positioning the patient in an area with proper substrate and away from structures that may interfere with standing, maintaining a quiet and calm environment, etc. are very important. Familiar personnel to verbally reassure the elephant during this potentially anxious and confusing period might be helpful, but caution is advised as a recovering elephant may be suspicious or anxious of the intentions of even generally trusted personnel.

Weaning from Supportive Care

In preparation for reversal, a weaning process is initiated to incrementally decrease or discontinue anesthesia maintenance drugs, supportive care (i.e., IV fluids, etc.), and ventilatory support. This phase can be unpredictable and challenging in some patients so a well thought out plan including notification of potential dangers with an alert staff is advised. All nonessential monitoring devices and equipment are removed from the recovery area but should be kept close in case of emergency. A portable ECG and pulse oximeter (e.g., Sentier Vetcorder Pro™) are ideal to replace larger monitoring devices during reversal since they provide valuable information and can be easily removed when it is time to leave quickly. Only experienced staff with essential duties remain at the patient's side.

Reversal Drugs

Alpha-2 Adrenoreceptor Antagonists

While historically many alpha-2 antagonists (including yohimbine, tolazoline and idazoxan) have been available, atipamezole has largely gained favor for reversal of alpha-2 agonist drugs. It is a specific alpha-2 antagonist available as a concentrated compounded formulation (25 mg/mL; Zoo Pharm, Fort Collins, CO) or less concentrated small animal preparation (5 mg/mL, Antisedan®; Zoetis US). Due to the potential for side effects following IV administration, it is recommended (by the manufacturer) that atipamezole is administered intramuscularly. In an emergency, IV administration of a partial dose may be considered. Both routes generally result in a quick and smooth reversal of agonist medications such as xylazine, detomidine, medetomidine, and dexmedetomidine (Meyer et al. 2021; Plumb 2022). Examples of atipamezole use are documented in the literature (Luders et al. 2016; Bouts et al. 2017). "Resedation" is possible and likely explained by a differential elimination half-life of some alpha-2 agonist drugs relative to atipamezole. Animal species may also play a role in this phenomenon.

Ultrapotent Opioid Antagonists

The preferred antagonist for rapid reversal of a captive opioid-anesthetized elephant in the United States is naltrexone (50 mg/mL; ZooPharm), which can be given intravenously or intramuscularly. It is considered a complete opioid antagonist with a species-dependent and usually long duration of action, which minimizes the chance for renarcotization (Horne & Loomis 2014; Kreeger & Arnemo 2018a; Burroughs et al. 2021; Meyer et al. 2021). Naltrexone reversal is recommended at 10 mg for each 1 mg of thiafentanil and 20 mg for each 1 mg of etorphine (Lance & Kenny 2012; Meyer et al. 2021a; Wildlife Pharmaceuticals Ltd. 2022c). Higher doses of naltrexone of 25–50 mg per 1 mg of thiafentanil or etorphine have also been used safely in captive elephants by an author (J.Z.) and others (Cerreta et al. 2019). In free-ranging African elephants, a reversal combination of 5 mg of naltrexone plus 2 mg of diprenorphine per 1 mg of etorphine or thiafentanil can be used (Burroughs et al. 2021). Diprenorphine is a mixed opioid agonist-antagonist that has been used successfully to antagonize the effects of opioids in captive settings in the United States and when immobilizing elephants in Africa (Horne & Loomis 2014; Kreeger & Arnemo 2018a; Meyer et al. 2021; Wildlife Pharmaceuticals Ltd. 2022d). Diprenorphine is manufactured as Activon® (Wildlife Pharmaceuticals Ltd.) specifically for reversal of etorphine (Captivon®, Wildlife Pharmaceuticals Ltd.). The final dose of the antagonist should be based on the total amount of UPO used for induction, supplementation, and maintenance of anesthesia.

The ability to rapidly reverse alpha-2 and opioid-anesthetized elephants is extremely valuable, especially during clinical emergencies or following extubation at the end of a procedure, when ventilation can no longer be supported and it is important to recover the patient. Since emergence can be very rapid, all nonessential personnel and equipment must be at a safe distance from the recovery area when naltrexone is given.

Characteristics and Times Following Opioid Reversal in the Captive Elephant

The etorphine- or thiafentanil-anesthetized elephant generally has similar characteristics on reversal but emergence and standing are sometimes unpredictable. The actual time to each of the key characteristics will vary depending on other drugs, the patient, and procedural factors including the length of anesthesia, type and reversibility of the other agents, reversal drug, dose, route of administration and the elephant's physical and physiologic status and inherent behavioral characteristics.

The following is a review of the clinical reversal characteristics of a typical uncomplicated anesthesia of an elephant anesthetized with a UPO and medetomidine, and reversed with IV naltrexone and IM atipamezole.

- 0–2 minutes post reversal: Return of palpebral reflex, intermittent shallow breaths, weaning off ventilatory support, all patient-side personnel on alert to exit.
- 2–3 minutes post reversal: Initial swallowing against the endotracheal tube, return of deeper and more regular spontaneous respirations, if intubated ventilatory support is stopped, all unnecessary personnel exit.
- 3–4 minutes post reversal: Purposeful ear, tail, and trunk movement, eyes wide open and responsive, extubation occurs (see next section) following return of deep and productive spontaneous respiration.
- 4–5 minutes post reversal: The favorite keeper should begin talking to the patient to offer comfort and reassurance during recovery, return of normal respiration through the trunk, ear flapping, head movement with trunk sniffing and probing.
- 5–10 minutes post reversal: Increasing awareness leading to first purposeful movements, favorite keeper offering encouragement to stand, first attempt to move to sternal then to standing, unsteady on feet, standing base wide.
- 10–20 minutes post reversal: Progressive return to preanesthetic state, steady on feet and walking normally, return of urination/defecation, trainers may attempt to reestablish relationship but with caution.

  Note that standing times can be as quick as 2–3 minutes or delayed as long as 30 minutes and are dependent on many factors.

Extubation

The extubation process must be a coordinated effort and is a balance between safety for the patient and safety for personnel. All tie-downs for the endotracheal tube are removed and the balloon cuff is deflated. Ventilation may continue but weaning is advised by decreasing respiratory rate and depth. Deeper, more regular spontaneous respirations, swallowing reflex, and return of purposeful movement of eyes, ears, and legs are indicative of time to extubate. The use of mouth straps to open the lower jaw may be necessary to remove the endotracheal tube and protect the balloon cuff from molar damage. A distinctive rumbling sound is sometimes heard following extubation as the soft palate falls back into normal position under the glottis and breathing returns through the trunk. If possible, oxygen can be insufflated through the trunk while the animal continues to recover.

The Process of Standing

It is beneficial to understand the basic biomechanics of how an elephant stands. Strength and coordination during standing are very important in these large animals so providing full reversal for the elephant will ensure full recovery. Since anxiety and confusion may occur as drug effects wane, the area must be kept quiet and calm with only familiar personnel present. The goal is to reduce early and unsuccessful attempts to stand, which may be frustrating, exhausting, and potentially dangerous for the elephant. This is especially true for animals with physical disabilities that may affect standing.

Following appropriate reversal, the recumbent elephant moves lateral to sternal and then stands by elevating its front half prior to the rear, similar to the movement of the domestic horse and rhinoceros, but with one important modification: due to its great weight and size, to obtain sternal position, an elephant uniquely initiates this process by throwing its independent (i.e., upper) rear leg caudally to create the momentum necessary to assist the front half of its body to roll to sternal position. As it rolls, the front legs are extended forward while the rear legs are tucked under its body. The elephant will now first stand by lifting the front half of its body followed by the rear. Since the throwing of the leg assists in gaining sternal position, ideally the elephant's feet and legs should be positioned 6–8 feet safely away from any wall or solid structure to allow this unique movement.

Once standing, it is not uncommon to see a transitory paresthesia and slight lameness of the dependent front leg, especially following prolonged recumbency with less than ideal padding. It is characterized by a dropped elbow and buckling at the fetlock, which usually persists for 2–5 minutes so the elephant should be kept calm and in place while presumably normal nerve function and muscle perfusion return. Delay in standing or failure to stand following reversal is a significant potential complication and could evolve into a medical emergency. It is difficult to quantify the amount of time which an elephant should take to stand following reversal since there are many factors involved, including age, physical status, preexisting conditions, duration of recumbency, and procedural repercussions. Prolonged recumbency in an adult healthy elephant is defined here as a procedure in which the anesthetized patient is maintained in the lateral position for over 1.5–2 hours. If the recumbent, fully reversed, and alert elephant does not stand within 20–30 minutes or after three to five vigorous attempts following periods of rest, intervention should be considered. The response should be rapid and include initiation of the previously discussed and practiced contingency plan for assisted standing. Mental fatigue and

physical exhaustion may occur after intense unsuccessful attempts to stand and cause the recumbent elephant to lose motivation to stand, leading to further delays and complications.

Managing Prolonged Recumbency

The cause of a failure to stand or delayed attempts to stand may be the result of a known preexisting condition, repercussion of the medical/surgical intervention, myopathy or neuropathy that developed from recumbency (Dunlop et al. 1994), frustration from poor footing, or a combination of these. It is reasonable to compare the etiologies of a delayed recovery of an elephant with those of the domestic equine (Muir & Hubbell 2009; Bidwell 2015; Gozalo-Marcilla & Ringer 2021) or recumbency in the domestic bovine, also known as "downer cow syndrome". This is a difficult situation where veterinary leadership, teamwork, and experience are required to determine the etiology and manage this potentially life-threatening incident. The elephant patient may be anxious and unpredictable under these stressful conditions so extreme caution is necessary.

Since incomplete reversal is a possibility, repeat administration of antagonists should be considered. Enthusiastic verbal encouragement to stand from favorite personnel should be attempted, especially in those patients who appear conscious and responsive. Obtaining patient vitals and a blood sample should be considered to assist in identifying the cause as long as this can be done safely. Small amounts of favorite foods and water may be offered if needed to influence the animal's well-being and cooperation. If available, introducing a familiar companion elephant into the recovery area or in an adjacent pen with clear visual or trunk-to-trunk contact can be considered. Consider offering pain relief, improved substrate, or modification of other environmental conditions if these are possibilities. If conservative attempts fail, assisted standing protocols must be initiated.

A strategy to physically assist a recumbent elephant to sternal and then standing positions requires prompt intervention, a well-defined plan with backup options, safety considerations, specialized equipment, and trained personnel. Each situation will vary in complexity so options need to be explored and practiced prior to anesthesia, especially for patients expected to have difficulty standing. Allow the patient time to rest and become completely alert and aware before initiating assistance. A crucial step for the laterally recumbent elephant is to first achieve sternal recumbency, which may motivate it to stand on its own. If the patient is making unsuccessful attempts to reach sternal recumbency, manual assistance can be considered to help push the patient to sternal recumbency (Fig. 44.17). Due to inherent dangers, this topic should have been previously discussed and assistance provided only by willing, physically capable, experienced personnel while working exclusively along the dorsum of the elephant and away from the reach of the trunk and legs. As the elephant rocks back and forth during normal attempts to move to sternal recumbency, personnel can take advantage of the momentum and make timely efforts to push the elephant into sternal recumbency. Introducing a tractable, favorite herd mate into the recovery area may comfort and encourage the patient to stand.



Figure 44.17 If an overhead hoist or other lifting devices are not available, physically capable trained personnel may be necessary to assist and encourage the patient to stand. Using this female African elephant's momentum during its attempts to stand, the team was successful in assisting her to sternal position prior to standing. Photo courtesy of J.R. Zuba with permission from Dr. Jackie Gai.

If conservative attempts to stand are unsuccessful the use of heavy machinery will be necessary. Due to the great weight of adult elephants, access to an overhead lift system, such as a hoist or crane, with lifting straps or a sling is fundamental and has been used successfully (Fig. 44.18) (Fowler 1995; Fowler et al. 2000; Phair et al. 2014; Cerrata 2019). A large animal rescue lift system (Häst Tripod Large Animal Rescue Frame) capable of lifting an elephant is now commercially available. If straps cannot be applied prior to recumbency, a strap guide (Häst Large Animal Rescue Lift System) can be used to pass lifting straps under the thoracic and inguinal areas of the recumbent elephant, which can then be attached to a lift system. It is worth noting the recent availability of animal rescue and disaster response organizations such as Animal Search and Rescue (ASAR; https://asartraining.com), which provide specialized equipment and training to zoo personnel to assist standing and lift recumbent animals, including elephants.



Figure 44.18 For procedures performed outdoors, a crane or other lifting devices may be necessary to assist an elephant to stand following prolonged anesthesia, especially older patients or those with preexisting conditions. Photo courtesy of J.R. Zuba.

Postprocedure Monitoring

All anesthetized elephants should be monitored closely for 24 hours following recovery, including an overnight watch for all debilitated patients or those that do not appear fully recovered at the end of the procedure day. Within the first hour of recovery from a predominantly opioid and alpha-2 anesthetic (and reversal), the elephant should be alert, responsive and clear-headed, steady on their feet, and manage to urinate and defecate. An elephant may be distrustful and reluctant to interact with trainers immediately after a procedure so all personnel need to be cautious. Once the elephant appears to be clinically normal, access to small amounts of food and water can begin at approximately 1–2 hours following a satisfactory recovery, with 25% incremental increases over the next 24 hours. Ideally, the recovering elephant should be isolated and monitored for normal behavior, appetite, and excretions for 24 hours, but the social needs of the individual must also be considered.

Summary

Providing safe and effective anesthesia for captive African (*Loxodonta africana*) and Asian (*Elephas maximus*) elephants poses significant clinical challenges. These include unique anatomy, physiology, and behaviors, and the need for specialized equipment, medications, facilities, and trained personnel. With recognition that there is much to still be learned, this chapter provides practical information relative to anesthetizing captive elephants to maximize the chance of a successful outcome. The authors hope to have also communicated that this is a significant undertaking and success depends on each member of the team.

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Manufacturers

3M Healthcare
DanInject USA, Austin, TX, USA
Häst, Floyd, VA, USA
In Case of Anesthesia, La Jolla, CA, USA
iSTAT, Abbott Laboratories, Abbott Park, IL, USA
JD Medical, Phoenix, AZ, USA
JZ PICTURE, San diego, California
Mallard Medical, Redding, CA, USA
Mila International, Inc., Florence, KY, USA
NexGen Pharmaceuticals, Weatherford, TX, USA
Piedmont Plastics, San Diego, CA, USA
Species 360, https://species360.org/products-services/zoo-aquarium-animal-management-software-2/
Sentier, Waukesha, WI, USA
Tegaderm Film, 3M Healthcare, St. Paul, MN, USA
Wildlife Pharmaceuticals Ltd., White River, South Africa
Zoetis Inc., Kalamazoo, MI, USA
Zoetis US, NJ, Kalamazoo, Michigan, USA
Zoo Pharm, Fort Collins, CO, USA

45

Nondomestic Equids

Chris Walzer

Introduction and Taxonomy

The Equidae family encompasses the zebras, asses, and horses. These descended some 50 million years ago from the "dawn horse" (*Hyracotherium*), with the *equus* emerging in the Pleistocene, about 1.5 million years ago. The taxonomy of the nondomestic equidae is controversial; the International Species Information System (ISIS) lists eight wild species with several subspecies, three zebras and one wild ass in Africa, and three wild asses and the Przewalski's horse in Asia. They are distributed solely throughout the Old World, from the deserts of Namibia across the plains of eastern Africa to the high-altitude semi-deserts of central Asia. In addition to the wild equidae, feral horses and donkeys (or burros) exist on all continents except Antarctica. Generally, the present-day equids exploit the semiarid grasslands, where they play a key role in the functioning of natural grazing systems. Within their natural range, many equids are subjected to extreme weather conditions. For example, temperatures range from −45°C in the winter to 40°C in the summer, with diurnal temperature ranges in excess of 35°C at the reintroduction site for Przewalski's horses in the Dzungarian Gobi in Mongolia. The equidae utilize a great range of altitudes within their present-day distribution, 60 m b.s.l. (Danakil: Somali wild ass) and 5000 m a.s.l. (Tibet: Kiang) (Strauss 1995). For further information concerning the status and geographical distribution of the various subspecies, the reader is referred to the IUCN/SSC Equid specialist group publications (Moehlman 2002; Kaczensky et al. 2018). Of particular importance in the captive and medical management of wild equids is an understanding of their two distinct social systems (Moehlman 2002). In the equids of the arid habitats, some males defend territories, preferably near water sources, which confer mating rights over females when they enter the territory. Asses and Grevy's zebra form loose groups, and the only long-term relationship occurs between mother and offspring for a period of 2 years. Asses in central Asia may aggregate to loose groups in excess of several 100 individuals. The other equid species form predominantly family groups, so-called harem groups. In this system, lifelong relationships between adult individuals are formed. Young males form bachelor groups. The various social systems must be considered when managing these species in general, but especially the removal of individual animals from a harem group during anesthesia must be critically evaluated.

Anatomy and Physiology

The anatomy and physiology of the wild equids is similar to that of their domesticated counterparts (Table 45.1). The mountain zebras (*Equus zebra hartmannae* and *Equus zebra zebra*) are distinguished from other zebra species by a "grid iron" pattern formed by stripes on the rump and a small dewlap on the throat (Duncan 1992). The Grevy's zebra (*Equus grevyi*) is the largest wild equid. They are easily recognizable on the one hand due to their size, and on the other due to the large ears and distinct fine stripe pattern. The plains zebras (*Equus burchelli* spp.) are one of the most abundant ungulate species in Africa. Subspecies can be distinguished by the variations in their stripe patterns. The classification and number of the subspecies is controversial. The African wild asses are sympatric throughout their range with the domestic African donkeys, and it is probable that the genomes of the wild and domestic asses are extensively mixed. Unlike the Przewalski's horse and the domestic horse, the wild asses and donkeys have the same number of chromosomes and appear similar. Differences persist in leg colors, counter shading, and shoulder crosses. The Asian wild asses (*Equus onager, Equus kiang*, and *Equus hemionus*) vary little in size, but skeletal and color differences allow the various subspecies

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Table 45.1 Biological data of the wild equids.

	Birth Weight	Adult Weight	Life Expectancy	Reported Gestation Length	Nursing in Months
Przewalski's horse	45	250–375	33	330–340	6–8
Asian wild ass	25–30	200–250	29	330–360	6–9
African wild ass	20–30	250–300	24	360	4–6
Grevy's zebra	20–30	350–450	35	387–428	6–13
Plains zebra	33	350–450	29	365–375	6–10

Sources: Adapted from Strauss G. 1995. Einhufer. In: *Krankheiten der Zoo- und Wildtiere* (R Göltenboth, H-G Klös, eds.), pp. 189–200. Berlin: Blackwell Wissenschafts-Verlag; Duncan P, ed. 1992. *Zebras, Asses, and Horses: An Action Plan for the Conservation of Wild Equids*. Gland: UCN.

to be distinguished. The Przewalski's horse (*Equus ferus przewalskii*) is closely related to the domestic horse; although they are distinct in the number of chromosomes (Przewalski's horse $2n = 66$, domestic horse $2n = 64$) their hybrids are fertile (Ryder et al. 1978). The Przewalski's horse has an erect mane, and the proximal aspect of the tail has short guard hairs. Most Przewalski's horses have a dark stripe along the back and distinct horizontal stripping of the palmar aspects of the front legs. Latest genetic research has shown that the Przewalski's horse is most probably not the direct ancestor of the present domestic horses, but more likely a sister taxa (Wallner et al. 2003).

Physical Restraint of Equids

Although physical restraint cannot be recommended for any wild equid, except possibly newborn foals, nonchemical capture methods have been employed in the zoo-born Przewalski's horse. In the course of the various reintroduction projects to Mongolia, specific techniques and methods have been developed to facilitate loading. For the first time in 2002, nonchemical capture and crating was possible for the majority of zoo-born horses. The system was based on training each individual horse to feed in large crates over a period of several weeks. The crates were subsequently closed using a remote system and the horses moved into smaller transport crates (Fig. 45.1) (Walzer et al. 2004). In 2005, a similar simplified system was also used successfully in Takhin Tal, Mongolia, to move eight horses into the west of the Gobi B Strictly Protected Area (Schönpflug & Walzer, unpub. data, 2005).

Individual transport crates for equids are based on the IATA recommendations and have been adapted over the years for this specific airfreight transport scenario but are most probably beneficial for all equid transports (IATA 2006). Head and neck movement in the crate has been limited to reduce the risk of a horse turning onto its back while inside the crate at takeoff during air transport



Figure 45.1 Nonchemical capture of the zoo-born horses. Individual horses are fed in large crates over a period of several weeks. The crates are subsequently closed using a cable-controlled remote drop-door system.



Figure 45.2 Head and neck movement in transport crates is restricted with padding to reduce the risk of a horse turning onto its back at takeoff during air transport.

(Fig. 45.2). The headroom of the crates is additionally lined with high-density foam mats to limit abrasions and trauma due to head-rubbing. Alternatively, and for land transport, equids can be mass crated (Openshaw 1993).

Vascular Access Sites and Monitoring

Vascular access is easily performed in the various equid species. As a routine measure, an intravenous (IV) catheter should be placed during all equid anesthesia procedures, as this provides constant venous access if an emergency should arise or additional drugs must be provided. The jugular veins provide an excellent venous access site for standard "over-the-needle" catheters. Large-bore catheters should be used to provide adequate fluid flow rates. At least 14 standard wire gauge (swg) should be used (Taylor & Clarke 2007). These can be placed either with the flow or against the flow. Placing catheters against the flow (towards the head) is often easier and reduces the risk of air entrainment (Taylor & Clarke 2007). Alternative venous access sites are the distal branches of the saphenous vein and the external thoracic vein. Arterial access and catheter placement is most easily achieved in the facial and transverse facial artery. These sites can be used to determine the pulse rate, collect arterial blood samples for blood gas analysis, and direct blood pressure monitoring. The handling and storage of arterial blood samples may affect blood gas values (Klein et al. 2005).

In general, anesthesia monitoring in the wild equid species is analogous to that in the domestic horse. Anesthesia monitoring should be implemented as soon as the animal is fixed. Sequential rectal temperature measurements, thorax excursion to determine breaths per minute, and auscultation for heart rate are the absolute minimum in anesthesia monitoring. Relative percentage oxyhemoglobin saturation measured with a battery-powered pulse oximeter (e.g., Nellcor NP-20, Nellcor Incorporated, Pleasanton, CA, USA) is useful to determine arterial oxygenation and gives a good insight into respiratory function. Pulse oximeter probes can be affixed to the tongue, nasal septum, and plucked ear (Fig. 45.3). Several excellent reviews have been previously published and the reader is referred to these (Saint John 1992; Taylor & Clarke 2007).



Figure 45.3 Portable pulse oximeter probe affixed to the tongue of an Asiatic wild ass.

Intubation

Endotracheal intubation is easily achieved in the equid species. For intubation, the head is extended. When using almost-straight silicone endotracheal tubes (ETs), these can be advanced directly into the trachea. When using the older curved red-rubber type ETs, the ET is initially advanced with the concave curve dorsally until the soft palate is dislodged from the epiglottis and then rotated 90° and passed on down the trachea (Taylor & Clarke 2007).

Chemical Restraint and Capture

Oral Sedation

Varying degrees of sedation can be achieved using acepromazine as granules (Vetranquil 1%, Albrecht, Germany) or as a paste (Sedalin, Chassot, Switzerland) at a dosage of 0.5–1.5 mg/kg per os (PO). The granules are mixed into moistened pelleted feed or the paste is placed in apples, both of which are then readily consumed by the animal. Though this is not sufficient for subsequent physical restraint, it has proven valuable as a transport and preimmobilization sedation (Wiesner 1993).

Parenteral Sedation

Various drugs, especially alpha-2 agonists and acepromazine (Vetranquil 1%, Albrecht), have been used to sedate wild equids. Detomidine (Domosedan, SmithKline Beecham Animal Health) at 20–80 mg/kg intramuscular (IM) has been used successfully in some wild equids (Morris 1992; Vitaud 1993). In contrast to the experiences gained with detomidine, these authors warn against using the alpha-2 agonist medetomidine (Dormitor, SmithKline Beecham Animal Health) alone as a preanesthetic due to the occurrence of significant ataxia (Morris 1992). Similarly, romifidine (Sedivet, Boehringer, Germany) has been shown to cause ataxia (Wiesner & von Hegel 1990). Acepromazine is used at a dosage of 0.15–0.25 mg/kg IM. Furthermore, azaperone at a dosage of 200 mg has been suggested for the sedation of zebras (Burroughs 1993a). Several other drugs would potentially be useful in sedating equids, but are impracticable in their use due to the large volumes necessary.

Long-acting Neuroleptics

When long-term sedation is required, as during a transport process, this is best achieved using one of the long-acting neuroleptics (LANs). This group of drugs can be used

Table 45.2 Suggested dosages for long-acting neuroleptics in selected wild equids.

Drug	Burchell's Zebra	Hartmann's Zebra	Przewalski's Horse	Onset of Sedation	Duration
Haloperidol	0.3 mg/kg	0.28–0.35 mg/kg	0.2–0.3 mg/kg	5–10 minutes	8–18 hours
Zuclopenthixol	50–100 mg/adult	50–100 mg/adult	50–100 mg/adult	1 hour	3–4 days
Perphenazine	100–200 mg/adult	200 mg/adult	150–200 mg/adult	12–16 hours	10 days

Sources: Based on Swan GE. 1993. Drugs used for the immobilization, capture, and translocation of wild animals. In: *The Capture and Care Manual* (AA McKenzie, ed.), pp. 2–64. Pretoria: Wildlife Decision Support and the South African Veterinary Foundation; Walzer C, Baumgartner R, Robert N, et al. 2000. Medical aspects in Przewalski horse (*Equus przewalskii*) reintroduction to the Dzungarian Gobi, Mongolia. Proceedings of the American Association of Zoo Veterinarians, pp. 7–21.

to reduce anxiety and stress during long-distance translocation, and for reintroduction into novel enclosures and habitats. As a result of the delayed absorption of the neuroleptics, it is prudent to combine a long-acting tranquillizer with a short-acting analog (Ebedes 1992). Haloperidol belongs to the butyrophenone group of neuroleptics with a longer duration of activity. It is available in Europe as a 5-mg/mL injectable solution (Haldol, Janssen-Cilag, Vienna, Austria) that can be applied IM and IV. Furthermore, 1- and 10-mg tablet forms (Haldol, Janssen-Cilag) for oral application are also available. It is important to note that in Europe haloperidol is also available as a decanoate ester (haloperidol decanoate, Janssen-Cilag), an oily form that results in a long-term deposit. Haloperidol decanoate results in a prolonged sedation of up to 25 days and its effects are generally unsatisfactory due to adverse side effects such as inappetence and central nervous system symptoms (Swan 1993). Zuclopenthixol acetate is a thioxanthene similar to the phenothiazine group of tranquillizers. Through esterification with the acetate and dissolution in a vegetable oil, absorption and duration has been extended. It is available as a 50 mg/mL injectable solution (Ciatyl-Z-Accuphase, Bayer, Leverkusen, Germany). Similar to haloperidol, zuclopenthixol is also available in some countries as a decanoate ester; again, the duration is extended, but once again the effect seems inadequate (Swan 1993). Perphenazine is a phenothiazine derivate with a piperazine side chain. It is available as a 100 mg/mL injectable solution in the enanthate ester form, dissolved in a sesame oil (Decentan Depot, Merck KgaA, Darmstadt, Germany). When compared with haloperidol and zuclopenthixol, perphenazine has a markedly prolonged duration of action that can subsist for 10 days. These neuroleptics have been used successfully in various zebra species (Swan 1993) and in Przewalski's horse (Atkinson & Blumer 1997; Walzer et al. 2000a). Extrapyramidal symptoms (EPS), a neurological side effect, causes a variety of symptoms, for example involuntary movements, tremors, changes in breathing and heart rate, and inapetenz have been recorded as the most important side effects of LANs. The EPS can be treated with biperidine (Akineton, Knoll, South Africa) and diazepam (Valium; Roche, Switzerland). The use of long-acting neuroleptics has greatly facilitated the in-crate phase during flight (36 hours) and reloading of Przewalski's horses. This author presently recommends treatment with a combination of 0.2–0.3 mg/kg haloperidol (Haldol, Janssen-Cilag) and 150–200 mg/adult equid perphenazine (Decentan-Depot, Merck KgaA). It is important to carry out this treatment at least 12–24 hours prior to transport or anticipated stressor influence (Table 45.2).

Anesthesia

Applying drugs over a greater distance requires specific remote delivery systems. For an excellent review of the various available systems, the reader is referred to Kreeger et al. (2002) and Chapter 5 in this book. The author recommends the use of a CO_2-propelled dart gun, such as the Daninject JM model (Daninject JM™, Wildlife Pharmaceuticals, Fort Collins, CO, USA). Previous authors have warned against using high-velocity gun systems (e.g., the Cap-Chur® system) in zebras due to their thin skin (Burroughs 1993b). When working in the wild, this author prefers to use new 3-mL darts discharged by expanding compressed air (Daninject, Wildlife Pharmaceuticals). Old darts are not used, as these are never as accurate. By shortening the dart stabilizers to 3 cm, the effective range is 80 m under ideal conditions (Lengger et al. 2002). However, this distance is significantly reduced in windy conditions. A sufficiently long dart needle of 55 mm is required to efficiently dart an Asian wild equid in good condition during the late summer and fall due to significant layers of fat in the rump region. For zebras, a needle length of 25–30 mm has previously been recommended (Burroughs 1993b). In captive zebras, this is most probably too short, and the use of 55 mm should be considered. The use of wire barbs or collars on the needle to securely retain the dart in the animal is recommended to enable complete drug expulsion. Once an animal is successfully darted, one should attempt to keep it in sight. However, it is very important at this



Figure 45.4 The head of a horse should be fixed at all times during an immobilization procedure. The knee is best placed laterally on the maxilla.

stage to not disturb the animal any further by chasing it or approaching before the drugs have taken full effect. Once the animal has become recumbent, an approach on foot from behind and immediate fixation of the head is recommended (Fig. 45.4). Be aware that in the first few minutes of recumbency, the animal may become aroused by voices or loud noises and attempt to rise and flee further. Anesthesia monitoring should be implemented as soon as the animal is fixed.

The agent of choice for wild equid immobilization and anesthesia is the potent opiate etorphine. The opiates interact in the central nervous system with stereo-specific and satuarble receptors (Kreeger et al. 2002). Various receptors have been identified. These are classified as κ, δ, σ, μ receptors. A major advantage in the use of the opiates is the specific opiate antagonists that allow for the complete reversal of the anesthetic effects. Whereas some agents can be classed as sole antagonists (e.g., naltrexone), others have agonist–antagonist properties (e.g., diphrenorphine). The opiate ethorphine is an analog of thebaine and is in humans 500 times more potent than morphine (Jasinski et al. 1975; Kreeger et al. 2002). Etorphine at 2.45 mg/mL is available in Europe and many other parts of the world in combination with acepromazine 10 mg/mL (Large Animal Immobilon, C-Vet Veterinary Products, Leyland, UK). Furthermore, ethorphine is available as a mono substance at 4.9 and 9.8 mg/mL (M99, Vericore Ltd., Dundee, UK). All products are supplied in a container together with the antidote diprenorphine or M5050 in the respective adequate dosages. The use of diprenorphine to antagonize etorphine in nondomestic equids may increase the likelihood of renarcotizations. In North America, due to difficulty in obtaining ethorphine, a similar, more potent opiate, carfentanil (Wildlife Pharmaceuticals Ltd.) has been used extensively in equids (Allen 1992, 1994, 1997; Klein & Citino 1995). However, the effects of carfentanil cannot be equated with those of ethorphine as the procedure is markedly rougher with significant muscle contractions (Morris 1992). In the past years, several additional nonnarcotic immobilization protocols have been developed and used more or less successfully in wild equids (Matthews et al. 1995; Morris 1992; Vitaud 1993). For prolonged surgical procedures, intubation and inhalation anesthesia with isoflurane or halothane is recommended.

For wild equid anesthesia, this author presently recommends a combination of the opiate etorphine (M99, C-Vet Veterinary Products, Lancashire, UK), the sedative alpha-2 agonist detomidine-HCl (Domosedan, Orion Corp. Farmos, Turku, Finland), and the mixed antagonist-agonist opioid buthorphanol (Torbugesic, Fort Dodge Animal Health, Fort Dodge, IA, USA). Detomidine acts on the alpha-2 adrenergic receptors, where it inhibits the release of norephinephrine. Butorphanol is a μ-opioid receptor antagonist that alleviates the marked respiratory depression induced by the ethorphine at the μ receptor and potentiates the sedative effect at the κ and σ receptors. Furthermore, this combination has significantly limited the ethorphine specific pacing, which greatly reduces the distance an equid travels after darting. This is particularly important in open steppe habitats, where equids darted without the addition of butorphanol can cover several kilometers before becoming recumbent. However, the combination still allows for "walk-in" crate loading. Etorphine is reversed with the opioid antagonist naltrexone at a rate of 20:1 (Trexonil, Wildlife Laboratories Inc., Fort Collins, CO, USA). Naltrexone has a longer half-life than the antagonist-agonist diprenorphine (Revivon, C-Vet Veterinary Products) and eliminates in- and post-transport renarcotization. Renarcotization is an effect that occurs when using opioids. Several hours after antagonist application, the animals once again come under the influence of the opioid agonist (Kreeger et al. 2002). Especially in equids captured in the wild, this effect could be fatal as it potentially makes an individual more prone to predation and injury. However, it is important to note that due to the long half-life, a subsequent anesthesia induction with etorphine (or any other opioid), in case of emergency, would not be possible, and an alternative method (e.g., the alpha-2 agonists medetomidine and ketamine) needs to be considered (Table 45.3).

Chemical Capture of Equids in the Wild

Przewalski's Horses

Due to the general lack of cover in the Gobi area, wild Przewalski's horses are extremely difficult to approach in the field. During the past years, we have employed various methods to get within shooting range, such as approaching

Table 45.3 Selected anesthetic protocols for wild equids.

Species	Drug 1	Drug 2	Additional Drugs	Antagonist	Comments	Reference
Kulan (*Equus hemionus*)	4.2 mg etorphine	17 mg ACP	30 mg xylazine	6 mg diprenorphine + 0.125 mg/kg yohimbine	Total dose for adult	Kreeger (1996)
	0.016 mg/kg etorphine	0.067 mg/kg ACP		0.042 mg/kg diprenorphine + 0.4 mg/ kg nalorphine	$n = 27 + 49$	Strauss (1992, 1999)
	5.4 mg etorphine		150 mg ketamine	250 mg naltrexone	Total dose for adult, $n = 3$ wild	
	4.4 mg etorphine	10 mg butorphanol	10 mg detomidine	6 mg diprenorphine	$n = 17$ wild	Walzer et al. (2006)
Kiang (*Equus kiang kiang*)	0.012 mg/kg etorphine	0.05 mg/kg ACP		0.025 mg/kg diprenorphine	$n = 26 + 10$	Strauss (1992, 1999)
Somali wild ass (*Equus onager*)	0.017 mg/kg etorphine	0.07 mg/kg ACP		0.045 mg/kg diprenorphine	$n = 14$	Strauss (1992, 1999)
Przewalski's horse (*Equus ferus przewalskii*)	0.008 mg/kg etorphine	0.033 mg/kg ACP	0.033 mg/kg detomidine, 0.033 mg/kg buthorphanol	0.16 mg/kg naltrexone + 0.04 mg/kg atipamezole IV	$n = 34$ wild	Walzer et al. (2000b, 2006)
	0.018 mg/kg etorphine	0.075 mg/kg ACP	0.16 mg/kg xylazine	0.045 mg/kg diprenorphine IV	$n = 32 + 41$	Strauss (1992, 1999)
	0.07–0.1 mg/kg medetomidine	1.8–2.6 mg/kg ketamine		0.17–0.23 mg/kg atipamezole	$n = 11$	Matthews et al. (1995)
	0.6 mg/kg romifidine	3.3 mg/kg TZ		2.5–3 mg/kg tolazoline IV	$n = 15$	C. Walzer (unpubl. data, 2002)
Mountain zebra (*Equus zebra*)	0.35 mg/kg romifidine	1.8 mg/kg TZ		2.5–3 mg/kg tolazoline IV	$n = 9$	Wiesner & von Hegel (1990)
	4–6 mg etorphine	80 mg azaperone		9.6–14.4 mg diprenorphine	Total dose for adult, high dose for male	Kreeger (1996)
	0.009–0.01 mg/kg etorphine	0.037–0.044 mg/kg ACP		0.045 mg/kg diprenorphine IV	$n = 53 + 69$	Strauss (1992, 1999)
Plains zebra (*Equus burchelli*)	0.0085–0.01 mg/kg etorphine	0.035–0.04 mg/kg ACP		0.045 mg/kg diprenorphine IV	$n = 54 + 21$	Strauss (1992, 1999)
	5.5–8.3 mg/kg TZ	0.06–0.08 mg/kg detomidine			$n = 11$, long recovery	Vitaud (1993)
	0.017 mg/kg etorphine	0.017 mg/kg medetomidine	0.24 mg/kg azaperone	0.23 mg/kg naltrexone IM	$n = 5$, pilot study	Gaudio e al. (2019)

ACP, acepromazine; IM, intramuscular; IV, intravenous; TZ, telazol/tiletamine-zolazepam.

on a motorcycle and horseback or waiting at water points. Using a combination of 2.5–3.0 mg of etorphine, 10 mg of detomidine, and 10 mg of butorphanol, 14 horses have been successfully captured in the wild (and 35 procedures in the very large adaptation enclosures, 20–30 ha) in Mongolia (Walzer et al. 2006). Initial effects were noticed after 3–5 minutes when the animal exhibited a stiff, high-stepping gait and became ataxic. Induction to lateral recumbency occurred within 5–10 minutes. Procedures lasted on average 35 minutes. Following IV antagonist application anesthesia was smoothly reversed without any signs of excitement, and the animals were back on their



Figure 45.5 The head of all equids should be fixed to the ground for as long as possible following antagonist application to prevent premature uncoordinated attempts at getting up, as these could result in injury.



Figure 45.6 An Asiatic wild ass being darted in the rump musculature from a moving jeep (60 km/h) at a distance of approximately 10–15 m on a parallel track.

feet within 2 minutes. It is important to note that the head of all equids should be fixed to the ground for as long as possible following antagonist application to prevent premature uncoordinated attempts at getting up, as these could result in injury (Walzer et al. 2006) (Fig. 45.5).

Asiatic Wild Ass

Throughout its range, the wild ass is extremely skittish—most probably due to poaching activities—and in some areas, flees human presence at several kilometers' distance (e.g., in Great Gobi B SPA). We have employed four distinct techniques to capture this species in the wild. In the summers of 2002 and 2005, we used a modified high-pressure CO_2 dart gun (Daninject JM, Wildlife Pharmaceuticals Ltd.) from a pre-placed hide, 60–80 m distant from water points. This method was especially useful in the south Gobi as the khulan are readily approached in the area. Some water points additionally offer good cover that allows for a shooting distance of 40–55 m. If possible, it is a distinct advantage to take a position high above the animal (e.g., cliff face), as they are unwary of danger from above. As open water is lacking in large parts of the distribution range in the south Gobi, the wild ass must dig to a depth of approximately 45 cm to access ground water. At this time, it is very difficult for the animal to see movements in its vicinity. Furthermore, the use of ground water increases the amount of time the animals have to remain stationary, which additionally greatly facilitates darting.

In 2003 and 2005, we also employed a chase method where the khulan was darted from a moving vehicle. This method had previously been used to collar a wild Bactrian camel (*Camelus bactrianus ferus*) and is traditionally employed by wild ass poachers with 12-gauge shotguns (Blumer et al. 2002). When using the local UAZ jeeps it is important to remove the window from the passenger side and to provide seatbelts for the driver and shooter. If using the Daninject JM CO_2 dart gun, a short 4-cm barrel can be used instead of the standard barrel as this greatly facilitates movement in the jeep. Once an animal is identified, it is chased until the jeep is able to approach within approximately 10–15 m on a parallel track (see Fig. 45.6). It is then easily darted in the rump musculature using standard pressure settings. It is essential to define a chase cut-off time before the procedure is started. Our experience has shown that a cut-off time of 15 minutes is adequate for the Asiatic wild ass. To date, we have captured six animals with this very time-efficient method. The shortest chase time was 2 minutes and the longest 13 minutes. In all cases, induction was extremely rapid and smooth (4–8 minutes), and body temperature was below 40°C. A severe limitation to this method is that one is only able to capture males or juveniles without foals. A chase of a female with a foal would result in (permanent) separation of the young from the mare and is therefore unacceptable.

Additionally, we used a video-enabled remote-controlled CO_2 gun (Walzer & Boegel 2003) at several water points in attempts to capture khulan in 2003 and 2005. To date, this method has not been successful for wild ass mainly due to the abundance of water in the areas it was employed. In the authors' view, this method has great potential in areas with small waterholes that the animals have to visit.

Finally, due to geomorphological constraints, capture events in Iran and Kazakhstan required a novel approach employing capture corals. In the Bahram-e-Goor protected area in Iran, two small capture corals with remotely triggered doors were built and baited with water and fodder.

Following several weeks of pre-baiting, 15 individuals were successfully captured (Walzer et al. 2006). In the Altyn Emel national park in Kazakhstan a large multi-segmented capture coral was built and wild ass were driven into the coral using 4 × 4 vehicles. Two drives resulted in the capture of 50+ individuals (Levanov et al. 2013). At both sites individuals were selected from the coral and remotely darted with the combination described below then individually walked out into a processing enclosure. Following sampling and collaring the animals were either released (Iran) or treated with long-acting neuroleptics and loaded into crates for translocation to a release site (Kazakhstan).

In all wild ass procedures, anesthesia was induced with a single 3-mL dart containing a combination of 4.4 mg of etorphine (M99, C-Vet Veterinary Products, Lancashire, UK), 10 mg of detomidine–HCl (Domosedan, Orion Corp. Farmos), and 10 mg of butorphanol (Torbugesic, Fort Dodge Animal Health). Anesthesia was initially reversed with an IV combination of 200 mg of naltrexone (Trexonil Wildlife Laboratories Inc.) and 20 mg of the alpha-2 antagonist atipamezole (Antisedan, Orion Corp. Farmos). Reversal was rapid and generally smooth, but some signs of excitation related to radio collar placement (head shaking) were noted. Subsequently, the opioid antagonist-agonist diprenorphine (Revivon, C-Vet Veterinary Products) was used. This eliminated head shaking and provided a smoother reversal. All animals were standing and alert approximately 2 minutes following administration of the antagonists.

Zebras

The chemical capture of zebras has been described previously (Burroughs 1993b). Similar to the Asiatic wild equids, zebras are very difficult to approach in the wild. The techniques employed are similar to the ones described earlier, with various mass-capture bomas and drop-wall boma techniques employed (Laubscher et al. 2015). Additionally, darting individuals from a helicopter is recommended (Burroughs 1993b).

Surgical Field Anesthesia

For some procedures, it can be necessary to extend and deepen the anesthesia as the chemical capture drug combinations at the doses provided do not offer the necessary depth of anesthesia for surgical procedures because significant muscle contractions and uncontrollable movements can occur. Following recumbency, an IV catheter is placed and an IV infusion of guaifenesin-ketamine-xylazine (1 L of 5% guaifenesin) (Myolaxin, Vétoquinol UK Ltd., Buckingham, UK), 1000 mg of ketamine (Ketamidor, Richter Pharma, Wels, Austria), and 500 mg of xylazine (Rompun, Bayer Austria Ges.m.b.H, Vienna, Austria) is started. Nasal oxygen at a flow rate of 10 L/min is provided. An adult Przewalski's horse received on average 733 mL of the triple drip at an average rate of 12.6 mL/min. Despite oxygen supplementation, most equids will become hypoxemic and slightly hypercapnic throughout the procedure.

Approximately 10 minutes before the surgical procedure is finished, the IV infusion should be stopped. Subsequently, the opiate anesthesia components from the capture event are reversed with 150 mg IV naltrexone. This multidrug procedure is well adapted for surgical anesthesia in Przewalski's horses and most likely for other wild equids in a field setting. However, it is strongly recommended that adequate anesthesia monitoring is available for the early recognition of critical respiratory and metabolic problems (Walzer et al. 2009) (Figs 45.3 and 45.7).



Figure 45.7 Field anesthesia and surgery setting in the Hortobágy National Park, Hungary. Following induction with etorphine-detomidine-butorphanol, surgical-depth anesthesia is maintained with a so-called intravenous triple-drip consisting of guaifenesin-ketamine-xylazine.



Figure 45.8 A radio-collared Przewalski's horse rising following the reversal of the opiate anesthesia components with 150 mg of naltrexone.

Fig. 45.8 shows a horse post antagonism getting up.

Chemical Capture of Captive Nondomestic Equids

Although not currently available, carfentanil has been extensively studied as an immobilizing agent for nondomestic equids (Allen 1990, 1992, 1994, 1997; Klein & Citino 1995). Etorphine was not available to zoo and wildlife veterinarians working in the United States for several years, so carfentanil was used as a primary immobilizing agent for nondomestic equids (Allen 1992, 1994, 1997). There are several disadvantages of using carfentanil versus ethorphine as an immobilizing agent for nondomestic equids. Oftentimes, nondomestic equids immobilized with carfentanil have to be assisted into recumbency or be given supplemental anesthetic induction agents to achieve complete immobilization (Allen 1992, 1994; Klein & Citino 1995). Supplemental anesthetic agents are given IV after the animal has been partially immobilized by carfentanil. Ketamine, glyceryl guaiacolate, or propofol are often used to get adequate muscle relaxation and complete immobilization (Zuba & Burns 1998). The delivery of carfentanil by dart into the muscles of the neck or shoulder will result in faster induction times and less morbidity (Allen 1992, 1994, 1997). Significant respiratory depression is commonly seen with carfentanil immobilizations (Allen 1992, 1994). This can often be successfully treated with IV administration of doxapram and the delivery of intranasal oxygen (Allen 1992, 1994, 1997). Most nondomestic equids immobilized with carfentanil alone experience a significant tachycardia, which may be due to the stress of the procedure and inadequate immobilization (Allen 1992, 1994). Additionally, renarcotization may occur in nondomestic equids immobilized with carfentanil.

Renarcotization seems to be more common in the Somali wild ass (*Equus onager*) when immobilized with carfentanil alone (Allen 1997). Carfentanil, when used alone, was not adequate for the immobilization of Grevy's zebra (*Equus grevyi*) unless unacceptably high doses were used (Allen 1997).

Grevy's zebra (*Equus grevyi*) can be immobilized with carfentanil in combination with other drugs in a staged immobilization protocol (Klein & Citino 1995). First, detomidine (0.1–0.15 mg/kg) is given IM. Then, approximately 20 minutes later, carfentanil (0.098 mg/kg) in combination with ketamine (2 mg/kg) is given IM. In one study, this combination was compared to medetomidine and ketamine in combination. Both study groups experienced significant hypertension with these combinations (Klein & Citino 1995). The preferred method for immobilizing captive Grevy's zebra is to use etorphine in combination with detomidine or detomidine and acepromazine (see Table 45.3).

Although carfentanil has been used to immobilize captive nondomestic equids, etorphine is the preferred primary immobilizing agent. Diprenorphine, in most cases, will adequately antagonize the effects of etorphine, but in one comprehensive review of renarcotization in nondomestic equids, renarcotization was relatively common in zebra and onager when using diprenorphine to antagonize etorphine (Allen 1990). The use of naltrexone to antagonize etorphine typically does not result in any episodes of renarcotization in nondomestic equids.

Thiafentanil is a potential alternative to carfentanil and etorphine in situations where etorphine is difficult to obtain. A study in captive Grevy's zebra compared thiafentanil and etorphine-based combinations (Stuchin et al. 2019). Immobilization with thiafentanil in combination with an alpha-2 agonist (medetomidine or detomidine) and ketamine was compared to etorphine in combination with an alpha-2 agonist with or without ketamine. Induction times were longer with thiafentanil-based protocols and the addition of ketamine in the protocol tended to prolong recoveries (Stuchin et al. 2019). Thiafentanil appears to be a viable alternative to etorphine but more work is required to determine an appropriate dose of thiafentanil to optimize induction time.

Recently, due to opioid import restrictions and a perceived human health risk, nonopioid combinations have been used in captive wild and feral equids. Ninety free-roaming feral horses (*Equus ferus caballus*) in the Danube delta were immobilized remotely using a single disposable 6-mL dart containing a combination of 30 mg of medetomidine and 775 mg of ketamine. Eighty-one horses had an uneventful mean induction of 7.2 minutes with good muscle relaxation and a median recumbency time of 67 minutes. Ten horses required supplemental ketamine

intravenously due to incomplete immobilization (Rosu et al. 2021). A recent study compared two alpha-2 agonist-based protocols with standard etorphine protocols for general anesthesia of captive kulans. A total of eight kulans were individually separated and darted using a combination of 3 mg/kg ketamine, 0.09 mg/kg medetomidine-0.3 mg/kg midazolam, and 0.2 mg/kg butorphanol while an additional seven kulans received 250 mg/animal tiletamine and 250 mg/animal zolazepam, 0.09 mg/kg medetomidine and 0.2 mg/kg butorphanol. The authors recommend these two protocols for prolonged medical procedures in captive kulan. It is, however, critical to note that the use of highly potent alpha-2 agonists such as the 40 mg/mL medetomidine used in this study constitutes a considerable risk to humans due to the absence of a proven antagonist for humans when compared to opioids with a clinically proven antagonist such as naltrexone (Haymerle et al. 2010).

Analgesia and Analgesic Techniques

In general, analgesia and analgesic techniques will be similar in wild horses and domestic horses, although dosages may vary. The following reference contains updated information regarding systemic analgesics and local anesthetic techniques in domestic equids. (Doherty et al. 2022).

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46

Tapirs

Budhan Pukazhenthi, Rebecca Richard, Paulo Rogerio Mangini, and Dawn Zimmerman

Introduction

Tapirs are perissodactyls belonging to the Family Tapiridae. Currently, there are four species recognized by the IUCN Red List. Three species belong to the New World (Baird's, lowland, and mountain) and one to the Old World (Malayan). All species of tapirs are herbivores and feed on leaves, shrubs, fruits, and roots. They also are considered "gardeners of the forest" as they consume fruits and facilitate seed dispersal via feces.

Population sizes of wild tapirs are highly variable. According to the IUCN Red List, all species except the lowland tapir are endangered. Lowland tapirs are listed as vulnerable, with decreasing populations. Population sizes are ~2500 (mountain; Lizcano et al. 2016), <5500 (Baird's; Garcìa et al. 2016), not known but decreasing (lowland; Varela et al. 2019), and ~2000 (Malayan; Traeholt et al. 2016). Global ex situ populations of tapir are eight (mountain), 58 (Baird's), 505 (lowland), and 183 (Malayan) animals (Species360 2020). As with most rare and endangered species, all four tapir species could benefit from management of ex situ populations. However, none of the tapir species under human care in zoo/breeding centers are considered self-sustaining.

Tapirs have been studied both in situ and ex situ. In situ efforts have focused on population estimation, ecology/habitat use, and disease exposure. These studies often warrant the safe capture of animals under field conditions. Extensive in situ research has been reported for at least three species of tapirs. Due to the diverse habitat types in which tapirs are found, different approaches are required for the capture of tapirs. For example, Baird's tapir, lowland tapirs, and Malayan tapirs may be captured using snares, pit traps, or box traps. However, the steep terrain mountain tapir habitat does not permit capture using these methods.

This chapter focuses on the general characteristics of tapirs, drug delivery options, intubation, sedation/tranquilization options, anesthesia options, anesthetic complications, and future research needs.

Body Weight

Amongst all four species of tapirs, mountain tapirs are the smallest and Malayan tapirs are the largest. Accurate estimates of body weight for wild tapirs are lacking. Under field conditions, most body weights are estimates, although body weights of ex situ managed animals serve as good starting points when calculating anesthetic dosages (Table 46.1).

Physical Restraint

Tapirs are extremely elusive in the wild and are well adapted for their environment. Animals can hide in dense vegetation and navigate the terrain very efficiently. In free-ranging conditions, tapirs are often captured by attracting the animal to bait stations, box traps, pit-fall traps or using tracking dogs for locating the animals and then lassoing or darting them. Tapirs have a predilection for water when threatened or pursued, therefore under field conditions additional care is warranted to prevent animals from entering water before or after administration of anesthetic drugs. Irrespective of the capture method, all wild tapirs are first anesthetized before handling to ensure the safety of both the animal and the capture team.

Under ex situ conditions, tapirs often are managed through direct contact. Although tapirs are docile animals, there are several reports of severe injuries to handlers, therefore current Association of Zoos and Aquariums

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Table 46.1 Recommended dose and supplemental dose.

Species	Drug combination	Reversal	Comments	Reference
Mountain tapir	Carfentanil (5.4 µg/kg) + ketamine hydrochloride (0.26 mg/kg) + xylazine (0.13 mg/kg) IM	Yohimbine (0.2 mg/kg) IV and naltrexone (100–200 mg/kg), half IV, half SC	Effective in male, female, and juvenile animals	Miller-Edge (1994)
	Ketamine hydrochloride 400–500 mg; 2.8 mg/kg + xylazine (400 mg; 2.2 mg/kg + butorphanol (10 mg; 0.05–0.1 mg/kg)	Yohimbine hydrochloride (40 mg; 2.2 mg/kg) or Atipamazole (20 mg; 0.06 mg/kg) to reverse Xylazine + naltrexone (40 mg; 2.2 mg/kg) to reverse butorphanol	Effective in wild tapirs Induction time: 3–5 minutes Ketamine hydrochloride supplementation (50–100 mg IV or IM) to maintain anesthetic plane	Davis-Powell (pers. comm.)
	Detomidine (0.05 mg/kg) + butorphanol (0.15 mg/kg) IM as preanesthetic and supplemented with ketamine hydrochloride (1–2 mg/kg) IM		Anesthesia can be maintained with isoflurane via a face mask or endotracheal tube Bradycardia has been reported in at least one animal that was managed using atropine sulfate (0.025–0.04 mg/kg) IM	Richard (pers. comm.)
	Butorphanol (0.125 mg/kg) + medetomidine (0.04 mg/kg) IM used as a preanesthetic Anesthesia then induced using diazepam (0.03 mg/kg) + ketamine hydrochloride (1.25 mg/kg) IV	Naltrexone (0.9 mg/kg) + atipamezole (0.2 mg/kg) + flumazenil (0.003 mg/mL) IM	Resulted in light anesthesia Average recovery time was about 7 minutes No adverse effect reported	Richard (pers. comm.)
	Butorphanol (0.15 mg/kg) IM	Naltrexone (0.6–0.9 mg/kg) IM, six times the induction dose is preferred for optimal reversal	Effective sedation was achieved Most applicable for minor procedures in tractable animals and/or juveniles	Richard (pers. comm.)
	Ketamine (1.5 mg/kg) + medetomidine (0.015 mg/kg) + butorphanol (0.15 mg/kg) IM	Naltrexone (0.7–0.9 mg/kg) + atipamezole (0.075 mg/kg) IM	Effective anesthesia for semen collection by electroejaculation Average induction time was 3 minutes and recumbency was achieved within 5 minutes Naltrexone must be five or six times the butorphanol dose Atipamezole must be five times medetomidine dose Recovery time was about 2 minutes (to initial head control) and 5–10 minutes to standing	Richard & Mangini (pers. comm.)
Baird's tapir	Etorphine (1.88 mg) + acepromazine (7.7 mg) IM	Diprenorphine hydrochloride (three times the etorphine dosage used)	Field anesthesia	Parás et al. (1996)
	Detomidine (0.065–0.13 mg/kg) + butorphanol (0.13–0.2 mg/kg) IM	No reversal		Trim et al. (1998)
	Ketamine hydrochloride (2.2 mg/kg) IV, then an additional dose of ketamine hydrochloride (1.5 mg/kg) 20 minutes later	No reversal	Animal intubated and anesthesia maintained with isoflurane Complications included hypoxemia when animal was allowed to breath air	Trim et al. (1998)

Table 46.1 (Continued)

Species	Drug combination	Reversal	Comments	Reference
	Butorphanol (40–50 mg) + xylazine (100 mg)	Naltrexone (50 mg) IM + tolazoline (1200 mg) no sooner than 30 minutes from the last administration of ketamine	Field anesthesia for a 200–300 kg animal Ketamine hydrochloride (187 ± 40.8 mg/animal) or constant rate of infusion of propofol (50–200 μg/kg/min) to maintain anesthesia Time to sternal recumbency: 11 minutes Return to standing after reversal: 12 minutes	Foerster et al. (2000)
	Etorphine hydrochloride (1.96 mg) + acepromazine (5.9 mg)	Diprenorphine hydrochloride (5.88 mg)	Field anesthesia for a 200–250 kg animal Relatively short induction time	Hernandez (2014)
	Butorphanol (0.15–0.2 mg/kg) + detomidine (0.06 mg/kg) IM, ketamine (1–2 mg/kg) to reach or maintain lateral recumbency Boluses of propofol (0.2–2.2 mg/kg per bolus) as supplement	Naltrexone and yohimbine hydrochloride	Ex situ anesthesia Optimal for semen collection by electroejaculation Also effective in female tapirs	Pukazhenthi et al. (2011)
	Butorphanol (0.13–0.2 mg/kg) + acepromazine (7.7 mg/animal) + detomidine (0.065–0.13 mg/kg) + ketamine hydrochloride (2.2 mg/kg) IM	No reversal	Rapid and smooth recovery	Trim et al. (1998)
Lowland tapir	Detomidine (0.17 mg/kg) PO followed in 20 minutes by carfentanil (7.88 ± 1.85 μg/kg) PO	Yohimbine (0.2 mg/kg) IV + naltrexone (100–200 mg), half IV, half SC	Sternal or lateral recumbency reached in 10–11 minutes of carfentanil administration Smooth recovery with animal standing within 2–5 minutes of administration of reversal	Pollock & Ramsey (2003)
	Ketamine hydrochloride (3.5–4.0 mg/kg) + xylazine (2–2.2 mg/kg) IM supplemented with ketamine hydrochloride (1.4 mg/kg) IM	Tolazoline (4 mg/kg)	Effective in captive, semicaptive, and wild tapirs	Blanco Márquez & Blanco Márquez (2004)
	Telazol (2.5–2.8 mg/kg) supplemented with ketamine hydrochloride (1.2–1.5 mg/kg) IM	Tolazoline (4 mg/kg)	Effective in captive, semi-captive, and wild tapirs	Blanco Márquez & Blanco Márquez (2004)
	Tiletamine/zolazepam (0.83–1.25 mg/kg) + ketamine (0.40–0.60 mg/kg) + medetomidine (0.004–0.006 mg/kg) OR Detomidine (0.04–0.06 mg/kg) OR Romifidine (0.03–0.05 mg/kg)	Atipamezole (0.05–0.06 mg/kg) IV or IM given no sooner than at least 35 minutes from the last administration of tiletamine/zolazepam	Induction time: 2–5 minutes Anesthesia duration: 30–40 minutes Good muscle relaxation, normal cardiorespiratory parameters, and smooth recovery Atropine sulfate (0.025–0.04 mg/kg) to control excessive salivation/nasal secretions	Mangini & Medici, (1998); Mangini et al. (2001); Mangini (2014); Medici et al. (2014); Quse & Fernandes-Santos (2014); Fernandes-Santos et al. (2020)

Table 46.1 (Continued)

Species	Drug combination	Reversal	Comments	Reference
	Medetomidine (0.008–0.01 mg/kg) OR Detomidine (0.07–0.09 mg/kg) OR Romifidine (0.09–0.11 mg/kg) OR Xylazine (0.42–0.56 mg/kg) + atropine (0.04 mg/kg) then wait 10 minutes to tiletamine/zolazepam (4.11–5.6 mg/kg)	Atipamezole (0.05–0.06 mg/kg) IV or IM given no sooner than at least 30–35 minutes from the tiletamine/zolazepam administration	Alpha-2 adrenergic agonists used as preanesthetic agent (IM) 10–15 minutes before tiletamine/zolazepam (IM) Induction time: 15–20 minutes after tiletamine/zolazepam administration Anesthesia duration: 40–50 minutes Best muscular relaxing, cardiorespiratory parameters, and smooth recovery obtained with medetomidine, followed by romifidine, detomidine, and xylazine Duration for full recovery was 1–3 hours after arousal	Mangini et al. (2001); Mangini (2014); Medici et al. (2014)
	Butorphanol (0.15–0.17 mg/kg) + medetomidine (0.012 mg/kg) + ketamine (0.6–0.7 mg/kg)	Naltrexone (0.3–0.35 mg/kg) + atipamezole (0.04 mg/kg) single solution, administration could be given half IM, half IV, no sooner than at least 35 minutes from the last administration of ketamine	Induction time: 4–6 minutes Anesthesia duration: 30–40 minutes Recovery time: 1–2 minutes after reversal Atropine may be required to control excessive salivation and/or nasal secretions	Medici et al. (2014); Quse & Fernandes-Santos (2014); Quse & Fernandes-Santos (2020)
	Methadone (0.15 mg/kg) + detomidine (0.05 mg/kg) + ketamine (1–2 mg/kg)	Naloxone (0.01–0.02 mg/kg) + yohimbine (0.1 mg/kg) single solution, administration could be given half IM, half IV, no sooner than at least 35 minutes from the last administration of ketamine	Induction time: 5–6 minutes Good muscle relaxation Recovery time: 1–2 minutes after reversal Atropine (0.02–0.04 mg/kg) may be required to control excessive salivation and nasal secretions	Quse & Fernandes-Santos (2014); Mangini (pers. comm.)
	Butorphanol (0.15–0.20 mg/kg) + medetomidine (0.003–0.005 mg/kg)	Atipamezole (0.06 mg/kg) + naltrexone (0.6 mg/kg), single solution	Induction time: 10–15 minutes Anesthesia duration 30–40 minutes Average recovery time 1 minute after reversal Atropine sulfate (0.02–0.04 mg/kg) may be required to control excessive salivation and nasal secretions	Velastin et al. (2004); Medici et al. (2014)
	Detomidine (0.05–0.075 mg/kg) IM, wait 15 minutes to administer midazolam (0.1 mg/kg) IV + ketamine (2 mg/kg) IV	Yohimbine (0.15 mg/kg) IV, recovery at 3–5 minutes	Induction time: 8–12 minutes Anesthesia duration: 45–60 minutes	Ferreira (1997)
	Detomidine 0.04 mg/mL + midazolam 0.1 mg/mL + ketamine 4 mg/mL in 234 mL of sterile saline infused at 1 mL/kg/h rate	No reversal drugs used	Administered via slow IV Good muscle relaxation Minimal cardiorespiratory depression Atropine (0.04 mg/kg) IM 10 minutes before adrenergic alpha-2 agonists Reduces salivation and bradycardia	Ferreira (1997)

Table 46.1 (Continued)

Species	Drug combination	Reversal	Comments	Reference
	Xylazine 1.72 mg/mL + midazolam 0.1 mg/mL + ketamine 4 mg/mL infused at 1 mL/kg/h rate	No reversal drugs used	Slow IV anesthesia Good muscle relaxation, minimal cardiorespiratory depression Ideal for biological samples collection and small invasive procedures Atropine (0.04 mg/kg) IM 10 minutes before adrenergic alpha-2 agonists Reduces salivation and bradycardia	Ferreira (1997)
	Butorphanol (0.12 mg/kg) + azaperone (0.5 mg/kg)	No reversal drugs used	Induction time: 14–20 minutes Anesthesia time: 100–130 minutes	Velastin (2007)
	Azaperone 0.6–0.9 mg/kg + medetomidine 0.006–0.01 mg/kg		Single IM injections	Baiva et al. (2024)
	Ketamine (2–3 mg/kg) + butorphanol (0.15–0.18 mg/kg) + detomidine (0.05–0.075 mg/kg)	Naloxone (0.08–0.1 mg/kg) + yohimbine (0.2–0.3 mg/kg) single solution, administration could be IM or IV, no sooner than 30 minutes from the last administration of ketamine	Induction time: 3–5 minutes Anesthesia time: 40–50 minutes Ideal for semen collection via electroejaculation Atropine (0.02–0.04 mg/kg) required in 20–25% of procedures to reduce salivation and respiratory secretion	Santos et al. (2019); Mangini (pers. comm.)
	Xylazine (0.8 mg/kg) + butorphanol (0.4 mg/kg)	Yohimbine (0.36 mg/kg) + naltrexone (0.4 mg/kg) single solution IV, 30–40 minutes after last ketamine dose	Induction time: 12 minutes Anesthesia time: 45 minutes Suitable to induce deeper anesthesia with ketamine (1 mg/kg) IV application or isoflurane inhalation, allowing surgical procedures	Quse & Fernandes-Santos (2014)
Malayan tapir	Butorphanol (0.15–0.24 mg/kg) + medetomidine (0.01–0.03 mg/kg) or xylazine (0.3–0.35 mg/kg) IM	Naloxone/naltrexone (0.6 mg/kg) + yohimbine (0.2–0.3 mg/kg) or tolazoline (4 mg/kg) IM or IV	For supplemental anesthesia, ketamine hydrochloride (0.5 mg/kg) IV or IM can be administered	Janssen (1996); Quse & Fernandes-Santos (2014); Miller et al. (2000)
	Etorphine (2.45 mg) + acepromazine (10 mg) IM then guaifenesin IV until intubation		Isoflurane to maintain anesthesia	Lambeth (1998)
	Medetomidine (0.012–0.018 mg/kg) + butorphanol (0.012–0.018 mg/kg) + ketamine hydrochloride (5–7 mg/kg) IM	Atipamezole (0.07–0.09 mg/kg) + naltrexone (0.36–0.47 mg/kg) IM	Supplemental ketamine hydrochloride and/or guaifenesin (IV) was administered to achieve optimal level of anesthesia for semen collection by electroejaculation	Tipkantha et al. (2011)
	Ketamine hydrochloride (3 mg/kg) + butorphanol (0.13 mg/kg) + medetomidine (0.013 mg/kg) IM	Naltrexone (0.4 mg/kg) + atipamezole (0.06 mg/kg) IM	Induction time: 2–4 minutes Anesthesia duration: 50 minutes Full recovery time: 10–15 minutes after reversal Ideal for semen collection by electroejaculation	Tipkantha (pers. comm.)

IM, intramuscular; IV, intravenous; PO, per os; SC, subcutaneous.

guidelines recommend "protected contact" to minimize risk of injury to animal handlers (AZA Tapir TAG 2013).

Tapirs are relatively easy to train using positive reinforcement techniques. Animals can be "scratched down" using a hand brush or an outdoor broom. This is accomplished by scratching the animal's dorsum, neck, or the abdomen until the animal lays down in lateral recumbency. When combined with desensitization training, simple health assessments including physical examination, blood collection, transabdominal ultrasound examinations, and intravenous (IV) catheterization can be accomplished without the use of anesthetic drugs. For animals that are noncooperative or procedures that warrant extensive manipulation of animals, use of chemical immobilization should be considered.

Drug Delivery Method

In free-ranging conditions, most drug delivery is accomplished via remote dart projection or pole syringe. In captivity, drug delivery can be accomplished via hand-injection (intramuscular [IM] or IV), pole syringe, or remote delivery. Sites for administration and delivery methods are indicated in Fig. 46.1. Tractable animals may be scratched down to sternal or lateral recumbency to allow administration of the induction dose by hand-injection in the hindquarters while the animal is relaxed. Tapirs may preferably tolerate injection in the hindquarters or over the shoulder region.

Vascular Access

The most common options for venous access in tapirs include the femoral, saphenous (Fig. 46.2), cephalic, jugular, and auricular veins. The jugular vein provides the best location for collection of large volumes of blood



Figure 46.2 Intravenous administration of supplemental anesthetic drug via the saphenous vein in a lowland tapir. Photo credit: Budhan Pukazhenthi.

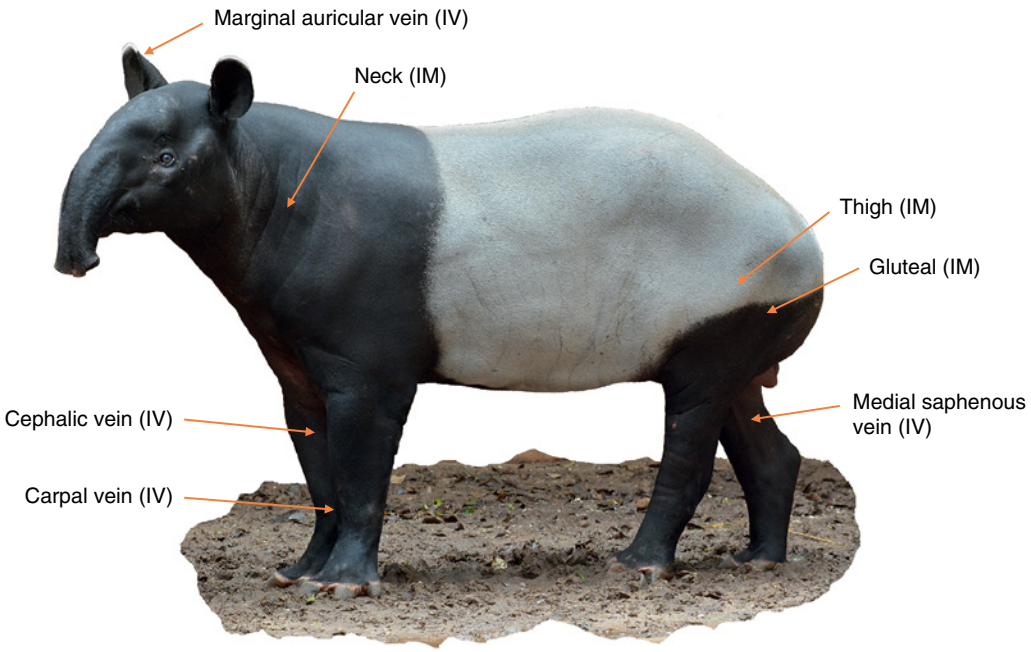


Figure 46.1 Preferred sites for administration of drugs and/or fluids in tapirs. For remote delivery of anesthetic drugs, the best sites are the thigh, gluteus, and shoulder. IM, intramuscular; IV, intravenous. Photo credit: Budhan Pukazhenthi.

or administration of IV fluids. This can be accomplished using an indwelling catheter or a large-volume syringe. The femoral and saphenous veins also provide relatively easy vascular access. Blood collection or drug administration is best achieved using a 19-gauge butterfly catheter. Small volumes of blood also can be collected from the marginal auricular vein using a 21-gauge butterfly catheter.

Intubation

It is not uncommon for sedated tapirs to produce excessive salivary secretions. While atropine is often used to decrease salivation (see Table 46.2), intubation is recommended to avoid airway obstruction and allow access for respiratory intervention. Tapirs can be blind intubated with a 16–20-mm internal diameter endotracheal tube for most adult animals (see Hernandez et al. 2014). Should intubation prove challenging due to anatomical considerations (including the narrow caudal pharyngeal space, long dental arcades, and muscular caudal tongue limiting easy visualization of the pharynx), visualization of the epiglottis may be facilitated by placing the animal in sternal recumbency and fully extending the head. Use of a long stylet to guide the endotracheal tube between the vocal folds may allow successful passage of the tube. Once the tube is in place, the cuff should be inflated and the tube secured using a gauze bandage. During long procedures, adult tapirs almost always benefit from oxygen supplementation via either intubation or nasal insufflation. If respiratory support is warranted, tracheal insufflation of oxygen or positive pressure ventilation (20–30 cmH_2O) can be provided. Under field conditions, a manual resuscitator bag can be used to improve oxygenation. Use of capnography, in addition to blood pressure and pulse oximetry, may further enhance monitoring of respiratory efficiency and minimize the risk of ventilation/perfusion mismatch.

Table 46.2 Body weight (range) of male and female tapirs.

Species	Male (kg)	Female (kg)
Mountain tapir	140–204	145–170
Baird's tapir	185–284	218–344
Lowland tapir	198–205	171–221
Malayan tapir	295–385	340–430

Sedation/Tranquilization/ Anesthesia Techniques

As with all large mammals, anesthesia of tapirs warrants extreme care. Although similar anesthetic protocols can be used for both wild and captive tapirs, close attention must be paid to the stress or excitement state of each individual animal (Mangini 2006). Stress/excitement is one of the most important factors affecting the response to anesthesia in most wild tapirs. Free-living tapirs, captured via remote dart projection or traps, are usually more susceptible to the effects of acute stress than their captive counterparts. Stress responses are particularly important when adrenergic alpha-2 agonists are used in the anesthetic protocol because of the reduced efficacy of these drugs under moderate or high stress conditions. This is especially common when animals are pursued on foot for darting. Additionally, the dart volume, duration of induction, and time to recumbency are important factors to consider when choosing an anesthetic protocol to use in wild tapirs.

Standard anesthetic monitoring is easily accomplished in most tapirs. Oxygen saturation should be maintained between 95% and 100%, similar to equids, and can be measured using pulse oximetry with transducer placement on the tongue, gingival, or preputial/vulvar folds; oxygen saturation levels below 90% are indicative of ventilation/perfusion mismatch. Spontaneous respiration rates for tapirs under anesthesia are generally in the 20–30 breaths per minute range, but when mechanical ventilation is employed, rates between 4 and 7 breaths per minute with an inspiratory duration of 1 second are generally sufficient to allow appropriate oxygenation. End-tidal capnography further facilitates anesthetic monitoring and ranges between 35 and 55 mmHg for either spontaneously ventilated or mechanically ventilated patients. Dorsal recumbency, as with equid species, will significantly negatively impact oxygenation due to atelectasis and decreased perfusion of dependent muscle groups, and may require the use of positive inotropes to maintain appropriate perfusion, particularly over prolonged periods. Transient apnea may be noted with induction doses of propofol and with high levels of isoflurane (one animal), which may be countered by decreasing the inhaled anesthetic and/or administration of doxapram (0.3 mg/kg IV).

In addition to oxygen saturation and respiration, heart rate, blood pressure, and electrocardiography (ECG) also are important for anesthetic monitoring. A recent study described the normal ECG parameters for lowland tapirs anesthetized using a combination of ketamine hydrochloride, detomidine, and medetomidine (Santos et al. 2019; Table 46.3).

Table 46.3 Parameters in DII (lead II) for *Tapirus terrestris* (*n* = 11; Santos et al. 2019).

Parameter	Average	±SD
Heart rate (bpm)	63	±22
PR interval (s)	0.19	±0.06
Duration of QT (s)	0.40	±0.14
Duration of QRS (s)	0.08	±0.02
Duration of P (s)	0.05	±0.02
Amplitude of P (mV)	0.16	±0.07
Amplitude of R (mV)	0.74	±0.41
Mean electric axis (EEM)	70.00	±81.22

SD, standard deviation.

Tapirs, like horses, do not vomit. However, spontaneous drainage of stomach contents from the nose is not uncommon, even after a 36-hour fasting period prior to anesthesia. Elevating the head with the nose oriented down may minimize the risk of aspiration but does not entirely alleviate passive regurgitation. Regurgitated fluid is usually brownish-red in color.

Appropriate padding should be employed to minimize ventilation/perfusion mismatch in the dependent muscle groups; padding the face may additionally mitigate any transient damage sustained from pressure on the facial nerve. Physical therapy of the down limbs during anesthesia may be useful in maintaining blood flow to the distal extremities and thus improve recovery.

Mountain Tapir

Under field conditions, mountain tapirs have been anesthetized using a combination of ketamine, xylazine, and butorphanol via dart projection (Davis-Powell, pers. comm.; Table 46.1). An initial effect was observed within 3 minutes and the animal was recumbent within 5 minutes. In a few cases, anesthesia was supplemented with an IV or IM injection of ketamine hydrochloride. This protocol yields about 30 minutes of anesthesia that permits blood collection, trans-abdominal ultrasound examination, and placement of a satellite tracking collar. Anesthesia is reversed using a combination of yohimbine hydrochloride and naltrexone administered intramuscularly. In most cases, the animal is standing within 10 minutes of reversal.

A similar protocol includes detomidine (0.04 mg/kg) combined with butorphanol (0.2 mg/kg IM). Anesthesia can then be induced with propofol (2 mg/kg slow IV) to effect. This combination can be supplemented with ketamine hydrochloride (0.5 mg/kg) administered intravenously. Anesthesia is reversed using atipamezole (0.05–0.1 mg/kg IV or IM) and naltrexone (0.9 mg/kg IM). It is important to note that propofol induction frequently results in transient apnea, therefore such protocols should include intubation and manual ventilation if indicated to maintain oxygenation.

Furthermore, a combination of butorphanol (0.125 mg/kg IM) and medetomidine (0.04 mg/kg IM) has been used as a preanesthetic. Anesthesia is then induced with diazepam (0.03 mg/kg) and ketamine (1.25 mg/kg) administered intravenously. Anesthesia is reversed with naltrexone (0.9 mg/kg), atipamezole (0.2 mg/kg), and flumazenil (0.003 mg/kg) administered intramuscularly.

Mountain tapirs can also be sedated using butorphanol at 0.15 mg/kg IM, which is adequate for minor procedures such as minor hoof repair or trimming. Butorphanol may be reversed with naltrexone (0.6–0.9 mg/kg IM), with six times the induction dose (0.9 mg/kg) recommended as some animals may recover slowly at lower doses. Decreasing the induction dose of butorphanol may be warranted in animals with compromised health conditions. As noted previously (Hernandez et al. 2012), tapirs may be sensitive to alpha-2 agonists or may require higher doses of reversal due to delayed clearance of the drug.

Another preferred anesthetic combination for mountain tapirs consists of ketamine (1.5 mg/kg), medetomidine (0.015 mg/kg), and butorphanol (0.15 mg/kg) administered intramuscularly. This combination has been successfully used in several captive mountain tapirs, providing 45–50 minutes of reliable anesthesia at a surgical plane suitable for moderately invasive procedures such as power dentistry, oral examination, and semen collection by electroejaculation (Pukazhenthi et al., unpub. data). It is important to note that at least 30 minutes should expire following ketamine hydrochloride administration before reversal of alpha-2 agents. Anesthesia is reversed with naltrexone (0.7–0.9 mg/kg) at five to six times the butorphanol dose and atipamezole (0.075 mg/kg) at five times the medetomidine dose. Reversal drugs are administered intramuscularly and animals are typically standing within 10 minutes of administration.

Baird's Tapir

Under free-ranging conditions, adult Baird's tapirs have been anesthetized using etorphine hydrochloride (1.88 mg) and acepromazine maleate (7.7 mg) administered intramuscularly via a dart (Parás et al. 1996) (Fig. 46.3). Anesthesia is reversed with diprenorphine hydrochloride (5.6 mg IM). Use of carfentanil or etorphine in tapirs



Figure 46.3 Intravenous administration of supplemental anesthetic drug via the cephalic vein in a Baird's tapir. Photo credit: Budhan Pukazhenthi.

managed in human care has mostly been eliminated due to the availability and efficacy of alpha-2 agonist combinations. A combination of butorphanol (40–50 mg) and xylazine hydrochloride (100 mg) has been used successfully in adult Baird's tapirs. However, this protocol requires the administration of additional ketamine hydrochloride (~187 mg/animal) or a constant rate infusion of propofol (50–200 μg/kg/min). Animals are generally sternal within 11 minutes of darting. Anesthesia reversal is accomplished using naltrexone (50 mg IM) and tolazoline (1200 mg IM). Animals return to standing within 12 minutes of administering the reversal (Foerster et al. 2000).

In zoological collections, Baird's tapirs have been anesthetized using a combination of acepromazine (7.7 mg/adult animal), butorphanol (0.13–0.2 mg/kg), detomidine (0.065–0.13 mg/kg), and ketamine hydrochloride (2.2 mg/kg) without reversal (Trim et al. 1998). Animals can also be anesthetized using a combination of butorphanol (0.15–0.2 mg/kg), detomidine (0.06 mg/kg), and ketamine hydrochloride (1–2 mg/kg) with supplemental boluses of propofol (0.2–2.0 mg/kg per bolus). The depth of anesthesia provided is adequate for semen collection by electroejaculation, trans-abdominal ultrasonography, and rectal examination. Anesthesia is reversed using naltrexone and yohimbine hydrochloride IM (Pukazhenthi et al. 2011).

Lowland Tapir

Under free-ranging conditions, lowland tapirs can be anesthetized using a number of combinations with favorable results. These include a combination of two dissociative agents, tiletamine hydrochloride/zolazepam (0.83–1.25 mg/kg) and ketamine hydrochloride (0.004–0.6 mg/kg), and an alpha-2 agonist (medetomidine 0.004–0.006 mg/kg or detomidine 0.04–0.06 mg/kg or romifidine 0.03–0.05 mg/kg) administered in a single IM injection yields a stage 3 anesthesia allowing biological sampling, treatment of wounds (suturing), placement of radio collar, and other low invasive manipulation for 30–40 minutes. The average induction time is 2–5 minutes to lateral recumbency. When medetomidine is present, this combination yields excellent muscle relaxation, cardiorespiratory parameters, and smooth recovery. If excessive salivation or respiratory fluids is observed, atropine (0.025–0.04 mg/kg IM) can be administered. Anesthesia can be reversed using atipamezole (0.05–0.06 mg/kg IV or IM). However, it is not uncommon to observe various adverse effects, including excitation, head shaking, pedaling, apnea, and ataxia during recovery; these effects may be mitigated by administering midazolam (0.03 mg/kg) IM 30–40 minutes after induction of anesthesia with tiletamine hydrochloride/zolazepam (Mangini et al. 2001; Mangini 2014; Quse & Fernandes-Santos 2014).

When tapirs are captured in traps, alpha-2 adrenergic agonists can be used as a preanesthetic agent (IM) 10–15 minutes before tiletamine/zolazepam administration. Choices include medetomidine (0.008–0.01 mg/kg), detomidine (0.07–0.09 mg/kg), romifidine (0.09–0.11 mg/kg), or xylazine hydrochloride (0.42–0.56 mg/kg). Animals reach sternal recumbency within 15–20 minutes after tiletamine/zolazepam administration. This combination yields 40–50 minutes of immobilization with good muscle relaxation and cardiorespiratory parameters. Anesthesia is reversed with atipamezole (0.05–0.06 mg/kg IV or IM) (Mangini et al. 2001; Mangini 2014; Medici et al. 2014).

A second combination that includes butorphanol (0.15–0.17 mg/kg), medetomidine (0.012 mg/kg), and ketamine hydrochloride (0.6–0.7 mg/kg) administered via a single IM injection yields good immobilization for 30–40 minutes with a 4–6-minute induction time. Anesthesia reversal is accomplished using naltrexone (0.3–0.35 mg/kg) and atipamezole (0.04 mg/kg) IM, or delivered half IM and half IV, at least 30 minutes after the initial injection of anesthetics. Average recovery time is 1–2 minutes after administration of the reversal drugs.

A combination of methadone (0.15 mg/kg), detomidine (0.05 mg/kg), and ketamine hydrochloride (1–2 mg/kg) intramuscularly in a single injection also yields good anesthesia under free-ranging conditions. Induction is within 5–6 minutes and results in good muscle relaxation. This anesthetic combination is fully reversible using naloxone (0.01–0.02 mg/kg) and yohimbine hydrochloride (0.1 mg/kg). For best results, reversals are administered half IM and half IV no sooner than 35 minutes after the last dose of ketamine hydrochloride. The average time to recovery

is about 1 minute after reversal (Quse & Fernandes-Santos 2014; Mangini, pers. comm.).

Anesthesia also can be achieved using a combination of butorphanol (0.15–0.2 mg/kg) and medetomidine (0.003–0.005 mg/kg) in a single IM injection. The induction time is slightly prolonged (10–15 minutes) and yields 30–40 minutes of good immobilization. In the event of excessive salivary and/or nasal secretions, atropine (0.025–0.04 mg/kg IM) can be administered. This protocol is fully reversible with atipamezole (0.06 mg/kg) and naltrexone (0.6 mg/kg), and the animal is usually standing within a minute post reversal (Velastin et al. 2004; Medici et al. 2014).

Under ex situ conditions, lowland tapirs can be anesthetized using a combination of detomidine (0.4–0.75 mg/kg), midazolam (0.1 mg/kg), and ketamine hydrochloride (2–4 mg/kg). In this case, detomidine is administered IM first and after 15 minutes both midazolam and ketamine are administered intravenously. Induction is achieved within 8–12 minutes after IV administration of midazolam and ketamine, and anesthesia lasts for 45–60 minutes. Anesthesia can be reversed with yohimbine hydrochloride (0.15 mg/kg IV) and recovery is observed within 3–5 minutes (Ferreira 1997).

Another combination of ketamine hydrochloride (3 mg/kg), butorphanol (0.18 mg/kg), and detomidine (0.065 mg/kg) administered via a single IM injection was most effective for semen collection using electroejaculation, as well as for ECG evaluations (Santos et al. 2019; Mangini, pers. comm.). The induction time was 3–5 minutes, resulting in sternal or lateral recumbency. This combination yielded a deep plane of anesthesia that lasted for 45–50 minutes. Although excessive salivation and nasal secretions were observed, these symptoms could be controlled via administration of atropine sulfate (0.02–0.04 mg/kg IM). Anesthesia can be reversed with naloxone (0.08–0.1 mg/kg) and yohimbine (0.2–0.3 mg/kg) administered IM or IV no sooner than 30 minutes after the last administration of ketamine hydrochloride.

In addition to the above, combinations of butorphanol (0.12 mg/kg) and azaperone (0.5 mg/kg) (Velastin 2007), medetomidine (0.006–0.01 mg/kg) and azaperone (0.6–0.9 mg/kg) (Biava et al. 2014), or xylazine (0.8 mg/kg) and butorphanol (0.4 mg/kg) (Quse & Fernandes-Santos 2014) also are successful. All injections are administered via an IM injection. Reversal of anesthesia is achieved using yohimbine (0.36 mg/kg) or naltrexone (0.4 mg/kg).

Slow IV infusions also are effective. Specifically, combinations of detomidine (0.04 mg/kg), midazolam (0.1 mg/kg), and ketamine hydrochloride (4 mg/kg) can be mixed with 234 mL of sterile saline solution and administered intravenously (1 mL/kg/h). Alternatively, detomidine can be substituted with xylazine hydrochloride (1.72 mg/kg) to achieve similar results. Atropine sulfate (0.04 mg/kg) can be administered to control excessive salivation and bradycardia (Ferreira 1997). Anesthetic recovery can be achieved without the use of any reversal drugs (Ferreira 1997).

Malayan Tapir

Tranquilization for loading and transporting Malayan tapirs has been successful with acepromazine (0.75 mg/kg) and diazepam (0.05 mg/kg per os [PO]), which can be administered the day prior and lasts approximately 48 hours (Quse & Fernandes-Santos 2014).

Successful immobilization of Malayan tapirs has been reported with butorphanol (0.15–0.24 mg/kg) in combination with detomidine (0.035–0.05 mg/kg) or medetomidine (0.01–0.03 mg/kg) or xylazine (0.3–0.35 mg/kg) IM (Janssen 1996; Quse & Fernandes-Santos 2014; Miller et al. 2000). If supplemental anesthesia is needed, ketamine can be administered at 0.5 mg/kg IV or IM (Janssen 1996; Quse & Fernandes-Santos 2014). Reversal is achieved with naloxone/naltrexone (0.6 mg/kg; Miller et al. 2000) in combination with yohimbine (0.2–0.3 mg/kg) or tolazoline (4 mg/kg; Miller et al. 2000) IM or IV (Janssen 1996; Miller et al. 2000).

Complications and Other Considerations

The most common adverse effects during tapir anesthesia induction or recovery are apnea, arterial hypotension, and ataxia/agitation; Quse & Fernandes-Santos 2014). Ataxia has been particularly noted in protocols with ketamine (Hernandez et al. 2014). Additional anesthetic emergencies include hypothermia, hyperthermia, bradycardia, and low oxygen saturation (Quse & Fernandes-Santos 2014). The low surface area to body mass ratio of tapirs may increase their likelihood of hyperthermia. Animals should be recovered in the shade with continual temperature monitoring with methods to decrease temperature, such as bathing in fresh water or moving to a well-ventilated area, readily available (Quse & Fernandes-Santos 2014; Medici et al. 2007). As it is also possible for tapirs to become hypothermic, procedures should be planned during mild temperatures and animals should be kept off of wet surfaces and shielded from cold air currents (Quse & Fernandes-Santos 2014; Medici et al. 2007).

While aspiration pneumonia is rare in tapirs, it has been reported, and steps should be taken to mitigate the risk. In order to reduce the chance of gastric reflux, food and water should be withheld for 18–24 hours prior to anesthesia. Animals may be intubated to minimize this risk.

As hindgut fermenters similar to horses, tapirs can be at risk of gastrointestinal disease following anesthesia (Hernandez et al. 2014). Atropine should be used with discretion as it has been associated with decreased motility in horses. Additional post-anesthetic risks include depression, self-injury, and re-narcotization. There have also been reports of tapirs returning to a deeper plane of anesthesia following protocols with medetomidine or detomidine, suggesting alpha-2 agonists may act longer in tapirs than their reversal agents (Hernandez et al. 2014).

It should be noted that the same anesthetic protocol could induce different responses (some adverse), even when applied to a same individual on different occasions (Mangini 2014). Apneic episodes can be reversed by external chest stimulation or via manual ventilation. However, recurrent apnea may require the use of doxapram hydrochloride (0.05–0.3 mg/kg IV). When alpha-2 adrenergic agonists are used and a persistent irregular respiratory rate is observed, partial doses of an alpha-2 adrenergic antagonist (yohimbine hydrochloride or atipamezole or tolazoline) may be administered to restore normal respiration, but this also could result in reversal of anesthesia. When animals experience bradycardia, atropine sulphate (0.02–0.04 mg/kg IM) can be administered (Mangini 2014; Quse & Fernandes-Santos 2014).

Other complications include potential ileus secondary to alpha-2 agonists or opioid administration, as has been noted in equine species (Merritt et al. 1998; Lester 2002). Postprocedural anorexia may occur in some ex situ managed tapirs, which might warrant feeding preferential food items for a few days to stimulate appetite for certain animals. Finally, myopathy or, more severely, rhabdomyolysis is always a potential consequence of general anesthesia is larger animals. Capture myopathy has been diagnosed in tapirs based on clinical signs and pathologic changes (Andrade et al. 2001; Castellanos 2013). The clinical outcome can be fatal, and increased likelihood of mortality has been associated with high stress capture events and concurrent infectious disease processes. Maintaining perfusion, appropriate blood pressure, fluid support, and careful positioning may all help alleviate the risk of muscle compromise during anesthetic events.

Analgesia and Analgesic Techniques

Given the similarities between tapirs and equids, most equine analgesics and analgesic techniques are applicable for clinical management of tapirs. Likewise, all contraindications relevant to equids also are pertinent to tapirs. Common analgesics include nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids. Among NSAIDs, phenylbutazone (3 mg/kg PO once daily [SID]) can be administered for orthopedic pain (e.g., chronic degenerative joint disease) as well as for soft tissue pain such as that associated with trauma, foot or dental disease. IV formulations of phenylbutazone are also available but should be administered with caution as extravascular injection may result in severe sloughing of the perivascular soft tissues, therefore IV administration is only recommended via catheterization. Other drugs include flunixin meglumine (1.1 mg/kg), which can be delivered via various routes. In rare cases, administration of flunixin has caused clostridial myositis in the horse (Jeanes et al. 2001). Other NSAIDs include ketoprofen (2 mg/kg SID IV or IM) and meloxicam (0.1–0.2 mg/kg PO SID). As with equids, the concurrent use of a gastro-protectant such as omeprazole is recommended when NSAIDs are administered to tapirs. Opioids such as tramadol (3–6 mg/kg PO twice daily) and butorphanol (0.02–0.05 mg/kg IM or IV every 4–6 hours) also are effective for pain management in tapirs.

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Rhinoceroses

Robin W. Radcliffe and Peter vdB. Morkel

The Rhinocerotidae

Introduction

Like the fabricated creature in Albretch Dürer's famous lithograph, the rhinoceros has long been a source of mystery, myth, and intrigue. Part unicorn and part armored beast, the current knowledge of rhinoceros anesthesia likewise represents a melding of pure art and hard science. Today rhinoceros anesthesia is relatively commonplace, yet no less demanding in practice.

The Rhinocerotidae are truly living fossils – a remnant and archaic mammalian family represented by only five extant species in four genera restricted to Africa and Asia. The relic survivors belie a one-time place of dominance among vertebrate organisms with over 150 fossil rhinoceros species discovered by paleontology across four continents (Prothero 2005). Yet, only five rhinoceros species are extant, four of which are critically endangered from poaching and loss of habitat, while the fifth is under constant relentless poaching pressure with current population numbers scarcely sustaining losses, and only through great resource investment from conservationists (Foose & van Strien 1997; Emslie & Brooks 1999).

Field anesthesia made possible the rhinoceros conservation success stories of the twentieth century (Harthoorn & Lock 1960; Player 1972; Meadows 1996) and remains a critical tool for proactive rhinoceros management programs incorporating translocation, ear-notching, radiotelemetry, microchip implantation, proactive horn trimming, and other techniques designed to secure the conservation of both African and Asian species (Dinerstein et al. 1990; Dinerstein 2003; Kock et al. 1990, 1995). Historical rhinoceros anesthesia protocols were based on highly effective reversible opioid combinations, yet new anesthesia techniques continue to improve efficacy and safety for both animals and human personnel (Fig. 47.1).

Taxonomy and Evolutionary History

The odd-toed ungulates of the order Perissodactyla include three living families: the rhinoceroses, horses, and tapirs. As the order name denotes, all Perissodactylids bear weight on one (equids) or three (rhinoceroses and tapirs) digits. Rhinoceroses and tapirs are among the most primitive of the world's large mammals and are further grouped into the suborder, Ceratomorpha based on a similar ancient body plan. The stout body of the rhinoceros is graviportal or designed for weight bearing with limb modifications to support large mass rather than the long angular limbs of equids in the suborder, Hippomorpha, specialized for speed.

The Perissodactyla enjoyed a period of extraordinary diversity in the Eocene epoch 34 to 55 million years ago before climate change presumably limited species radiation, culminating in extinction of 10 of the 14 perissodactyl families by the end of the Oligocene (Radinsky 1969). Prehistoric rhinoceroses in particular, as interpreted from fossil evidence, represented a far bigger group of organisms than exist today and included both horned and hornless forms. In fact, rhinoceroses were once the most common large herbivore in North America for most of the last 50 million years (Prothero & Schoch 2002). An extinct hornless rhinoceros, named Paraceratherium (also called Indricotherium), is known to science as the largest land mammal that ever lived, measuring over 6 m at the shoulder and weighing an estimated 20 tons (Prothero & Schoch 2002; Prothero 2005).

Biology and Morphology

The Rhinocerotidae are large terrestrial herbivores that have evolved either a browsing (black, Sumatran, Javan) or grazing (white, greater one-horned) strategy to process large quantities of fibrous feeds or simple grasses, respectively. As such, they share bulky elongated skulls, dental

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Figure 47.1 Helicopter-assisted aerial slinging of a black rhinoceros (*Diceros bicornis*) by its feet during translocation operations in the Kaokoveld of northwestern Namibia.

patterns largely devoid of canines and incisors (retained to various degree in the Asian species), and prehensile or wide, flat lips in the browsers and grazers, respectively. Like the equids, fermentation takes place in the cecum and colon. The rhinoceros gut is less efficient than that of ruminants since the microfloral protein formed in the hindgut is largely unavailable to the animal. As a result, rhinoceroses must eat more, have a relatively fast passage of gut contents, and possess limited time to reabsorb water from the feces. Therefore, rhinoceroses must drink every day or every second day, making it a water-dependent species rarely found more than 15 km from a water source.

Despite their often-conspicuous absence in many fossil rhinoceroses, the single horn (*Rhinoceros* sp.) or pair of horns (*Ceratotherium*, *Diceros* and *Dicerorhinus* sp.) is certainly the most distinguishing feature of the living Rhinocerotidae, giving name to the group literally as the *nose-horned beasts* (Prothero & Schoch 2002). Rhinoceros horns differ from true horns of the Artiodactyla by having no central core of bone. Instead, the tubular hair-like keratin filaments are



Figure 47.2 The distinctive hair coat of a Sumatran rhinoceros, a feature linking the primitive *Dicerorhinus* genus with its prehistoric past. Image courtesy of Mohd Khan bin Momin Khan, Malaysia Department of Wildlife and National Parks.

compressed in a linear fashion and set on a bony protuberance of the skull (Raubenheimer et al. 2015). Underneath the horns, the skull incorporates extensive nasal bones and sinuses – structures inordinately prone to complications from trauma during capture and translocation.

Rhinoceros skin is thick, with several centimeters of primarily collagenous dermis, with the Asian species having subdermal plates and heavy skin folds (Cave & Allbrook 1958; Shadwick et al. 1992). The greater one-horned rhinoceros of Asia is perhaps best known for the exaggerated armour-like plates or folds first popularized in the famous Dürer woodcutting of the Middle Ages. The epidermis, however, is very thin (1 mm) and heavily keratinized, incorporating extensive vasculature, which may predispose the rhinoceros to pressure necrosis, particularly in calves (Cave & Allbrook 1958; Gandolf et al. 2006). Significant body hair is an antiquated trait retained in all but one living species, the Sumatran or "hairy rhinoceros" so-called for its shaggy coat of hair (Fig. 47.2). Wild *Dicerorhinus* have shorter more bristly coats than their captive relatives, a trait providing protection for the skin from the numerous biting insects that share its environment. Hair, a primordial trait of many fossil rhinoceroses, including the woolly rhinoceros *Coleodonta* and massive one-horned hairy *Elasmotherium*, eloquently links the Sumatran rhinoceros with its long and prosperous past.

Rhinoceros Immobilization and Capture

Rhinoceros Capture Beginnings

Before widespread application of chemical capture techniques, early African rhinoceros capture operations utilized ropes and a chase vehicle (made famous in the film

Hatari staring John Wayne and Hardy Kruger). Although dangerous to the operator and stressful to the animal, some teams in East Africa became remarkably proficient at this form of capture. Chemical capture of rhinoceroses was first attempted with the dissociative anesthetic phencyclidine and the curariform muscle relaxant gallamine triethiodide. In 1960, during Operation Noah, many black rhinoceroses (*Diceros bicornis*) were saved from the rising waters of the newly constructed Lake Kariba, bordering Zambia and Zimbabwe, using these novel techniques (Child & Fothergill 1962; Condy 1964; Harthoorn & Lock 1960; Meadows 1996). Phencyclidine and gallamine were succeeded by the easily reversible opioids, first morphine and diethylthiambutene followed quickly by the more potent opioids including etorphine HCl (M99) (King & Carter 1965; King 1969; Keep et al. 1969). Over the past 60 years, etorphine has become the standard opioid for capture of the African and Asian rhinoceroses, with fentanyl citrate (Sublimaze), carfentanil citrate (Wildnil), and thiafentanil oxalate (Thianil) proving useful alternatives. Pioneering investigation by early practitioners such as Toni Harthoorn, Eddie Young, Ian Hofmeyr, Ian Player, and many others provided the foundation on which future rhinoceros chemical capture methods, including the present work, are based (Player 1972; Harthoorn 1973; Young 1973).

Remote Drug Delivery: Equipment and Darting Techniques

An assortment of remote drug delivery equipment is available for rhinoceros capture, including new developments, yet some of the early systems are still in common practice today, attesting to their simple and dependable design. In captive and boma situations all darting systems can be utilized, but nylon darts (Daninject or Telinject with 60 × 2 mm smooth needles) are preferred as they are quiet and relatively atraumatic. The authors prefer to hand-inject (using appropriate human protective safety measures) or pole-syringe *captive* rhinoceroses, including animals held in bomas, to eliminate the excitability that typically follows from the noise and impact of projectile darting.

For field capture of rhinoceroses on the ground or from a helicopter a robust and reliable darting method such as the Cap-Chur system is preferable, although it is a matter of personal preference, with many operators also using DanInject® or disposable Pneudart®/Motsumi® darts. Dart barrels made of aluminum or stainless steel are the most durable for field use, especially since power settings and impact energy are high, wind or down drafts from the helicopter can be significant, and the operator is often forced to shoot through vegetation. The dart needle should be 5–6 cm long for adult rhinoceroses. Rhinoceros skin can plug the lumen of a dart needle unless the needle has a relatively thick wall and narrow lumen (Cap-Chur NCL needles) or the tip is bent over (Fauncap dart needles) or the point is sealed and side ports are provided. The needle must preferably have a bead, low barb, or small collar about 25 mm from the base to hold the dart in the thick skin, although many operators successfully use 60-mm smooth needles in field conditions. A novel spiral-threaded needle was developed by Deon Joubert specifically for use on thick-skinned pachyderms; the dart needle can be easily removed by screwing it out of the animal, thereby reducing skin and tissue trauma (Fig. 47.3; Joubert Capture Equipment, Hadison Park, Kimberley, South Africa).

Proper dart placement is essential to ensure good drug deposition. The dart should be placed perpendicular to the skin for deep intramuscular (IM) injection (the thick skin of a rhinoceros often makes an angled shot ineffective). When darting from the helicopter, the muscles of the rump or the upper part of the hind leg offer the best targets. In the boma or on foot, any large muscle mass can be used for dart placement, although the neck and shoulder are



Figure 47.3 Robust dart needles for the capture of free-ranging rhinoceroses demonstrating the various design configurations of needle tip and barb. The spiral-threaded needles on the right are less traumatic and can be screwed back out of thick rhinoceros skin. Photograph courtesy of Joubert Capture Equipment, South Africa.

preferable. To avoid bounces, a dart should not hit too hard; some practitioners even say that the dart must land on the rhinoceros (C. Moueix, pers. comm. 2019). Antibiotics are routinely infused into dart wound sites, and intramammary mastitis preparations work well for this application.

Recumbency and Positioning

Recumbency and positioning are critical considerations for safe anesthesia of rhinoceroses whether in a zoological setting or in the wild. Prior to induction in captivity, thick padding or heavy mats should be utilized to protect recumbent animals from the concrete floors common in these environments. Myositis and neuropathy are serious potential complications. Traditionally, rhinoceroses immobilized in the field were maintained in or moved into sternal recumbency, however, irreversible muscle damage has developed in this position (especially if the rhinoceros goes down on a slope facing upwards with the full weight on its hind legs) as a result of occlusion of the blood supply to the limbs. Although uncommon, problems even occur with careful "placement" of the legs in an apparently natural position. With the rhinoceros in lateral recumbency, blood flow to the limbs is improved and circulation to the muscles allows delivery of oxygen and dissipation of carbon dioxide and heat generated while running. With the animal in lateral recumbency, the legs should be physically "pumped" up and down by hand every 20 minutes to aid circulation. The weight must be taken off the lower legs to "pump" them effectively; this is accomplished by two or more people lifting the upper legs and rolling the animal partially onto its back about 45° from horizontal. We recommend that all black rhinoceroses that have undergone any degree of exertion be placed in lateral recumbency for at least a few minutes.

The decision to move white rhinoceroses onto their sides should be based on several factors, including the degree of exertion, presence of muscle tremors, and duration of recumbency. White rhinoceroses often experience significant muscle rigidity, paddling, and even convulsions under opioid anesthesia; these effects are exacerbated by lateral positioning but tend to resolve with time. Importantly, the paddling and rigidity can be controlled by the post-induction administration of butorphanol, which improves blood gases by reducing the tremors and related oxygen consumption of muscles in etorphine-immobilized white rhinoceroses (Buss et al. 2018). Therefore, white rhinoceroses should be positioned initially in sternal recumbency until complete relaxation is achieved (Kock et al. 1995).

The position in which a rhinoceros is placed during recumbency is also an important consideration for respiratory function. In black rhinoceroses, it has been shown that arterial oxygen hemoglobin saturation (SaO_2) and partial pressures (PaO_2) are higher in sternal than lateral posture. Consistent with observations in domestic animals and humans, the black rhinoceros has greater dead space in lateral compared to sternal posture as indicated by a lower end-tidal carbon dioxide and higher dead space ratios and volumes in lateral (Morkel et al. 2010). The most appropriate posture for rhinoceroses during anesthesia must be based on the circumstances of each capture and should strike a balance between maintaining respiratory function while providing optimal circulation to the limbs. An oblique dorsal recumbency is probably ideal, with regular turning onto the opposite side every 20–30 minutes and a few minutes before reversal. This may require quite a few assistants in large adult rhino and provision must be made for about 10 strong assistants for longer procedures.

Eyes and Ears

The eyes of the recumbent rhinoceros must be shielded with a large towel or appropriate-sized blindfold to prevent retinal damage from direct sunlight, dirt accumulation, and corneal abrasion from the environment. For black rhinoceroses undergoing translocation, the use of a muslin cloth wrapped tightly around the face several times and secured to the horn with cable ties is preferred to a simple blindfold (Fig. 47.4). This technique serves to fix the eyes in a closed position and quiets the rhinoceros during crate transport. Before blindfolding, foreign material should be washed from the eyes using physiologic saline. The ear canals are plugged with cotton wool or a cloth while the



Figure 47.4 Attachment of a muslin cloth blindfold to aid in crate transport of the black rhinoceros (*Diceros bicornis*). Note the use of cable ties in front of the caudal horn to secure the blindfold over both eyes.

rhinoceros is anesthetized, leaving tabs for quick removal. Alternatively, when a large number of rhinoceroses are to be immobilized, two cloth-covered cotton wool plugs can be joined with cord so they remain together. If the rhinoceros is being transported, its ears are normally blocked for the trip. However, in white rhinos or animals that are pushing, it is better to remove the ear plugs since a stimulated rhino is less inclined to push than one protected from external stimuli. Caution should be used on removal of the earplugs as the sudden auditory stimulation can result in excitement or aggression.

Anesthesia Monitoring

A one-off thorough clinical examination with regular monitoring of vital functions (respiration, temperature, heart rate, capillary refill time) must be conducted for the duration of anesthesia. The focus should be on monitoring respiratory and cardiovascular function as well as thermoregulation since hypoxia and hyperthermia are common life-threatening sequelae. These functions are very much dependant on the degree of exertion and excitement before and during induction and must be kept in mind during the evaluation. Careful monitoring is especially important in old, debilitated, very young, and heavily pregnant animals or animals that become recumbent in a shorter than normal time (less than 5–6 minutes after darting). Any residual dart contents should be checked to see if they were injected, especially if more than one dart was used, as the success of drug delivery may dictate protocols for anesthetic monitoring and antidote administration.

Pulse oximetry (SpO_2, peripheral oxygen saturation of hemoglobin) provides an indirect measure of the arterial oxygen saturation of hemoglobin (SaO_2) and is a valuable aid to help monitor blood oxygenation and pulse in anesthetized rhinoceroses. However, it should not be a replacement for thorough patient monitoring. Without simultaneous correlation with arterial blood gases, pulse oximetry is a tool best used to monitor trends in oxygen saturation. SpO_2 values often fluctuate so the pulse oximeter should be observed for at least 1 minute; if the SpO_2 does not consistently read above 80% or is declining, an intervention is warranted. Based on higher oxygen affinity of white rhinoceros hemoglobin, it has been suggested that SaO_2 levels (calculated from PaO_2 by blood-gas devices and ranging from lows of 40% up to 98%; Kock et al. 1995; Atkinson et al. 2002) in rhinoceroses underestimate the true oxygen saturation of hemoglobin when calculations are made using human formulae (Bush et al. 2004; Haymerle et al. 2016). Historically, the sensor clip was attached to the pinnae of the ear after careful scraping with a sharp blade to remove the epidermis, but this technique has been linked to falsely elevated oxygen saturation of hemoglobin (SpO_2 90–100%) in hypoxemic animals (PaO_2 below 30 mmHg), presumably from measurement of blood that is exposed to air (Meyer, pers. comm., 2020). The use of a transflectance probe under the third eyelid or on the mucosa of the oral cavity, penis, vulva, or rectum is a better alternative. A cloth is placed over the sensor as ambient light can affect the reading. In animals with excessive muscle rigidity or tremors, as is common in immobilized white rhinoceroses, the sensor may fail to obtain an accurate reading. A reflectance probe held against the nasal mucosa works well (applied beyond the pigmented area) and has also been used with varying success on the inner surface of the lips, against the gums, on the conjuctiva and in the rectum or vagina. With experience, the color of the blood can be used as a crude indicator of blood oxygenation in the absence of sophisticated equipment, especially arterial blood collected from the inner surface of the pinnae.

Respiratory Gases: Oxygen and Carbon Dioxide

Respiratory depression is the most significant life-threatening complication encountered during routine anesthesia of the rhinoceros (Heard et al. 1992; Kock et al. 1995; Atkinson et al. 2002; Bush et al. 2004, 2005; Fahlman et al. 2004). Rhinos experience respiratory depression and perfusion-ventilation inequalities because of large body size, positioning, muscle rigidity, abdominal organs pressing on the diaphragm, and sensitivity to the respiratory depressant effect of strong opioids, more specifically the μ-opioid receptors (Bush et al. 2011). Severe respiratory compromise with hypoxemia, hypercapnia, and acidosis is more common with long captive procedures or under field conditions where higher doses of opioids are used to shorten induction times (Heard et al. 1992; Kock et al. 1995). Among the African species, these physiologic changes are more prevalent in the white than black rhinoceros (Bush et al. 2004, 2005).

Respiration is the first and most critical function to be monitored in rhinoceroses under anesthesia. In the field situation it is valuable to have a reliable person who does nothing but watch respiration, noting the rate and depth by observing chest movement. Be sure there is a free flow of air in and out of both nostrils and that the blindfold does not restrict airflow. The lower nostril, in particular, should remain clear of obstruction so passive regurgitation of stomach contents is free to drain. A cloth sack can be placed under the head to limit inhalation of dust or other debris. When monitoring breaths on a bouncing vehicle as with an immobilized rhinoceros transported on a sledge where it is difficult to watch chest movement, a finger can be hooked in the nostril or a hand held close to the nares to feel for the warm exhaled air. Breathing should be deep

and regular. Respiratory rate is approximately 10–15 breaths per minute on induction, going down to 4–8 breaths per minute about 10 minutes post induction when using potent opioids. Respiration must be monitored for at least 30–60 seconds to obtain an accurate picture of ventilatory pattern as immobilized rhinoceroses often give two or three quick breaths followed by a period of apnea. Rhinoceroses often develop apnea when moved into a different position. Animals should be rolled slowly and watched for breathing. A painful stimulus often incites the apneic rhinoceros to take a breath. Observation of arterial blood color by sample collection from arteries located on the inner pinna of the ear provides a reliable early indicator of blood oxygenation. Dark red, almost black blood indicates poor oxygenation while a lighter red color is normal and correlates well with mucous membrane color.

If breathing is slow, the rhinoceros develops apnea, or blood oxygenation is poor (SpO_2 consistently less than 80%), partial reversal with nalbuphine (Nubain), diprenorphine (M50:50), or butorphanol (Torbugesic) or complete reversal with naltrexone HCl (Trexonil) are indicated. In white rhinoceroses, partial agonist-antagonists are given immediately on arrival at the immobilized animal. Nalorphine is no longer available in Africa so its use has largely been replaced by alternative partial agonist-antagonists (Tables 47.1 and 47.2). Butorphanol administered intravenously at 10–20× the etorphine dosage in milligrams produces similar effects to Nalorphine (Haw et al. 2014). Since black rhinoceroses stand up readily with very small volumes of partial agonists, caution should be exercised to avoid sudden arousal. Intravenous (IV) doxapram HCl (Dopram; black rhinoceros 200 mg, white rhinoceros 400 mg) provides a smaller, transient improvement in respiratory rate and depth, and is a good "kick-starter" if apnea occurs. Doxapram must be used with caution in white rhinoceroses as it causes central nervous system excitation and exacerbates muscle tremors; it is advisable to use Doxapram in conjunction with butorphanol and supplemental oxygen.

Nasal or tracheal insufflation of oxygen (O_2; 15–30 L/min) can produce a rapid and significant increase in blood oxygen saturation in an immobilized rhinoceros but must only be administered after butorphanol administration (Haw et al. 2014, 2015). Although it did not correct systemic acidosis or hypercapnia, O_2 insufflation did substantially improve oxygenation and anesthetic safety in field-immobilized rhinoceroses (Bush et al. 2004; Fahlman et al. 2004; Haw et al. 2014, 2015). A variety of factors influence pulmonary blood gas exchange, including dose of anesthetic drug, position of the rhinoceros during immobilization, size of the animal, pulmonary perfusion and pressures, and ventilation-perfusion matching. Oxygen supplementation at the flow rates commonly used for rhinoceroses appears to produce a more profound improvement of patient oxygenation (PaO_2 108–194 mmHg) in subadult African rhinoceroses compared to adults, perhaps indicating greater ventilation-perfusion mismatch with larger body size (Fahlman et al. 2004).

A control valve and flow meter are attached to the O_2 bottle and oxygen is administered via a flexible silicon or rubber nasogastric tube (edges rounded to prevent damage to nasal mucosa), measuring 2 m long and with 9–14 mm inside diameter (Fig. 47.5). Concurrent monitoring of the respiratory rate and depth, and blood oxygenation remains essential. Administration of a partial antagonist (nalbuphine or butorphanol) will temporarily increase the rate and depth of respiration, reducing tissue oxygen requirements by reducing metabolism (Buss et al. 2018) and should be administered before oxygen supplementation (Haw et al. 2014). Oxygen supplementation is a practical solution to enhance pulmonary gas exchange in immobilized rhinoceroses and if used wisely one bottle is sufficient for many animals, therefore we recommend immediate intranasal or tracheal insufflation of oxygen (avoid high flow rates that can induce hypercapnia) in all recumbent rhinoceroses. Within a few minutes vital statistics will provide information about respiratory function and in most situations if all physiologic variables are satisfactory the flow can be reduced or discontinued (Table 47.3). A small percentage of animals, however, will develop a physiologic crisis where continued oxygen supplementation is critical. Aluminum oxygen bottles are now available that are small and lightweight, making them convenient for helicopter use.

Capnography offers a useful adjunct to monitoring with pulse oximetry and many portable devices combine measurement of end-tidal carbon dioxide with oxygen saturation of hemoglobin. Capnography is common practice in human anesthesia as an aid to confirm placement of endotracheal tubes and for early warning of hypoventilation. In expired respiratory gases, capnography provides a direct measure of CO_2 eliminated from the lungs. It also gives an indirect measure of CO_2 production in the tissues and circulatory transport of CO_2 to the lungs, but perhaps more importantly, it provides a good indirect measure of ventilation. Capnography is a rapid noninvasive technique that offers reliable information about tissue CO_2 production, circulation, pulmonary perfusion, and alveolar ventilation and respiratory patterns. It can be readily measured in recumbent rhinoceroses by placing a cut-off endotracheal tube in the nostril to allow for passage of air over the detector or sampling tube. For rhinoceros capture, capnography is gaining acceptance by practitioners as a tool to enhance anesthetic safety by offering a quick method to detect ventilatory or circulatory failure (Morkel et al. 2010).

Table 47.1 Suggested doses for chemical restraint of adult wild rhinoceroses including supplemental agents used for respiratory support.

	Immobilization			Respiratory Support	
Rhinoceros Species	**Protocol**	**Reversal**	**Reference Comments**	**Protocol**	**Reference Comments**
White rhinoceros	2–3.5 mg etorphine + 40–90 mg butorphanol + 25–50 mg midazolam IM dart Detomidine, medetomidine, midazolam or azaperone can be added to this mix (a) for better muscle relaxation and often better blood oxygenation DMM and (b) to speed induction DMMA	Naltrexone at 40 mg per mg M99 IV (full reversal) OR 2–2.5 mg diprenorphine per 1 mg M99 IV (reverses M99, but not BT)	Bush et al. (2005, 2011) Reduces respiratory depression, hypoxia, tachycardia, muscle rigidity, and tremors, but with slower induction and an animal that may stay on its feet Avoid butorphanol in combination with etorphine in rough terrain where a quick induction is safer	Produces an immobile rhinoceros in ~10 minutes and crating *without* partial opioid reversal In case of inadvertent overdose or cardiopulmonary suppression give diprenorphine to reverse the M99 while preserving the sedative effects of the BT	Bush et al. (2005, 2011, unpubl. data) Reverse part or all of opioid effects based on desired outcome
	3–4.5 mg etorphine + 40–60 mg azaperone (replace azaperone with 10–20 mg detomidine if no transport) IM dart Consider 5–20 mg midazolam slowly IV for muscle relaxation	*For crate reversal*: 2.4 mg M50:50 per 1 mg M99 plus 1–2 mg naltrexone IV if pushing NTX will be a relatively lively wake up and one must be adequately prepared (i.e., animal close to crate, rope properly attached to head, well organized team, etc.) *For field/boma reversal*: naltrexone at 40 mg per mg M99 IV (full reversal)	Kock et al. (1995, 2006); Rogers (1993a) Still considered standard translocation protocol Morkel (unpubl. data); Kock et al. (1995)	All white rhinoceroses: 20 mg butorphanol per 1 mg M99 (20 × M99 considered minimum dose for white rhinoceros, reduce to 10× or 15× if light) OR 20–40 mg nalbuphine IV OR 20–30 mg nalorphine IV (no longer available in Africa) and/or 1 mg M50:50	Kock et al. (1995, 2006); Hofmeyr & Morkel (unpubl. data) Butorphanol is being used with greater frequency for its partial agonist properties in white rhinoceroses across Africa
Black rhinoceros	4 mg etorphine + 40–60 mg azaperone (replace azaperone with 100 mg xylazine or 10 mg detomidine) + 5000 IU hyaluronidase IM dart Azaperone can be increased to 200 mg for a quicker induction if no transport. Can also combine azaperone with alpha-2 agonists.	*For crate reversal*: 20 mg butorphanol per mg M99 OR 1–1.8 mg M50:50 IV *For field/boma reversal*: Naltrexone at 40 mg per mg M99 IV (full reversal)	Morkel (1989) Higher M99 doses for *Diceros bicornis bicornis* Kock (1992): Kock et al. (2006) Hyaluronidase is always recommended to speed induction, especially as black rhinoceroses (unlike white rhinoceroses) often run themselves into trouble	Give 5 mg butorphanol IV to increase respiration and heart rate and lighten the anesthesia. A 10-mg dose will considerably lighten anesthesia and the rhinoceros may stand. Animal less likely to stand if kept in lateral position and the rhinoceros can be easily pushed down, if necessary. *Note*: Do not use the white rhinoceros respiratory protocol in black rhinoceroses as it will cause arousal *Instead*: 5 mg butorphanol IV, titrate to effect Important to have animal lateral and pump legs every 20 minutes	Hofmeyr (unpubl. data); Morkel (unpubl. data); Kock et al. (2006)
	2–2.5 mg thiafentanil (thianil) + 2–2.5 mg etorphine IM dart Can also use thiafentanil alone at etorphine doses (i.e. up to 5 mg) but watch the respirations	Same	Rogers (1993b)		

(*Continued*)

Table 47.1 (Continued)

	Immobilization			Respiratory Support	
Rhinoceros Species	**Protocol**	**Reversal**	**Reference Comments**	**Protocol**	**Reference Comments**
Greater one-horned rhinoceros	2–2.5 mg etorphine + 10 mg acepromazine IM dart OR 0.7 mg carfentanil	Diprenorphine at 2.5 mg per 1 mg M99 IV Naltrexone at 100 mg per 1 mg carfentanil IV	Dinerstein et al. (1990) One sudden arousal noted Induction times longer for breeding males	Cardiopulmonary depression not reported, 6–10 breaths per minute Surround target rhinoceros with 10–15 trained elephants	Dinerstein et al. (1990)
Sumatran rhinoceros Transport	2 mg etorphine + 80 mg azaperone + 5000 IU hyaluronidase IM dart OR Use M99:BT:MDZ	Naltrexone at 50 mg per mg M99 IM or IV	Author suggestion (extrapolated from captive animals)	Treat like black rhinoceroses; muscle rigidity and tremors common Use 5 mg midazolam to relax Use 5 mg butorphanol for partial reversal of respiratory depression	Radcliffe et al. (2002, unpubl. data)
	80 mg butorphanol + 80 mg azaperone IM dart OR Use MED:BT:MDZ (see Citino (2019) in Table 47.1)	Naltrexone at 2.5 mg per mg BT IM or IV	Use for compromised animal in snare	If rhinoceros is approachable give 25–40 mg butorphanol IV rather than via dart Sumatran rhinoceroses are easily tamed and can even be fed into a crate; a temporary boma can be erected to facilitate capture and crating	Radcliffe et al. (2002, unpubl. data); Citino (2019, unpubl. data)
	Long-acting tranquilizer for Crate transport and boma confinement: 50 mg zuclopenthixol acetate	No antagonist (see respiratory support)	40 mg azaperone Calm agitated rhinoceroses during crate transport 50 mg zuclopenthixol Repeat dose at boma offloading	10–20 mg biperidin OR 5 mg diazepam For control of undesirable extra-pyramidal effects	Candra (2018) Zuclopenthixol is the only LA tranquilizer that has been used in a Sumatran rhinoceros

BT, butorphanol; IM, intramuscular; IV, intravenous; M99, etorphine; MED, medetomidine; MDZ, midazolam; NTX, naltrexone.
Sources: Candra, 2018 Indonesian Rhino Capture Team Report; Morkel unpubl. data; Radcliffe unpubl. data; Bush M, Citino SB, Grobler D. 2005. Improving cardio-pulmonary function for a safer anesthesia of white rhinoceros (*Ceratotherium simum*): use of opioid cocktails to influence receptor effects. Proceedings of the American Association of Zoo Veterinarians, American Association of Wildlife Veterinarians, and American Zoo and Aquarium Association Nutrition Advisory Group, pp. 259–260; Bush M, Citino SB, Lance WR. 2011. The use of butorphanol in anesthesia protocols for zoo and wild mammals. In: *Fowler's Zoo and Wild Animal Medicine Current Therapy 7* (RE Miller, ME Fowler, eds.), pp. 596–603; Kock MD, Meltzer D, Burroughs R, eds. 2006. *Chemical and Physical Restraint of Wild Animals: A Training and Field Manual for African Species*. Zimbabwe Veterinary Association Wildlife Group and International Wildlife Veterinary Services; Rogers PS. 1993a. Chemical capture of the white rhinoceros (*Ceratotherium simum*) or 1993b. Chemical capture of the black rhinoceros (*Diceros bicornis*). In: *The Capture and Care Manual* (AA McKenzie, ed.). Pretoria: Wildlife Decision Support Service and South African Veterinary Foundation.

Table 47.2 Suggested opioid reversal protocols for walking, crate loading and transport of adult African rhinoceroses.

Method	Use	Reversal Drug or Opioid	Technique for Crating or Translocation
Butorphanol or nalorphine walking and crating method	For opiate (M99)-immobilized rhinoceroses	*White rhinoceroses* *Walking*: 10–20 mg BT per mg M99 Add 1–2 mg M50:50 for adult bulls for walking or crating (Hofmeyr) OR 1 mg M50:50 plus 20 mg nalorphine. Give further incremental 10–20 mg nalorphine IV up to 75 mg (Kock 2006) Nalorphine no longer available in Africa *Crating*: 10–20 mg BT per mg M99 OR Diprenorphine (M50:50) at 2.4× etorphine dose IV Add 1–2 mg naltrexone to prevent pushing in crate. Can combine the naltrexone with diprenorphine, expect a relatively lively wake up so be properly prepared with head rope, position of crate etc. *Black rhinoceroses* *Walking*: Start with 5 mg nalorphine IV Give incremental 5-mg doses every 5–10 minutes up to 20–40 mg (Kock et al. 2006) *Crating*: 15 mg butorphanol IV per 1 mg M99 with rhinoceros's head in crate door (Hofmeyr) Add 1–2 mg M50:50 to preclude pushing OR 10–20 mg nalorphine per 1 mg etorphine 1–2 mg M50:50 IV may be necessary to prevent pushing (Morkel) OR Blindfold with tight muslin cloth and wake up with 1–2 mg IV M50:50 Avoid myopathy in crating process by ensuring rhino does not squat in crate; use prodder plus repeat 1–2 mg M50:50 or 5 mg butorphanol doses	• Blindfold rhino. After cleaning eyes of mud or other debris, wrap a 4-m piece of muslin (mutton) cloth to cover eyes completely. Attach three zip ties to secure muslin cloth forward of posterior horn (Note: The blindfold option is really for black rhinoceroses and although it can be used on white rhinoceroses as well there is much less need for it). • Position the rhinoceros's head close to or inside crate door: black rhinoceroses very important to have head in door, white rhinoceroses not critical. Keep ears plugged until crated or leave in for transport. • Place head rope. Use 20 m of soft nylon behind posterior horn with knot on side of head, passing rope end through hole in crate. • Place break rope on rear leg just below hock. Use 8 m of nylon rope. • Position eight people on head rope and four people on break rope. Can use a 4 × 4 pick-up truck for back-up on rope if not enough people for head rope. • Reverse. Wait 90–120 seconds. Use electric prodder or water in ear to stimulate rhinoceros to stand if does not do so by itself. • Walk rhinoceros into crate by pulling on head rope. Slow rhinoceros with break rope or go slowly with head rope. Guide rhinoceros by ground personnel. Slide and secure pipes in crate (most crates have horizontal pipes, some only have the doors). • If black rhinoceros pushes in crate give 1 mg naloxone or 0.6–1.2 mg diprenorphine IV. If white rhinoceros pushes give 1–2 mg naltrexone IV. Use prodder on head or shoulders and not on hindquarters since rhinoceros will tend to push/squat more with stimulation of hindquarters.
Butorphanol alone crating method	For awake rhinoceroses in zoo or boma environments	*White rhinoceroses* 50 mg butorphanol IV (Radcliffe) *Black rhinoceroses* 25–50 mg butorphanol IV at time of crating for conditioned animals (Radcliffe) *Boma black rhinos*: Start with 10 mg butorphanol IV and increase in 5-mg increments (Hofmeyr)	Butorphanol is a useful agent for crating and transport of crate-conditioned rhinoceroses in zoological settings. Combine with azaperone as needed Butorphanol provides excellent sedation without concerns of excessive head pressing in crate and occlusion of nostrils in corner No reversal required for butorphanol once rhinoceros is in crate

(*Continued*)

Table 47.2 (Continued)

Method	Use	Reversal Drug or Opioid	Technique for Crating or Translocation
Diazepam: nalorphine crating method	For field-immobilized rhinoceroses	*White and black rhinoceroses* 10–15 mg diazepam IV 10 minutes before "waking" rhino with reversal protocol (Morkel) Use standard crating methodologies above for white and black rhinoceroses after giving diazepam	Give diazepam to recumbent rhinoceros and wait 10 minutes Use the same crating procedure as above using diprenorphine alone (white rhinoceroses) or nalorphine combined with diprenorphine (black rhinoceroses) This protocol eliminates much of the pushing often observed in the crate following diprenorphine or nalorphine reversal procedures Diazepam provides good sedation for ~8 hours, especially in white rhinoceroses
Etorphine: azaperone boma crating method	For loading and transport of boma rhinoceroses	*White rhinoceroses* *Boma, crating*: 1–2.5 mg etorphine IM (higher dose for adult bull) plus butorphanol at 10× M99 dose plus 20 mg (subadult) or 40 mg (adult) azaperone *Note*: Butorphanol can also be given at time of recumbency rather than in the original dart, particularly if rhinoceros requires medical care or other procedures under recumbency (Buss) *White or black rhinoceroses* 0.7–1.2 mg etorphine IM (Kock et al. 2006) OR 0.3 mg and 0.5 mg M99 for black and white rhinoceroses, respectively, without need to reverse *Crate sedation*: 0.05–0.15 mg etorphine IM plus 100–200 mg azaperone (can put in same syringe) IM or 10–30 mg diazepam IM (not in same syringe) *Transport*: 50–150 mg zuclopenthixol acetate IM	Use low doses of etorphine to crate rhinoceroses from boma; combine with azaperone in black rhinoceros; wave white flag on pole to lure rhinoceros into crate Etorphine is the only agent to calm an excitable rhinoceros inside a crate Butorphanol is replacing nalorphine and diprenorphine for both respiratory support and arousal for crate loading in both white and black rhinoceroses. Use small incremental doses (5 mg or less) in black rhinoceroses as reversal is more dramatic and produces a lively rhinoceros *For crate sedation*: nalorphine sedation wears off ~5 hours post-crating; thereafter give etorphine every 2 hours for duration of trip If rhinoceros is not excitable, give azaperone up to 200 mg per 6 hours *Note*: More etorphine is not effective within 3–4 hours of diprenorphine use and 8–24 hours following reversal with naltrexone Avoid perphenazine in white rhinoceros (if going to boma) as it causes anorexia; low dose OK if going straight to field

BT, butorphanol; IM, intramuscular; IV, intravenous; M50:50, ; M99, etorphine.

Sources: Buss, unpubl. data; Hofmeyr, unpubl. data; Morkel, unpubl. data; Radcliffe, unpubl. data; Kock MD, Meltzer D, Burroughs R, eds. 2006. *Chemical and Physical Restraint of Wild Animals: A Training and Field Manual for African Species*. Zimbabwe Veterinary Association Wildlife Group and International Wildlife Veterinary Services; Rogers PS. 1993a. Chemical capture of the white rhinoceros (*Ceratotherium simum*) or 1993b. Chemical capture of the black rhinoceros (*Diceros bicornis*). In: *The Capture and Care Manual* (AA McKenzie, ed.). Pretoria: Wildlife Decision Support Service and South African Veterinary Foundation.

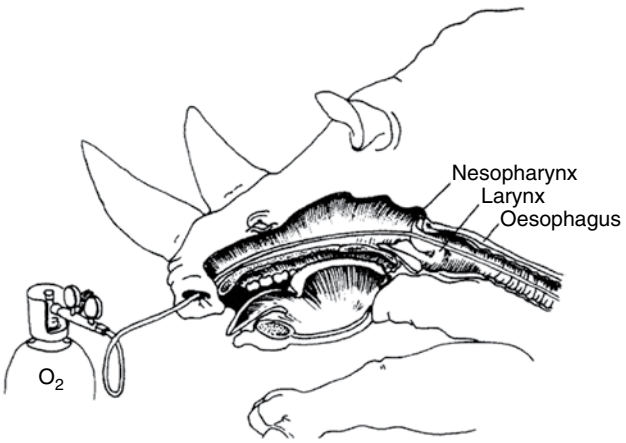


Figure 47.5 Illustration of the nasogastric tube tracheal insufflation technique for oxygen delivery in a recumbent white rhinoceros (*Ceratotherium simum*) under field conditions. Adapted from Bush et al. (2004), illustration courtesy of the South African Veterinary Association.

Table 47.3 Cardiopulmonary parameters in resting captive healthy white rhinoceroses (Citino & Bush 2007).

Parameter	Mean ± SD	Range
Heart rate (beats per minute)	39 ± 0.8	32–42
Respiration rate (breaths per minute)	19 ± 0.6	16–23
Rectal temperature (°C)	36.8 ± 0.1	36.6–37.2
Corrected indirect systolic pressure (mmHg)	160 ± 2.9	146–183
Corrected indirect diastolic pressure (mmHg)	104 ± 0.7	88–117
Corrected indirect mean pressure (mmHg)	124 ± 2.2	108–135
S_aO_2 (%)	97.2 ± 0.1	96.6–98
Arterial pH	7.391 ± 0.007	7.346–7.431
End-tidal CO_2 (mmHg)	45.1 ± 0.7	41.7–48
PaO_2 (mmHg)	98.2 ± 1.4	90.2–108.6
$PaCO_2$ (mmHg)	49 ± 0.9	44.4–53.7
Base excess (mmol/L)	3.5 ± 0.4	1.9–5.9
HCO_3^- (mmol/L)	29.3 ± 0.4	27.3–32.2

Body Temperature

Body temperature is an important variable and the best indicator of the degree of exertion and stress endured by the rhinoceros before induction. For every 1°C increase in body temperature above normal, there is an approximately 10% increase in oxygen consumption. A rhinoceros' body temperature varies slightly in relation to an inherent circadian rhythm, with a low at dawn and peak at dusk. Black rhinoceroses immobilized without excessive exertion have a rectal temperature of between 36.5 and 38.5°C, and anything over 38.5°C should be liberally doused with cool water. Young rhinoceroses tend to have a higher body temperature than adult rhinoceroses after running a comparable distance. Although drenching with water is important, it will not have a dramatic effect in lowering the core body temperature, as there is considerable thermal inertia in such a large mammal. It helps to fan the rhinoceros with branches or a portable leaf blower after the animal has been wetted with water. Holding leafy branches over the rhinoceros to provide shade can help lower the temperature, but it is important that people do not crowd around an immobilized rhinoceros and prevent air movement. A beach umbrella is the most efficient way to make shade: it is cheap, light, and easy to transport and can be folded to fit in the helicopter. A rhinoceros with a body temperature over 39°C must be processed quickly while a temperature greater than 41°C mandates immediate delivery of the antidote after dousing with water.

The rhinoceros, like other large mammals, is prone to hyperthermia during capture and translocation. The black rhinoceros appears to suffer a greater level of hyperthermia-related morbidity and mortality in the peri-capture period than the white rhinoceros. The goal of the capture team should be to minimize stress and exertion, and speed induction. The rise in body temperature can be documented while the animal is in recumbency following excessive exertion, however, a second phase apparently unrelated to the level of exertion appears to occur on crating. The mechanism of this hyperthermic response observed at variable periods after the rhinoceros enters the crate is not well understood, but could result from post-reversal agitation and muscle activity, a physiologic stress response, inadequate airflow inside the crate, or a combination of factors or mechanisms (Meyer et al. 2008). Simultaneous comparison of rectal and muscle temperatures in recumbent rhinoceroses demonstrates a 0.5°C (1°F) higher temperature in the muscle (Morkel et al. 2011). Since equilibration between rectal and muscle temperatures occurs slowly with time, a deep muscle thermistor can be a useful aid to measuring core body temperature. The probe is readily inserted into the dart site, but caution must be taken to avoid exposure to dangerous immobilizing drugs.

Additional options for temperature measurement in the rhinoceros include use of a handheld infrared thermometer (Fluke Hart Scientific Inc.) in the ear canal. In a recent pilot study deep-infrared ear temperatures were comparable to deep muscle temperatures, giving a reliable and rapid assessment of core body temperature. Surprisingly, the use of cotton or wool earplugs resulted

in ear canal temperature above deep muscle temperature and suggests that the inner ear in the rhinoceros may be an important site for cooling. In animals predisposed to hyperthermia (prolonged capture, high environmental temperature, etc.), rhinoceroses may benefit from removal of the earplugs and perhaps even application of some cooling mechanism to this site such as a cold pack (Morkel et al. 2010, 2011). Another tool that has been adopted to enhance temperature monitoring in rhinoceroses is the temperature microchip (LifeChip Inc.). After reaching equilibrium when implanted under the skin or into a muscle, chip temperatures were slightly lower than rectal temperatures.

Pulse and Blood Pressure

Heart rate is best obtained using a stethoscope while the pulse is readily palpable on the inside of the ear (medial auricular artery) or under the base of the tail (caudal artery). Pulse quality should be evaluated subjectively and compared with the pulse oximeter reading. It is often quite easy to visualize heart compressions by watching the chest wall or by feel with a hand placed over the cardiac window. The heart rate is usually 55–80 beats per minute (bpm) although it will be higher in rhinoceroses that have undergone marked exertion, especially in young animals (up to 140 bpm). Cardiovascular function and peripheral perfusion are assessed by capillary refill time and is measured by blanching the rhinoceros' gum for several seconds and then releasing. The observed delay or refill time should not exceed 2 seconds.

Hypertension is prevalent under etorphine anesthesia in black and white rhinoceroses (LeBlanc et al. 1987; Heard et al. 1992; Hattingh et al. 1994). Reports in white rhinoceroses anesthetized under field conditions noted reduction in blood pressures when azaperone tartrate (Stresnil) replaced fentanyl in etorphine-based combinations, an effect observed despite the higher dose of etorphine used in the cocktails containing azaperone (Hattingh et al. 1994; Buss et al. 2016). Sympathetic activation during immobilization of rhinoceroses is a very important factor that is not fully appreciated and may be the greatest cause of hypoxemia during etorphine immobilization (Meyer, pers. comm., 2020). Increased sympathetic nervous system action, peripheral vasoconstriction, and hypoxemia are purported factors in etorphine-induced hypertension in both rhinoceroses and equids (Daniel & Ling 1972; Heard et al. 1992). Opioid-related hypoxemia may induce sympathetic system stimulation and hypertension. Elevated heart rate is a good indicator of hypoxia; once hypoxia resolves the sympathetic response and associated hypertension disappear.

Rhinoceros Anesthesia in Captivity

Guidelines for Anesthesia of Captive Rhinoceroses

The large size of the rhinoceros belies an unexpected sensitivity to the opioid class of pharmacologic agents (Raath 1999). Surprisingly, the same dose of carfentanil citrate used to immobilize a 20-kg blackbuck (*Antelope cervicapra*) would also fully immobilize a 2200-kg white rhinoceros (*Ceratotherium simum*), making the rhinoceros over 100 times more opioid sensitive per unit mass than the average artiodactylid. This inordinate sensitivity of the Rhinoceros family to the opioid class – while responsible for the undesirable changes observed in cardiopulmonary function – also makes it possible to adapt less potent mixed agonist-antagonist opioid agents into anesthetic protocols for both captive and wild rhinoceroses (Radcliffe et al. 2000a; Walzer et al. 2000; Bush et al. 2005).

Planning for anesthetic events should include preparation of the subject and environment where these variables can be controlled. Depending on the purpose for anesthesia it is generally desirable to fast the animal for 12–24 hours prior to anesthesia (Radcliffe et al. 2000b). However, fasting is certainly not essential, as evidenced by the many successful field operations where capture of wild rhinoceroses is conducted in the absence of preanesthetic fasting. Water access should be denied for at least 12 hours and all water sources removed from the environment prior to drug delivery to prevent animals from losing consciousness while in a mud wallow or water pond. Both passive and active regurgitation of stomach contents are known, with the latter being very rare but quite spectacular (Radcliffe et al. 1998; Raath 1999). Passive regurgitation is common in immobilized rhinoceroses presumably secondary to drug- or hypoxemia-induced relaxation of the cardiac sphincter (Fig. 47.6). Because of the risks of regurgitation and inhalation pneumonia, great care must be taken with positioning of the head and nostrils, especially with animals in lateral recumbency.

Habitual patterns of behavior are important aspects of captive rhinoceros husbandry, facilitating close medical management. Anesthesia techniques should be adapted as part of these conditioning protocols. Regular visits by animal health staff to rhinoceros barns or bomas for acclimatization to the sights, sounds, and smells of the veterinary profession will help limit the stress of such procedures. In boma situations it is helpful to learn the nature of each animal, including its likes and dislikes, while also listening carefully to the keeper in charge of caring for the animal.



Figure 47.6 Passive regurgitation from the nares of a black rhinoceros (*Diceros bicornis*) forcefully expelled at expiration. The rhinoceros is positioned in sternal recumbency to help the reflux drain away from the airway.



Figure 47.7 Typical induction posture in adult white rhinoceros (*Ceratotherium simum*) under the effects of etorphine, illustrating characteristic head elevation, raised hackney action of forelimbs, and muscle rigidity. Image courtesy of Rolfe Radcliffe, Living Fossil Foundation.

African Rhinoceros Captive Anesthetic Regimens

White Rhinoceros (*Ceratotherium simum*)

The adult white rhinoceros is large and generally placid in captivity. Anesthesia with potent opioids is often associated with marked hypermetria, muscle rigidity, trembling, head shaking, and limb paddling (Fig. 47.7). These effects are undesirable and can be prevented by preanesthetic administration of the sedative or tranquilizer component of the cocktail and butorphanol post induction. In captive animals, initial dosing with IM azaperone or detomidine 20–30 minutes prior to induction with etorphine helps preclude muscle spasms and rigidity. With wild rhinoceroses, positioning in sternal recumbency until complete relaxation is achieved was deemed important in field practice (Kock et al. 1995).

Mixtures of etorphine or carfentanil combined with a sedative are standard agents for anesthesia of the captive white rhinoceros (Table 47.4). Doses ranging from 0.8 mg up to 3 mg of etorphine and 1.2 mg carfentanil are common (Heard et al. 1992; Walzer et al. 2000), however, supplemental opioids traditionally administered to extend anesthesia should be avoided as they have been linked to profound increases in pulmonary artery pressure and cardiac output, and decrease in arterial oxygen (Boesch et al. 2018). Following immobilizing doses of etorphine or carfentanil, other agents provide additional muscle relaxation and a deeper plane of anesthesia, including IV alpha-2 agents, propofol, guaifenesin, ketamine, and midazolam (Klein et al. 1997; Zuba & Burns 1998; Walzer et al. 2000; Kock et al. 2006). Muscle relaxation is critical for deep ventilation and to preclude the oxygen depletion and hyperthermia from muscle tremors inherent with the use of potent opioids. However, if used alone, these drugs may mask sympathetic activation that predisposes immobilized rhinos to tachycardia, cardiac hypoxia, and increased cardiac workload. Butorphanol does a good job of countering the adverse effects of sympathetic activation in white rhinoceroses.

Lower opioid doses are indicated in zoo-conditioned animals, yet the potent opioids are still associated with significant cardiopulmonary changes, especially as procedure length increases (Heard et al. 1992). One captive white rhinoceros immobilized with etorphine remained hypoxemic despite maintenance of inhalation anesthesia using intermittent partial positive pressure ventilation (Cornick-Seahorn et al. 1995). Hypertension is common while hypoventilation, pulmonary hypertension and shunting, and atelectasis induce hypoxia and hypercapnia (Heard et al. 1992; Bush et al. 2004).

Butorphanol combinations are replacing the use of more potent opioids for rhinoceros anesthesia in many zoological settings as safe and reliable anesthetic planes can be achieved for most procedures, including surgery (Radcliffe et al. 2000a–c). While not appropriate for all applications (i.e., fractious, nonconditioned animals or those with access to large areas) butorphanol combinations are highly effective. The author has used a mixture of butorphanol and azaperone for standing sedation and recumbent anesthesia in all four rhinoceros species maintained in captivity (white, black, greater one-horned, and Sumatran) with safe, predictable results (Radcliffe et al. 2000a,c; Radcliffe & Morkel 2007). Butorphanol doses for white rhinoceros range from 50 to 120 mg for an adult and from 10 to 20 mg for a calf or juvenile animal while azaperone doses range from 100 to 160 mg for an adult with supplemental doses given up to a maximum of 300 mg (Tables 47.4 and 47.5). IV butorphanol supplementation is effective at inducing

Table 47.4 Suggested doses for chemical restraint of adult captive rhinoceroses producing anesthetic planes from sedation to recumbency.

	Standing Sedation			Recumbency		
Rhinoceros Species	**Protocol**	**Reversal**	**Reference Comments**	**Protocol**	**Reversal**	**Reference Comments**
White rhinoceros	50–70 mg butorphanol + 100 mg azaperone IM hand-injection plus CRI	Naltrexone at 2.5 mg per mg BT IM or IV	Radcliffe et al. (2000a,b) Use CRI in long procedures	70–120 mg butorphanol + 100–160 mg azaperone IM hand-injection	Naltrexone at 2.5 mg per mg BT IM or IV	Radcliffe et al. (2000a) Supplemental IV dosing or CRI
	120–150 mg butorphanol + 5–7 mg medetomidine IM dart (Give 1–2 mg nalorphine IV to keep standing)	Naltrexone at 1 mg per mg BT Atipamezole at 5 mg per mg MED	Citino (2008)	120–150 mg butorphanol + 5–7 mg medetomidine (IM dart; recumbency ~20 minutes)	Naltrexone at 1 mg per mg BT Atipamezole at 5 mg per mg MED	Citino (unpubl. data) Improved analgesia for surgery
	0.8–1.5 mg etorphine IM dart	Naltrexone at 40 mg per mg M99	Portas (2004)	2–3 mg etorphine + 20–40 mg azaperone IM dart	Naltrexone at 40 mg per mg M99	Portas (2004)
				1.2 mg carfentanil IM dart	Naltrexone at 100 mg per mg M99	Portas (2004)
Black rhinoceros	25–50 mg butorphanol IV or IM hand-injection	Naltrexone at 2.5 mg per mg BT IM or IV	Radcliffe et al. (2000c; unpubl. data) Use for subadults and crating	1–1.5 mg etorphine + 100 mg azaperone IM hand-injection	Naltrexone at 50 mg per mg M99 half IV, half IM	Radcliffe (unpubl. data) Lower M99 doses with hand-injection
	1.5–2 mg etorphine + 2–3 mg medetomidine + 15–20 mg midazolam (Give 1–2 mg nalorphine IV to keep standing) IM dart	Naltrexone at 30 mg per mg M99 Atipamezole at 5 mg per mg MED	Citino (2019)	1.5–2 mg etorphine + 2–3 mg medetomidine + 15–20 mg midazolam (IM dart; recumbency ~15 minutes)	Naltrexone at 30 mg per mg M99 Atipamezole at 5 mg per mg MED	Citino (unpubl. data) Enhanced analgesia for dental surgery; midazolam to reduce aggression on recovery
	2–2.5 mg etorphine + 10 mg detomidine + 15 mg butorphanol IM dart	Naltrexone at 40 mg per mg M99 Atipamezole at 5 mg per mg DET	Portas (2004)	2.5–3 mg etorphine + 60 mg azaperone IM dart	Naltrexone at 20–40 mg per mg M99	Portas (2004)

Greater one-horned rhinoceros	100 mg butorphanol + 100 mg azaperone IM hand-injection	Naltrexone at 2.5 mg per mg BT IM or IV	Radcliffe & Lung (unpubl. data)	3.5–3.8 mg etorphine + 14 mg detomidine + 400 mg ketamine IM pole-syringe	150–300 mg naltrexone half IV, half IM No reversal DET	Atkinson et al. (2002)
	Medetomidine (4 µg/kg) Butorphanol (45–60 µg/kg) Midazolam (15–22 µg/kg)	Naltrexone at 1 mg per mg BT Atipamezole at 5 mg per mg MED	Citino (2019)	Etorphine (2 µg/kg) Medetomidine (3–4 µg/kg) Ketamine (0.1–0.15 mg/kg)	Naltrexone at 30 mg per mg M99 Atipamezole at 5 mg per mg MED	Citino (2019)
Sumatran rhinoceros	25–40 mg butorphanol IM hand-injection *Note*: Sumatran rhinoceroses are easily conditioned to chute restraint and can be hand-injected. Even wild rhinoceroses can be tamed quickly with feed and walked into a crate without use of drugs!	Naltrexone at 2.5 mg per mg BT IM or IV	Radcliffe et al. (2002) Use azaperone in longer procedures	30–50 mg butorphanol + 50–60 mg azaperone IM hand-injection	Naltrexone at 2.5 mg per mg BT IM or IV	Radcliffe et al. (2002) Higher doses for recumbency
				1 mg etorphine + 60 mg azaperone IM hand-injection	Naltrexone at 50 mg per mg M99 half IV, half IM	Radcliffe (unpubl. data) Azaperone 20 minutes prior to M99 or supplement midazolam
				10 mg butorphanol + 10 mg detomidine IM dart Wait 20 minutes 1.2 mg etorphine 5 mg acepromazine IM dart	150 mg naltrexone IV + 20 mg atipamezole IV	Walzer et al. (2010) 530-kg adult male; ketamine boluses (50 mg each) to extend anesthesia
	Adult female (wt. = 625 kg): 2.5 mg medetomidine (4 µg/kg) 20 mg butorphanol (31 µg/kg)	Naltrexone at 1 mg per mg BT Atipamezole at 5 mg per mg MED	Citino (2019) Excellent standing sedation for uterine endoscopy	Adult male: 4–5 mg medetomidine 40–50 mg butorphanol 20 mg midazolam	Naltrexone at 1 mg per mg BT Atipamezole at 5 mg per mg MED	Citino (2019) Combination for electroejaculation; supplement with glyceryl guaiacolate, medetomidine and ketamine

BT, butorphanol; CRI, constant rate infusion; DET, detomidine; IM, intramuscular; IV, intravenous; M99, etorphine; MED, medetomidine.

Sources: S.B. Citino, pers. comm., 2008, 2019. Use of medetomidine in chemical restraint protocols for captive African rhinoceroses. Joint Proceedings of the American Association of Zoo Veterinarians and the Association of Reptilian and Amphibian Veterinarians, Los Angeles, CA, pp. 108–109; Radcliffe, unpubl. data; Atkinson MW, Bruce H, Gandolf AR, Blumer ES. 2002. Repeated chemical immobilization of a captive greater one-horned rhinoceros (*Rhinoceros unicornis*), using combinations of etorphine, detomidine, and ketamine. Journal of Zoo and Wildlife Medicine 33(2):157–162; Portas TJ. 2004. A review of drugs and techniques used for sedation and anaesthesia in captive rhinoceros species. *Australian Veterinary Journal* 82(9):542–549; Walzer C, Goritz F, Hermes R, Nathan S, Kretzschmar P, Hildebrandt T. 2010. Immobilization and intravenous anesthesia in a Sumatran rhinoceros (*Dicerorhinus sumatrensis*). Journal of Zoo and Wildlife Medicine 41:115–120.

Table 47.5 Suggested doses for immobilization and anesthesia of rhinoceros calves in both captive and wild environments.

	Captive Calves			Wild Calves		
Rhinoceros Species	**Protocol**	**Reversal**	**Reference Comments**	**Protocol**	**Reversal**	**Reference Comments**
White rhinoceros	10–20 mg butorphanol IV for 66–159-kg calf (dose 0.13–0.15 mg/kg IV)	Naltrexone at 5 mg per mg BT	Gandolf et al. (2006) Heavy sedation Light anesthesia Mild resedation noted 8 hours post-reversal in one calf	*Calf*: 0.1–1 mg etorphine *Juvenile*: 1–2.5 mg etorphine *Subadult*: 2.5–3.5 mg etorphine (Note: above ranges represent calves of all sizes) *Note*: All white rhinoceroses, including calves, get IV BT at 10–20× the 1-mg M99 dose as soon as possible on recumbency to provide respiratory support OR 1 mg M50:50 plus 10 mg nalorphine IV	Diprenorphine at 2.5 mg IV per 1 mg M99 for transport Naltrexone at 40 mg per 1 mg M99	Kock et al. (2006) from South African National Parks Note: Always dart mother rhinoceros 30–60 seconds before calf (primarily for black rhinoceroses who easily split; in the case of white rhinoceroses, the calf rarely leaves the mother's side so one can wait longer or until mother goes down before darting the calf)
	2.5–5 mg butorphanol + 1.5–1.8 mg detomidine IM for 69–122-kg calf (dose 0.03 mg/kg BT plus 0.07 mg/kg DET)	Naltrexone at 4 mg per 1 mg BT Yohimbine at 0.125 mg/kg	Gandolf et al. (2006) Surgical anesthesia	*Calf*: 0.1–1 mg etorphine + 5–20 mg azaperone Subadult: 2.5–3.5 mg etorphine + 30–60 mg azaperone	Diprenorphine at 3 mg IV per 1 mg M99	Rogers (1993a)
Black rhinoceros	25 mg butorphanol IV for ~500-kg subadult calf	Naltrexone at 5 mg per 1 mg BT	Radcliffe et al (2000c) Heavy standing sedation	*Calf*: 0.1–1 mg etorphine Subadult: 2.5–3.5 mg etorphine	Naltrexone at 40 mg IV per 1 mg M99	Kock et al. (2006) from SANP
				Calf: 0.1–1 mg etorphine + 10–50 mg azaperone Subadult: 1.75–3.5 mg etorphine + 100 mg azaperone	Diprenorphine at 3 mg IV per 1 mg M99	Rogers (1993b); Kock et al. (2006) Note: Always dart mother rhinoceros 30–60 seconds before calf
				Note: Do not use the M50:50 plus nalorphine protocol in black rhinoceroses as it will cause arousal Instead: 5 mg butorpahnol or nalorphine IV; titrate to effect		
Greater one-horned rhinoceros	Butorphanol IV or IM Use white rhino as model	Naltrexone at 5 mg per 1 mg BT	Author suggestion based on use in African rhinoceros calves	*Calf*: 0.5–1 mg etorphine + 5 mg acepromazine *Subadult*: 2–2.5 mg etorphine + 10 mg acepromazine	Diprenorphine at 2.5 mg IV per 1 mg M99	Dinerstein et al. (1990) Same dose used for adult/subadult

BT, butorphanol; DET, detomidine; IM, intramuscular; IV, intravenous; M50:50, Diprenorphine; M99, etorphine.

Sources: Dinerstein E, Shrestha S, Mishra H. 1990. Capture, chemical immobilization, and radio-collar life for greater one-horned rhinoceros. *Wildlife Society Bulletin* 18(1):36–41; Atkinson MW, Bruce H, Gandolf AR, Blumer ES. 2002. Repeated chemical immobilization of a captive greater one-horned rhinoceros (*Rhinoceros unicornis*), using combinations of etorphine, detomidine, and ketamine. *Journal of Zoo and Wildlife Medicine* 33(2):157–162; Gandolf AR, Wolf TM, Radcliffe RW. 2006. Serial chemical restraint for treatment of decubitus ulcers in two neonatal white rhinoceroses (*Ceratotherium simum*). *Journal of Zoo and Wildlife Medicine* 37(3):387–392; Kock MD, Meltzer D, Burroughs R, eds. 2006. *Chemical and Physical Restraint of Wild Animals: A Training and Field Manual for African Species*. Zimbabwe Veterinary Association Wildlife Group and International Wildlife Veterinary Services.

recumbency in white rhinoceroses after initial drug delivery, if needed and desirable. IV dosing of azaperone without prior sedation has been associated with adverse extrapyramidal reactions in the horse and white rhinoceros, and should be avoided (Radcliffe et al. 2000a). Combinations of butorphanol and medetomidine offer another safe alternative that can produce dose-dependent anesthesia from standing sedation to surgical anesthesia for shorter procedures (Morkel & Nel 2019).

Inhalation anesthesia is possible in captive rhinoceroses where more invasive procedures requiring surgery or longer anesthesia times are indicated. Intubation in the rhinoceros is accomplished by hand or with an endoscope to guide placement of the endotracheal tube or a guide catheter into the airway. Unlike the horse, rhinoceroses have a unique, blind diverticulum in the dorsocaudal pharynx above the glottis. The anesthetist must be careful not to pass the tube into the diverticulum during intubation (Radcliffe et al. 1998).

A white rhinoceros was safely anesthetized to treat a surgical colic by sedation with butorphanol (80 mg) and detomidine (50 mg) followed by IV glyceryl guaiacolate (50 g) and three boluses of ketamine (200 mg per bolus) for induction (Valverde et al. 2010). Anesthesia was maintained for an additional 6 hours using isoflurane in oxygen delivered at 1–2% using a circle breathing system. Positioning for surgery and recovery were challenging, but made possible through the use of inflatable mats and the expertise of the local fire department. Although the rhinoceros eviscerated 3 days post surgery, the anesthesia and recovery were considered a success. Inhalation anesthesia together with a sling system facilitated laparoscopic-assisted transvaginal oocyte recovery in a black rhinoceros (Portas et al. 2006). Abdominal laparoscopy with insufflation of the abdomen is possible in rhinoceroses without general anesthesia by using a standing approach (Radcliffe et al. 2000b).

Black Rhinoceros (*Diceros bicornis*)

Black rhinoceroses appear predisposed to excitation during induction with etorphine, especially with remote drug delivery in zoological environments (Portas 2004). Using appropriate human safety practices, the stress of darting can be avoided by hand-injection, thereby alleviating much of the undesirable excitatory phase black rhinoceroses experience while also significantly reducing the total dose of opioid agents required (Radcliffe & Morkel 2007; Table 47.4). In bomas, to limit the "undesirable excitatory phase", great care should be taken to minimize the number of people and unusual objects close to the boma. Noise and movement should be avoided and, once recumbent, the rhinoceros' eyes should be covered and ears blocked as soon as possible. Significant induction risks include lacerations, limb and foot injuries, head trauma, damage to nasal sinuses, horn avulsion, and even death. With careful animal conditioning and procedure planning the risks of induction excitation are easily minimized. Likewise, antagonism of narcotic anesthesia in the black rhinoceros is characterized by rapid and powerful recoveries mandating extra care; never stand in front of a narcotized rhinoceros as arousal is often sudden and unpredictable (Kock et al. 2006).

As in the other rhinoceros species, potent opioids (primarily etorphine) have historically been used for anesthesia of captive black rhinoceroses with predictable results (Portas 2004). Zoo-conditioned animals require much lower doses of etorphine (1–1.5 mg) than their wild counterparts, especially when administered by hand-injection or pole-syringe (Table 47.4). Butorphanol alone or in combination with azaperone or detomidine HCl (Dormosedan) has also been used in the black rhinoceros, although its use is primarily limited to subadult animals, crating and translocation procedures, or well-conditioned animals since black rhinoceroses are easily excitable and may override drug effects (Radcliffe et al. 2000c). In addition to reversing the respiratory depressant effects at the μ receptors, butorphanol also antagonizes the powerful μ sedative effects, thereby greatly lightening anesthesia. For butorphanol use in the black rhinoceros, expect light planes of anesthesia and the need for frequent redosing. A more thorough discussion of mixed agonist-antagonist opioid cocktails and newer alpha-2 agents for use in both captive and field immobilization protocols for the African rhinoceroses can be found in the new techniques section of this chapter and in Tables 47.1 and 47.4.

Asian Rhinoceros Captive Anesthetic Regimens

Indian or Greater One-horned Rhinoceros (*Rhinoceros unicornis*)

Despite the common occurrence of Indian rhinoceroses in zoological parks and a propensity for foot problems necessitating chronic care, few published accounts of anesthesia in captive greater one-horned rhinoceroses exist (Atkinson et al. 2002; Portas 2004). One report combined injectable and inhalation anesthesia in a female *Rhinoceros unicornis* for ovariohisterectomy using etorphine and isoflurane in oxygen. The 7-hour long anesthesia (much of it in dorsal recumbency) was considered effective despite the animal succumbing to postsurgical complications (Klein et al. 1997). The most complete summary of captive anesthesia in this species, however, describes serial opioid-based anesthesia to facilitate long-term medical foot care in one animal. A combination of etorphine-detomidine (3–3.6 and 10–14 mg IM,

respectively) was given by projectile dart or etorphine-detomidine-ketamine (3.5–3.8, 14, and 400 mg IM, respectively) administered by pole-syringe (Atkinson et al. 2002). Use of the pole-syringe for drug delivery was preferred because darting was limited by a small target area among the peculiar anatomic neck folds and by drug selection for small dart volumes. While both drug combinations proved efficacious, subjective assessment suggested that the etorphine-detomidine-ketamine protocol produced more rapid induction, lowered the need for supplemental ketamine, and shortened reversal times (Atkinson et al. 2002).

The author has used butorphanol and azaperone (100 mg of each drug mixed in a syringe and given by hand-injection) to induce standing sedation in the Indian rhinoceros (Radcliffe & Lung, unpubl. data). A combination of butorphanol and detomidine (120 and 80 mg, respectively) produced sternal recumbency for surgical repair of a rectal prolapse (Bertelsen et al. 2004). As in the white rhinoceros, these protocols provide adequate muscle relaxation, sedation, and analgesia while being completely reversible with the pure opioid antagonists naltrexone or naloxone hyrdochloride (Narcan). Naltrexone is preferred unless short immobilization intervals are anticipated since renarcotization is common using naloxone alone; naloxone provides complete reversal for a short duration (~30–60 minutes) and is only suggested if repeat procedures are planned for the same day (Gandolf et al. 2000; Radcliffe et al. 2000a; Bertelsen et al. 2004; Portas 2004).

Javan or Lesser One-horned Rhinoceros (*Rhinoceros sondaicus*)

Rhinoceros sondaicus is the only rhinoceros not presently represented by captive specimens and was only extraordinarily displayed in zoological gardens during the seventeenth, eighteenth, and nineteenth centuries (Rookmaaker 1998). Although historical records indicate that at least 22 Javan rhinoceroses were captured between 1647 and 1939, only four survived long enough to reach zoo exhibits in Adelaide, Calcutta, and London (Rookmaaker 1998). The entire surviving wild population of Javan rhinoceroses can be found in Ujung Kulon National Park in West Java ($n \approx 72$). No accounts of Javan rhinoceros anesthesia exist, but techniques presumably would be analogous to the approaches used for the Sumatran rhinoceros (*Dicerorhinus sumatrensis*) or greater Asian one-horned rhinoceros (*Rhinoceros unicornis*), with size difference being a notable exception.

Sumatran Rhinoceros (*Dicerorhinus sumatrensis*)

Few reports of Sumatran rhinoceros anesthesia exist since captive specimens are rare. Etorphine (0.98–1.23 or 1 mg) combined with acepromazine (PromAce, 4–5 mg) or azaperone (60 mg) has been used to anesthetize captive Sumatran rhinoceroses (Portas 2004; Radcliffe & Morkel 2007). One adult male was immobilized on two occasions using a two-stage darting protocol. The first doses were considered inadequate and the authors subsequently recommended 10 mg of butorphanol plus 10 mg of detomidine IM followed 20 minutes later with 1.2 mg of etorphine and 5 mg of acepromazine IM, plus 50-mg supplemental doses of ketamine IV to extend the anesthesia period (Walzer et al. 2010). Darting of this animal likely contributed to long induction times (up to 40 minutes); Sumatran rhinoceroses are easily conditioned for hand-injection in a chute. As with the African species, muscle rigidity and cardiopulmonary depression are common with use of the potent opioids and preanesthetic administration of a tranquilizer is prudent to limit muscle tremors and improve respiratory function. Total azaperone doses should be kept to 100 mg or less as ataxia has been noted on recovery with higher doses in this species. Butorphanol has been combined with detomidine for standing sedation while the author routinely uses a mixture of butorphanol and azaperone for standing sedation and full recumbent procedures (Table 47.4; Radcliffe et al. 2002).

As with the African species, butorphanol combinations are preferred in captive Sumatran rhinoceroses to preclude the adverse cardiopulmonary changes associated with the use of more potent opioids. For adult animals butorphanol at a dose of 60–80 μg/kg with azaperone at 80–100 μg/kg and ranges of 30–50 mg and 50–60 mg butorphanol and azaperone, respectively, is recommended, with higher butorphanol doses being used on occasion to induce recumbency. Antagonism of the butorphanol effects is accomplished with naltrexone at a dose of 2.5 times the dose of butorphanol (Table 47.4; Radcliffe et al. 2002). Other tranquilizers may be used in place of azaperone such as the alpha-2 agonists, but care should be exercised as hypoxemia has been reported with use of these sedatives. Local anesthetics may facilitate invasive procedures, however, use of more potent narcotics such as etorphine or other pharmacologic agents such as ketamine and medetomidine may be indicated to induce surgical anesthesia.

New Captive Anesthesia Techniques

Although much has been learned about rhinoceros anesthesia, limitations still hinder safe and reliable procedures for these large mammals, especially where prolonged recumbency or surgery is required (Heard et al. 1992; Klein et al. 1997). Standing restraint where possible using mixed agonist-antagonists shows promise (Radcliffe et al. 2000a,b).

For the black rhinoceros, where potent opioids are still often preferred over mixed agonists, challenges include marked respiratory depression, inadequate muscle relaxation, need for frequent redosing, and incomplete analgesia in painful procedures. The incorporation of the potent alpha-2 agonist medetomidine with etorphine or butorphanol enhances sedation and analgesia in captive rhinoceroses (Citino 2008). Because alpha-2 agonists exacerbate respiratory depression and hypotension, contribute to dehydration, and alter thermoregulatory mechanisms, they must be used with caution in rhinoceroses of unknown health status, especially old and debilitated animals. However, under captive conditions where the health of an animal is known and a specific type of anesthesia is desirable, alpha-2 agents are effective supplements.

For the black rhinoceros, medetomidine (2–3 mg representing 2–2.9 μg/kg IM, 20 mg/mL solution) is combined with etorphine (1.5–2 mg representing 1.5–1.7 μg/kg IM; Citino 2008) and given by dart. The investigators were able to begin safe animal manipulations at approximately 9 minutes with full recumbency achieved in 15 minutes. This combination facilitated very painful procedures, including molar extraction and foot surgery, with the additional supplement of an IV guaifenesin-ketamine drip (1 g of ketamine in 1 L 5% guaifenesin solution) to enhance peripheral analgesia. Relaxation was excellent, with easy access to the oral cavity for dental surgery. Physiologic parameters were considered normal with concomitant nasal oxygen insufflation. Recovery from anesthesia was smooth and rapid, with no evidence of resedation or renarcotization using naltrexone at 30 mg per milligram of etorphine and atipamezole HCl (Antisedan) at 5 mg per milligram of medetomidine.

For white rhinoceros, where butorphanol has proven so effective in captive settings, the same investigator is using medetomidine (5–7 mg representing 2.47–2.81 μg/kg IM) and butorphanol (120–150 mg IM representing 62.5–64.9 μg/kg IM) to provide enhanced muscle relaxation and analgesia properties (Citino 2008). The animals can be manipulated within approximately 11 minutes of IM drug delivery with full recumbency in 20 minutes. The addition of medetomidine into these protocols has significantly improved muscle relaxation and analgesia properties for such painful ophthalmic procedures as eye enucleation and conjunctival flap surgery. As with the black rhinoceros, a 5% guaifenesin-ketamine drip was deemed useful for long procedures and to enhance peripheral analgesia. Antagonism was complete using naltrexone at 1 mg per milligram of butorphanol (204–262 μg/kg naltrexone) and atipamezole at 5 mg per milligram of medetomidine (25.4–31.2 μg/kg atipamezole).

Rhinoceros Anesthesia in the Wild

Guidelines for Anesthesia of Wild Rhinoceroses

Field anesthesia of Asian and African rhinoceroses is often undertaken to facilitate urgent conservation actions such as horn trimming, ear-notching, microchip application, radio-collaring, and horn transmitter implantation or translocation to protected areas (Dinerstein et al. 1990; Flamand et al. 1984). Ideally, rhinoceros capture operations should be conducted when environmental temperatures are lower than 25°C, usually in the early morning or late afternoon. Darting free-ranging rhinoceroses when ambient temperatures are high increases the risk of elevated body temperatures and associated physiological stress. If working in the late afternoon, a rhinoceros should not be darted unless there is sufficient daylight remaining (an hour is a minimum time to process the animal and deal with potential problems; Rogers 1993a,b). If a rhinoceros has run hard enough for its skin to become dark with sweat, the rhinoceros' body temperature will often exceed 39°C. Such an animal should not be darted or if it has already been darted, it must be drenched with water and processed quickly. If the temperature of an immobilized rhinoceros rises above 41°C, the antidote should be administered immediately and the animal released.

With good dart placement, recumbency should follow within 4–6 minutes post drug delivery (Morkel 1989, 1994; Kock et al. 2006). Induction is usually quicker in young rhinoceroses and longer in large bulls and heavily pregnant cows. If there are no signs at about 6 minutes, the rhinoceros should be darted again. Induction times of less than 3 minutes may indicate an overdose and it is important to get to such an animal quickly so that the respiration and other vital functions can be monitored; oxygen combined with a partial antagonist should be given, if necessary. In protocols incorporating thiafentanil (not recommended in white rhinoceroses), rapid inductions are expected and less of a concern. IV opioid use should be avoided due to risks of apnea, but if necessary give the opioid slowly while keeping a close eye on respiration. For the same reason caution must be exercised when giving midazolam or alpha-2 agonists by the IV route.

As a rhinoceros becomes affected by etorphine, its pace shortens, the forelegs are lifted higher in a classic "Hackney gait", and the head is elevated (Fig. 47.8). The rhinoceros then starts to blunder through bushes and slows down before going into lateral or sternal recumbency. In rough terrain rhinoceroses often run downhill once they are heavily narcotized and may easily injure

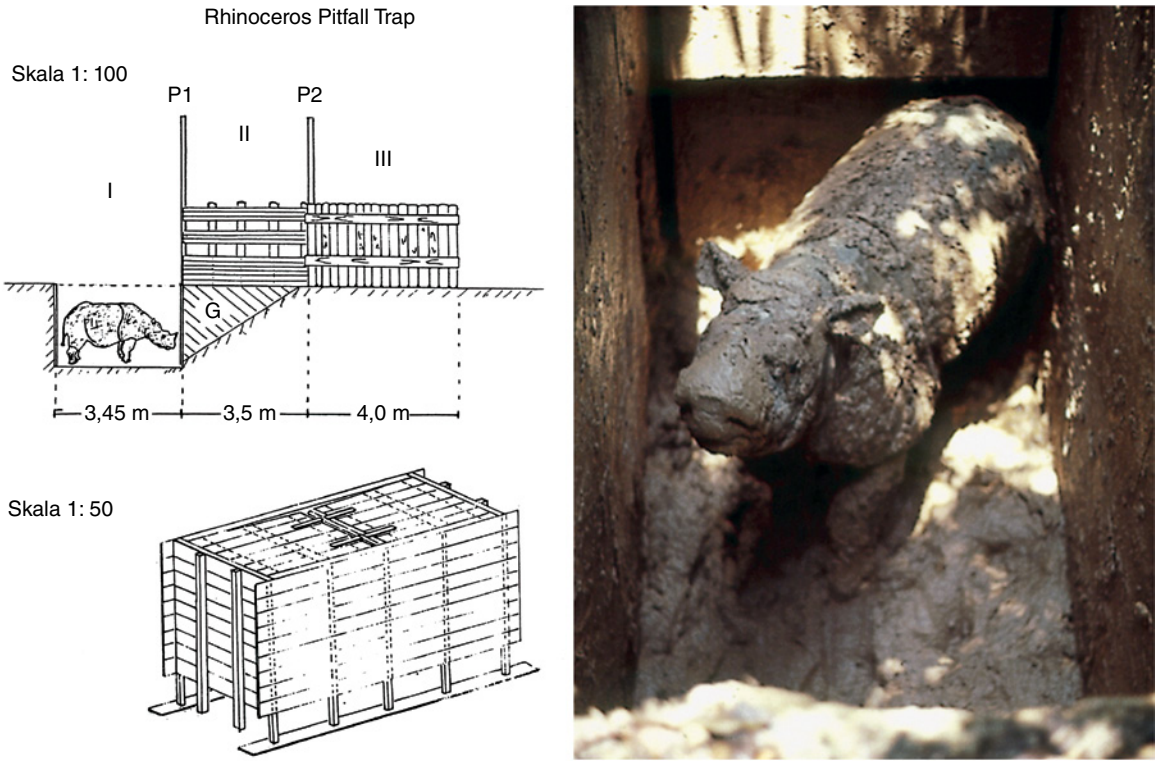


Figure 47.8 Diagrammatic sketch of pitfall capture method used in Indonesia's Riau Province for capture of wild Sumatran rhinoceros (*Dicerorhinus sumatrensis*). Sketches adapted from Sadmoko (1990), image courtesy of Mohd Khan bin Momin Khan, Malaysia Department of Wildlife and National Parks.

themselves by running into a gully or water source. With a quick induction, rhinoceroses usually go down in sternal recumbency. Occasionally the forelegs collapse first and the hindquarters remain elevated. In this situation the full weight of the abdominal organs press on the diaphragm and respiration may be compromised, especially in heavily pregnant females who have the weight of the fetus adding additional pressure. Such animals must be immediately pushed onto their sides. Most immobilized rhinoceroses will become fully recumbent, however, if the animal is still on its feet the brake rope can be placed around one of its rear legs, the blindfold over its eyes, and cotton wool in its ears.

On arrival at an immobilized rhinoceros a quick estimate of its age and body condition should be made. Older or debilitated rhinoceroses need special care. Nothing should impede respiration or push against the rhinoceros' belly, chest, or nostrils. On a slope, the rhinoceros should face uphill to alleviate pressure against the diaphragm. Field personnel must work quickly while the rhinoceros is recumbent – it helps to prepare a prioritized checklist before beginning each field capture exercise (Flamand et al. 1984; see also Box 47.1).

Box 47.1 Practical Strategies for Rhinoceros Field Anesthesia

- Darts should be tested and prepared ahead of time, loading the dart once you have visualized the rhinoceros, tailoring the dose for size, age, and condition of the animal. The rhinoceros should not be chased while the dart is being loaded. When darting from a helicopter get the dart in quickly and back off until the rhinoceros is nearing recumbency.
- Dart sites must be given special care in rhinoceroses because of the propensity for abscess formation. Rhinoceros skin is thick and tough, making drainage of subcutaneous infections unlikely without appropriate wound care. Intramammary antibiotics are often used, but in the face of growing antimicrobial resistance and a need for improved antibiotic stewardship, the authors suggest infusion of a noncytotoxic antiseptic directly into the dart wound.
- Tranquilizers are often combined with potent opioids to improve muscle relaxation in recumbent animals and to help sedate and calm the rhinoceros during transport.

- The addition of hyaluronidase, a hydrolytic enzyme that increases tissue permeability, greatly improves drug absorption and can markedly shorten the induction time.
- A lower opioid dose must be used for rhinoceroses that are in bomas, debilitated, old or where you cannot get to the immobilized animal quickly. *Be very careful with animals in poor body condition*. In most other situations underdosing of opioids is contraindicated for free-range capture of rhinoceroses.
- In general, any need for repeat darting of animals following partial or incomplete injection of immobilizing agents should redeliver the original full immobilizing dose. This is a useful rule for captive animals as well since repeat darting is often associated with excitation and prolonged drug effects if titration is attempted.
- A rapid induction shortens the period the rhinoceros is moving in a seminarcotized state and reduces injury, especially when immobilizing rhinoceroses in rough terrain. A quick induction also limits exertion and physiological stress, and associated elevations in body temperature, heart rate, and oxygen consumption.

Other Drugs and Immobilization Options

- Opiates: Carfentanil at 1–1.2 and 0.9 mg (captive white and black rhinoceros, respectively; Rogers 1993a, Portas 2004) and 3 mg for wild adult rhinoceros (Hofmeyr et al. 1975; De Vos 1978); etorphine at 1.8 mg plus 30 mg fentanyl OR fentanyl alone at 60 mg (black rhinoceros; Rogers 1993b; Kock et al. 2006); thiafentanil mixed with etorphine 2–2.5 mg thiafentanil plus 2–2.5 mg etorphine (avoid in white rhinoceros).
- Non-opiates: Medetomidine and butorphanol combinations (Morkel & Nel 2019).

Butorphanol and nalbuphine in African rhinoceros (Tables 48.2 and 48.3):

- To *improve respiration*, administer small incremental 5-mg doses of butorphanol or nalbuphine intravenously to effect (black rhinoceroses are very sensitive so be careful of sudden arousal). Butorphanol or nalbuphine may be used at 20–40 mg in a similar fashion for improving respiration in the white rhinoceros.
- To *walk a rhinoceros*, standard practice is now to give butorphanol at 10× (up to 20×) the etorphine (M99) dose (10–20 mg of butorphanol per 1 mg of M99) for white rhinoceros. Butorphanol can be incorporated into the initial dart or given at the time of recumbency or loading. Others give 1 mg of diprenorphine plus butorphanol followed by small incremental doses of butorphanol.
- For *transport*, wake white rhinoceros with 10–20 mg of butorphanol per 1 mg of M99 or give diprenorphine at 2.4× M99 dose (generally a lively wake up). Can also give 1–2 mg naltrexone with diprenorphine or later in transport to prevent pushing in crate. Can give 1–2 mg of diprenorphine intravenously if animal is pushing or collapsing in crate.

African Rhinoceros Wild Anesthetic Regimens

White Rhinoceros (*Ceratotherium simum*)

With the high doses of opioids used to speed induction under field conditions, the safe anesthesia of wild white rhinoceroses represents one of the most challenging branches of rhinoceros anesthesia (Table 47.1). Hypoxia, hypercapnia, hypertension, tachycardia, and acidosis are common physiologic abnormalities reported in anesthetized white rhinoceroses (LeBlanc et al. 1987; Heard et al. 1992; Hattingh et.al. 1994; Bush et al. 2004; Haw et al. 2014). A variety of techniques have been adopted to help alleviate the significant opioid-induced cardiopulmonary depression in African rhinoceroses. These include use of partial agonist-antagonist agents to reverse the μ-regulated opioid respiratory depression, respiratory stimulants such as doxapram, nasal or tracheal insufflation of oxygen, and incorporation of mixed agonist-antagonist agents into more potent opioid-based protocols to influence receptor effects (Kock et al. 1995; Radcliffe et al. 2000a; Bush et al. 2004, 2005; Fahlman et al. 2004; Haw et al. 2014).

Opioid doses for field anesthesia of adult white rhinoceroses range from 3 to 4.5 mg of etorphine plus 40–60 mg of azaperone or 10–20 mg of detomidine (Table 47.1; Rogers 1993a; Kock et al. 1995; Bush et al. 2004). When loading white rhinoceroses, lower azaperone doses (20–30 mg) are used to preclude recumbency in the crate (C. Moueix, pers. comm. 2019). Hyaluronidase (Hylase; 5000 IU) is often incorporated into darting protocols for rhinoceroses to shorten induction times (Morkel 1989). White rhinoceroses stopped moving 2–3 minutes sooner with hyaluronidase, but often remained standing (Kock et al. 1995). Fentanyl was once incorporated into drug cocktails for white rhinoceroses but is rarely used today (1 mg of etorphine is equipotent to 15 mg of fentanyl; Rogers 1993a). The parasympatholytic agent hyoscine was historically combined with opioids for its sedative and

amnesic properties as well as to induce "temporary blindness" by pupillary dilation (Player 1972; Rogers 1993a). However, its use is no longer widely accepted because of undesirable side effects and it is now considered obsolete (Kock et al. 1995; Raath 1999).

An extensive study of white rhinoceros anesthesia incorporating several drug protocols and 141 immobilizations over a 2-year period was conducted in Zimbabwe to enable dehorning operations (Kock et al. 1995). Initial immobilization mortality was quite high at 7% and was primarily attributed to hypoxemia and cardiovascular collapse. Subsequent captures utilized lower opioid immobilizing doses and simultaneously incorporated routine use of nalorphine (10–20 mg) or nalbuphine HCl (20–40 mg) to help improve respiration, especially in longer procedures where mortality was most prevalent. Of the various drug combinations tested (etorphine alone and in combination with fentanyl, xylazine, or detomidine), the etorphine-detomidine combination was considered superior because it was empirically judged as smoother and more rapid (no statistical significance). Pulse rates and creatinine phosphokinase (CPK) levels were significantly lower with the etorphine-detomidine combination, suggesting improved cardiac function and less muscle damage, respectively (Kock et al. 1995). Good muscle relaxation was observed without the rigidity and paddling common with use of potent opioids in the white rhinoceros. The ratio of etorphine to tranquilizer was critical and dose dependent, likely reflecting differences in drug pharmacology and onset of action.

An effective alternative for mitigating muscle rigidity in wild white rhinoceroses is the use of midazolam (Radcliffe & Morkel 2007; Table 47.1). Since immobilized white rhinoceroses are often first encountered in a standing position with a rigid body posture, IV midazolam at 5–20 mg is effective in inducing good muscle relaxation and recumbency. The Zimbabwe workers noted that even small incremental increases in etorphine in the initial immobilizing dose or redosing with etorphine resulted in poorer muscle relaxation and increased head shaking, jerking, and limb paddling (Kock et al. 1995). Midazolam has excellent muscle relaxation properties and is a useful adjunct in these situations.

Black Rhinoceros (*Diceros bicornis*)

Capture-related stress is a significant factor in field immobilization of the black rhinoceros, resulting in morbidity and mortality in the post-capture period (McCulloch & Achard 1969; Keep 1973). Rapid immobilization using high opioid doses in combination with hyaluronidase (or more potent agents such as thiofentanil alone or mixed 50:50 with etorphine) is the single most critical factor in reducing stress during black rhinoceros capture operations (Morkel 1989, 1994; Kock 1992). Furthermore, higher etorphine doses and use of hyaluronidase were associated with significantly shorter induction times, lower body temperatures, shorter distances moved, and reduced muscle damage, as evidenced by lower CPK and lactate dehydrogenase levels (Kock 1992). Although two accounts list 3 mg of etorphine as a standard opioid immobilizing dose for wild black rhinoceroses (Kock et al. 1990; Rogers 1993b), subsequent study suggests that 3 mg of etorphine is inadequate due to prolonged induction periods and associated capture stress (Kock 1992). Based on a review of published material and considerable author experience, 4 mg of etorphine is recommended as a good standard dose for an adult black rhinoceros bull or cow in good body condition (Table 47.1; Morkel 1989, 1994).

A scaled-down opioid dose should be utilized in young animals or those in poor body condition, but in all other circumstances a low dose of etorphine is contraindicated for free-range capture of the black rhinoceros (Kock et al. 2006). Azaperone is incorporated into etorphine-based African rhinoceros immobilization protocols at 40–60 mg total dose (Table 47.1). Black rhino immobilization and post crating tranquillization may be improved at higher azaperone dosages (180–200 mg in the dart) by reducing the stormy walking that typically follows partial antagonism with nalorphine or butorphanol (P. Nel, pers. comm., 2019). Concentrated (100 mg/mL) azaperone solutions should be carefully examined before use as they often crystallize under field conditions in cold temperatures. Xylazine or Detomidine (100 or 10 mg per adult, respectively) can be substituted for azaperone based on individual preference.

A disparity is evident in the opioid dose required for immobilization of the various subspecies of black rhinoceroses. The desert subspecies (*Diceros bicornis bicornis*) needs a slightly higher dose than the other subspecies. While 5 mg or even 6 mg of etorphine may be necessary for an adult *D. b. bicornis* in good condition, 4 mg is usually more than adequate for a comparable response in animals of the *D. b. minor* or *D. b. michaeli* subspecies. Not only is there variation between subspecies but there also appears to be some difference among individuals. The capture veterinarian must therefore be aware of these vagaries in dose response and be prepared to respond if an animal reacts unfavorably.

Asian Rhinoceros Wild Anesthetic Regimens

Indian or Greater One-horned Rhinoceros (*Rhinoceros unicornis*)

Techniques for field anesthesia of the greater one-horned rhinoceros were developed to meet research needs, including the elucidation of basic ecology, genetics, social

organization, and dispersal biology (Dinerstein et al. 1990; Dinerstein 2003). Furthermore, translocation programs are proving essential for reaching long-term population management goals for *Rhinoceros unicornis* in India and Nepal. Capture of wild greater one-horned rhinoceroses is usually conducted from atop trained elephants to facilitate finding and darting of rhinoceroses among the dense tall-grass habitats in the floodplain grasslands and riverine forests where these rhinoceroses flourish. In addition to providing an elevated platform, elephants (10–15 animals) are used to surround the target rhinoceros before and after darting to facilitate observation of the animal during induction and to prevent escape into open water (Dinerstein et al. 1990).

Adult greater one-horned rhinoceroses weigh an estimated 2000 kg, with males slightly larger than females. Dinerstein and colleagues immobilized 39 animals (representing 51 events) using a combination of etorphine and acepromazine (2–2.5 and 10 mg, respectively) delivered via remote IM injection either in the shoulder or rump using Cap-Chur darts with 5-cm needles (Table 47.1; Dinerstein et al. 1990). One adult female was immobilized with carfentanil (0.7 mg) and all animals were successfully reversed in the field using diprenorphine HCl (M50:50). Induction times were found to be significantly longer in breeding versus nonbreeding males, with the former group rarely moving far from the site of darting. A large disparity in induction times was noted across all age and sex groups, presumably related to variable drug delivery from dart placement among the thick skin folds characteristic of the species (Dinerstein et al. 1990).

Javan or Lesser One-horned Rhinoceros (*Rhinoceros sondaicus*)

There have been no published reports describing field capture or anesthesia of the Javan rhinoceros. As with the Sumatran rhinoceros, pitfall trap methodologies rather than stockade style traps are recommended for capture of lesser one-horned rhinoceroses in the rainforest environment provided the risks of flooding can be controlled (Nardelli 1987a; Sadmoko 1990). Field anesthesia is also possible, especially where animals are pushed out of the forest by human activities, and should be based on extrapolation of the best available information from the other Asian species.

Sumatran Rhinoceros (*Dicerorhinus sumatrensis*)

Several intensive operations have been conducted to capture wild Sumatran rhinoceroses using corral or stockade traps with little success (Abdullah 1987; Sadmoko 1990). In one instance an adult female Sumatran rhinoceros suffered severe head injuries and acute death following capture in a stockade trap from apparent panic-related self-trauma (Nardelli 1987b). Planned capture of wild Sumatran rhinoceroses in the forests of Southeast Asia has been most effective with the use of the pitfall trap. Pitfall traps (measuring 10 × 4 × 8 feet, length × width × depth) incorporate strong plywood walls to preclude landslides and a breakaway false ceiling that drops the animal into the excavated pit beneath (Fig. 47.8). Site selection favoring heavily used rhinoceros trails was considered the single most important criteria for success or failure of the pitfall trap (Abdullah 1987). Nevertheless, pitfalls suffer from significant problems. In many Sumatran rhinoceros areas poor drainage results in flooding of the pit despite careful preventive measures. Use of pumps to clear the flooded pits is recommended, but such equipment can delay capture due to the introduction of noise, smells, and other signs of human presence. Interference from nontarget species is also a common hazard; tapir, elephants, cattle, and even human beings have fallen into pitfall traps despite sign boards erected for the benefit of man (Abdullah 1987)!

Due to the dense nature of the rainforest environment and rare sightings of individual rhinoceroses therein, routine chemical capture techniques developed for Asian and African rhinoceroses are considered of high risk as an animal may be lost in the darting process. Increasingly, however, animals are being pushed from the jungle by human encroachment and once beyond the protective boundary of the forest are immediately threatened. In these circumstances, pitfall capture methods are not feasible and chemical capture techniques are indicated. Therefore, the capture process for an "at-risk" Sumatran rhinoceros found wandering within a Southeast Asian village or otherwise outside a protected area should be approached with careful planning of some urgency. Once the appropriate National Park, Rhinoceros Protection Unit (RPU), and sanctuary staff have been contacted the following stepwise approach to capture and translocation is suggested (Radcliffe et al. 2002).

Guidelines for Capture of Displaced Sumatran Rhinoceroses

Secure the Immediate Area

In the event a wild Sumatran rhinoceros is found wandering outside a protected area, the first priority should be to secure the area from villagers and would-be poachers to prevent the animal from being shot or otherwise harmed before capture or relocation of the rhinoceros is possible.

Determine Relocation Strategy

If possible, a small core group of decision makers should be formed to make immediate assessment of the risks and benefits of rhinoceros relocation. If the rhinoceros is unharmed and close to a protected area (<10 km), then it may be

desirable to move the rhinoceros without capture by pushing it back toward the forest. If the animal is injured or otherwise in need of medical attention or far (>10 km) from the forest, a decision should be made to capture the animal.

Make a Plan for Rhinoceros Capture

Considering the high risks associated with capture without using chemical restraint (i.e., the rhinoceros is physically restrained following an extensive stressful chase without the use of routine chemical capture methods), this approach is not considered safe or desirable (Fig. 47.9). The following are suggested guidelines and methodology for capture of at-risk Sumatran rhinoceroses outside a protected area.

Capture Method 1: Field Capture using Chemical Restraint

If a trained capture team is available (i.e., within 1 day's travel time) then it may be wise to have the RPU ranger staff carefully monitor and secure the rhinoceros and surrounding area from a distance without pushing the animal to run as the rangers await the capture team. A rapid induction and recumbency will be essential for safe capture of a tropical ungulate species such as the Sumatran rhinoceros that may risk drowning or suffer from capture myopathy.



Figure 47.9 Like the other rhinoceros species, the Sumatran rhinoceros (*Dicerorhinus sumatrensis*) is prone to capture myopathy. Here a wild "hairy" rhinoceros is restrained with a girth rope in hopes of moving the animal into a temporary boma. Hyperthermia is best avoided by limiting chase periods and liberal application of water. Image courtesy of Sugiyo, Wildlife Conservation Society, Indonesia Program.

For field anesthesia of the Sumatran rhinoceros, a combination of equal parts butorphanol and azaperone (80 mg each) is recommended for simplicity and its inherent safety for both rhinoceros and people alike (Table 47.1; Radcliffe et al. 2002). However, if a well-trained veterinary capture team is available then use of more potent opioids such as etorphine combined with azaperone and hyaluronidase (2 mg, 80 mg, and 5000 IU, respectively) or the newer etorphine-butorphanol-midazolam protocols may be considered depending on the situation (Bush et al. 2011). If the rhinoceros is already compromised from a chase or is restrained by a snare, the use of the safer butorphanol protocol is preferable to the potent opioids (Table 47.1). The butorphanol-azaperone combination may require confinement within a temporary boma or some additional restraint via a body or head rope to facilitate crating in healthy animals.

Capture Method 2: Field Capture by Erecting Temporary Boma

The Sumatran rhinoceros is perhaps the only species of rhinoceros that can be captured by human physical restraint alone, albeit after much chasing and associated capture stress. Therefore, if a trained capture team is not available and the rhinoceros is in immediate peril, physical capture can be a feasible option. To begin, the animal can be followed from a safe distance and without excessive chasing until the rhinoceros is located within an area where it is resting and approachable (i.e., in water or other suitable location; Fig. 47.10). Large rolls of shade cloth or tarpaulin are then carefully erected without disturbance to form a temporary boma surrounding the rhinoceros that will facilitate sedation, crating, and transport. Once the animal is restricted within the confines of the artificial boma, hand-injection or pole-syringe delivery of the butorphanol-azaperone combination will facilitate safe crating and transfer. The boma method is not likely to eliminate the long chase periods and accompanying stress, but it was effective in the recent capture and relocation of a young adult Sumatran rhinoceros in Indonesia (Fig. 47.9).

Sumatran Rhinoceros Transport

For Sumatran rhinoceroses that are conditioned to a crate prior to capture (i.e., captive animals or wild animals that allow crate training *in situ* such as in an oil palm



Figure 47.10 A wild Sumatran rhinoceros (*Dicerorhinus sumatrensis*) undergoing "hand translocation" without the use of chemical restraint after displacement from a protected forest reserve in Indonesia. Although this animal survived significant capture-related morbidity, chemical capture techniques are preferred if trained staff are readily available. Image courtesy of Chandra Putra, Way Kambas National Park, Sumatra.

plantation) there is often little need for sedation during transport. However, for animals captured in a pitfall trap, the use of both short-acting and long-acting tranquilization is indicated. In November of 2018, a Sumatran rhinoceros named Pahu was captured in a pitfall trap in East Kalimantan, Indonesia. The estimated 400-kg animal received 50 mg of zuclopenthixol acetate IM by pole-syringe shortly after capture, representing the first use of this long-acting tranquilizer in this species (Candra et al., unpubl. report). The zuclopenthixol acetate produced a calming effect during the 36 hours the animal remained in the pit while the capture team constructed a ramp and moved the transport crate into position. Two days after capture and while the animal awaited transport overland by truck, the rhinoceros became agitated in the crate and 40 mg of azaperone was given IM. The animal was calm within 20 minutes and 6 hours later the rhinoceros was loaded onto the back of a 4 × 4 pickup truck to begin transport to a nearby sanctuary. Following the 16-hour road transport the animal was given a second dose of 50 mg of zuclopenthixol acetate IM by pole-syringe immediately prior to off-loading into the sanctuary boma. The capture and translocation were a success.

Rhinoceros Crating and Transport

The moving or translocation of rhinoceroses is a specialized branch of rhinoceros anesthesia that has been practiced since the first African rhinoceroses were saved from the rising waters of Lake Kariba. The crating and relocation of rhinoceroses is now standard practice as urgent conservation measures, including enhanced animal monitoring and protected area management, have become effective tools in the fight against poaching (Hitchens et al. 1972; Flamand et al. 1984; Henwood 1989).

Walking a Rhinoceros

If a crate cannot be placed directly in front of the anesthetized animal, the rhinoceros can be "walked" a distance and guided into the crate (Fig. 47.11 and Table 47.2). When the rhinoceros becomes recumbent, the blindfold, cotton wool, head rope, and brake rope are applied. Four to six people are stationed on each rope, two people on each shoulder, one person to the side leading the team, and two people walking in front of the rhinoceros, clearing obstacles in its path. The rhinoceros is given small incremental doses of IV diprenorphine or butorphanol depending on species (Table 47.2). Butorphanol can be given IV at 10–20 times the etorphine dose to walk a white rhinoceros into a crate. Mixed opioid antagonists should be used with caution in black rhinoceroses and at lower doses with smaller increments compared to white rhinoceroses. Regardless of antidote used, a prodder is judiciously applied to the feet just above the nail, or to the muzzle or perineal area to get the rhinoceros to stand and keep it moving. After each dose, wait a few minutes (up to 10 minutes) and check the rhinoceros' response to the prodder or by squirting water in the ear. If there is no response, give another dose of the partial agonist-antagonist. Once the rhinoceros stands, it should begin to stagger forward and can then be readily guided with the head rope and by the people on the sides. If the rhinoceros moves too fast, go slowly with the head rope and pull the brake rope to slow the moving



Figure 47.11 "Walking" an etorphine-immobilized white rhinoceros (*Ceratotherium simum*) using ropes and trained personnel to guide and stabilize the narcotized animal.

rhinoceros. Particularly with young and fractious individuals it is important to slow the rhinoceros as it approaches the crate so it does not traumatize itself on entrance. A rhinoceros that charges too quickly into the crate can strike the far wall with such force to avulse the horn or crush the nasal bones. To preclude problems with loading, diazepam 10–15 mg IV 10 min before waking the rhinoceros helps to keep the animal calm when aroused in the crate.

Black Rhinoceros Crating

The recent decline in the availability and manufacture of the partial agonist-antagonist nalorphine in southern Africa has necessitated the use of alternative techniques for partial reversal and crating of black rhinoceroses in the field. Initial trials using similar agents such as nalbuphine and butorphanol have worked (sometimes quite well) although they have also been associated with irregular outcomes and responses in the black rhinoceros. Nalbuphine provides a satisfactory partial reversal that facilitates crating of black rhinoceroses, but appears to predispose crated animals to dog-sitting and squatting, which can lead to serious myopathy and inability to stand (Fig. 47.12). Butorphanol given in higher doses (25–30 mg for an adult animal) also provides a reliable partial reversal for crating of black rhinoceroses. However, such animals seem prone to head pressing in the crate and require constant supervision. Head pressing in the black rhinoceros seems to be correlated with too much opioid activity; this can be countered by using naloxone (one or two 0.4-mg ampoules) to lighten the opioid effect with a pure antagonist (P. Nel, pers. comm., 2019). If the rhinoceros is slightly too alert, one can manage the animal with azaperone, which does not cause head pressing.



Figure 47.12 Post-translocation myopathy in a black rhinoceros. Capture complications are more prevalent in animals that experience excessive chase periods, hyperthermia, or struggle to stand on crating. Image courtesy of Birgit Kötting, Etosha Ecological Institute, Namibia.

A novel approach to crating the black rhinoceros currently practiced in Namibia combines diprenorphine together with methods to limit noise and visual stimulus during transport. A muslin (mutton) cloth works well for both white and black rhinoceroses (Fig. 47.4). Animals remain remarkably tranquil, although some degree of chemical tranquilization is still necessary. The beauty of blindfolding is that a physical rather than a chemical means is used to calm the animal. The cloth must be placed with great care to avoid damage to the eyes or loss of the blindfold during crate transport. One should brush or blow any dirt from around the eyes and flush the eyes with saline, if necessary. Tying the blindfold properly takes two people – the secret is to start with a 4-m length of muslin cloth and place the middle point on the forehead directly behind the back horn. Both ends of the cloth are pulled tightly on either side of the head, making sure both eyes are closed in a normal manner. The cloth is wrapped under the jaw around the opposite side behind the back horn where it is tied securely. While wrapping, the cloth should be spread to cover the eye properly and hooked behind the jaw. Three heavy-duty cable ties 40 cm in length are used to secure the blindfold to the rhinoceros. Two ties are threaded through holes in the cloth fashioned above and forward of the eye and closed to form a loop. A third cable tie is threaded through the two loops in front of the back horn and pulled tight. The cable ties serve to pull the cloth forward securely over the eyes. If the cloth becomes loose during the journey, simply pull on a cable tie to tighten the blindfold.

Reversal and crating are then routine: a heavy hemp rope is secured around the head with a blindfold and threaded through the front of the crate. This rope will provide the forward pull on standing and will direct the rhinoceros into the forward part of the crate. A second rope is secured to one rear leg and is used as a break rope to simultaneously slow the momentum of the rhinoceros so it does not collide with the front of the crate, where horn or nasal trauma may result. A relatively high dose of diprenorphine (black rhinoceros adult 1.5–2 mg; subadult 1 mg) is given intravenously after positioning immediately in front of the crate door. The team remains quiet and the animal is not disturbed for 2 minutes. On standing, the rhinoceros is pulled forward into the crate while the break rope on the back leg slows the rhinoceros. Once inside the crate, the rhinoceros is secured by sliding three pipes into place at the rear of the crate and the rear doors are closed. This protocol consistently produces a lively and relatively awake

rhinoceros inside the crate that remains calm because of the combined use of a secure blindfold and earplugs.

Rhinoceroses blindfolded with muslin cloth travel well and can be given other sedatives, including azaperone (60–100 mg) or additional opioids (etorphine or butorphanol), during transport as needed. From about 4 hours onward an additional 0.05–0.1 mg of etorphine (usually with about 60 mg of azaperone) is administered, and can be repeated every 2 hours. The veterinarian (or someone with a high level of experience with opiates) must remain with the animal for the entire trip to evaluate and top-up as needed. Straightening with a prodder applied lightly to the forehead, neck or shoulder is often necessary in the first few hours. The muslin cloth can be kept on for as much as 36 hours. It is essential to put the cloth on tightly, make sure it is 100% clean, and ensure that no sand or dirt gets into the rhinoceros' eyes.

The beauty of the tight blindfold and blocked ears is that you can wake up the rhinoceros to a large degree (and therefore prevent pushing), but because the animal cannot see or hear it is very unresponsive and rarely gets excited – the effect is quite remarkable. However, the muslin cloth blindfold is inadequate by itself for crate transport and additional tranquilization using repeated ultra-low doses of etorphine and azaperone is essential along the road.

Tranquilization During Transport

All black rhinoceroses require tranquilization during transport (even most crate-conditioned animals) to preclude excessive struggle and associated trauma (Table 47.2). Other rhinoceros species tolerate transport better than black rhinoceroses, but still often benefit from some sedation. The veterinarian must always travel with the rhinoceros and be prepared to give additional sedatives or even narcotics if needed. It is imperative that the veterinarian anticipates the animal's tranquilization needs as waiting until the rhinoceros is alert and bouncing around will risk unnecessary trauma to both animal and attendant. Additionally, a cool animal is generally more relaxed than an overheated one.

Rhinoceroses settle into the rhythm of transport quite well after just a few hours. However, as the short-acting tranquilizers begin to wear off, the animal may become excited if suddenly startled (i.e., from stopping, off-loading, etc.). The rhinoceros can be redosed with tranquilizers while the vehicle is in motion or stop, inject, and start moving again immediately. In most instances, hand-injection is the best method to deliver additional tranquilizer. A 20-gauge, 1.5-inch needle is inserted into the lateral muscles of the neck while avoiding the nuchal region. Beware of the head and horn during neck injections. For restless individuals, the gluteal region also works well. Once the rhinoceros has settled, attach the syringe and inject the drug. A pole syringe can also be used, but hand-injection is preferred because it precludes the startled response resulting from the jab of the pole. Beware of coring, where the rhinoceros' skin may block the needle lumen. An IM injection takes 5–10 minutes for first effect; for a faster response, an IV injection into the ear vein is sometimes possible, although care must be taken to avoid the dangerous area around the animal's head and horn. Recumbency during transport can be beneficial or a potential problem in a crated rhinoceros, depending on the animal's position and duration of recumbency. If the rhinoceros lies down while the vehicle is moving, the rocking and bouncing action of the truck helps to facilitate limb circulation. Beware, however, if the rhinoceros lies down for a long period (>45 minutes) since the complications from compartment syndrome are serious. Rhinoceroses heavily sedated with opioids often struggle to work out a way to lie down; however, if they manage to do it once, they will lie down more easily thereafter.

Short-acting tranquilizers such as azaperone, xylazine or detomidine, and diazepam or midazolam are useful agents to produce a calming effect in rhinoceroses during transport. Azaperone is the tranquilizing agent of choice and can be repeated every 4–6 hours as needed (Rogers 1993a,b; Kock et al. 2006). A 40 mg/mL azaperone solution is a convenient preparation and mixes well with etorphine for IM administration to a fractious, crated rhinoceros. The administration of opioids, either alone or in combination with IM azaperone or diazepam, is the only effective way to preclude an excited black rhinoceros from traumatizing itself inside a crate (Table 47.2). Etorphine and azaperone (0.05–0.15 and 100–200 mg, respectively) are delivered by hand-injection or pole-syringe with sedation achieved in 5–10 minutes for durations of 2 hours or more.

Long-acting tranquilizers can help to calm an animal, but are inadequate by themselves to sedate an excited animal during transport. Zuclopenthixol acetate (Clopixol Acuphase, 25–150 mg per adult rhinoceros) takes about an hour to provide sedative effects after administration, while perphenazine enanthate (Trilafon, 200–400 mg per adult) takes about 12 hours for the first noticeable effects to appear (Swan 1993; Kock et al. 2006; Table 47.2). Perphenazine works well for the translocation of black rhinoceroses while caution should be exercised in white rhinoceroses as its use has been implicated in anorexia (Portas 2004; Kock et al. 2006). Higher doses of long-acting tranquilizers should be avoided before release from the crate or boma since it may cause animals to lie down, creating a hazard in hot environments or where predators are present.

Black Rhinoceros Off-loading from Crate

Black rhinoceroses, especially juveniles and subadults, are notorious for being aggressive and sometimes even self-destructive to themselves and the crating equipment (trucks, crates, etc.) at off-loading sites. In Namibia, where rhinoceroses are often moved from veldt to veldt without the use of bomas and adaptation periods, the capture team uses a technique for off-loading that is effective and largely eliminates the aggressive phase. At the off-loading site, the rhinoceros is resedated inside the crate using a low dose of etorphine (adult 0.1–0.2 mg) combined with azaperone (adult 80–120 mg) and allowed to narcotize over a period of several minutes. Once the rhinoceros is head pressing or otherwise sedated, the muslin blindfold and earplugs are removed and the etorphine antagonist administered. A standard dose of 12–18 mg of diprenorphine for an adult animal is administered by IM (not IV) injection and the crate doors are opened. As the rhinoceros regains its first levels of awareness it walks slowly from the crate even while still sedated and partially narcotized. These black rhinoceroses tend to walk directly away from the crate and into the veldt without the characteristic aggression and attack of the crate or related equipment. As the animal continues to walk away from the off-loading site it becomes more fully aware of its surroundings and ambulates from the site in a normal fashion. This protocol has largely eliminated the aggression and self-trauma that is often characteristic of black rhinoceroses at off-loading.

Alternative Rhinoceros Anesthesia Techniques

Antidote Choice

Following IV antidote administration, a recumbent rhinoceros will stand within 60–80 seconds. Response to the antidote is first noted as an increase in the depth and rate of respiration and movement of the ears and eyes. Rhinoceroses get to their feet quickly and are immediately strong and aggressive. A rhinoceros should always be moved into sternal recumbency before giving the antidote or it may bash its head on the ground as it attempts to rise from the lateral position. IM dosing of the antidote is often preferred for arousal of rhinoceros cow–calf combinations so the pair awake slowly and have time to join together without dashing off in opposite directions. If IV dosing is desired with recovery of cow–calf pairs, the cow is injected first, 30 seconds before the calf.

Out of tradition, opioid antagonists are dosed using empirically derived ratios rather than on a milligram per kilogram basis; for the pure opioid antagonist, naltrexone, dosage ratios of 20–50 times the etorphine milligram dose and 90–100 times the carfentanil milligram dose are considered standard for captive rhinoceroses (Swan 1993; Allen 1996; Kock et al. 2006). Renarcotization has been reported in the white rhinoceros, but it is a rare occurrence in the black rhinoceros (Kock et al. 1990; Portas 2004). Field workers frequently use lower naltrexone doses (12.5:1 naltrexone to etorphine ratio) without a problem (Kock et al. 1995), but sedative signs at these doses have been reported in white rhinoceroses and a minimum of 40:1 is therefore recommended to preclude renarcotization (Rogers 1993a; Kock et al. 1995; Portas 2004). While naltrexone is considered the agent of choice for complete reversal of narcotic anesthesia, a number of scenarios arise under both captive and field conditions where a full reversal of an opioid-based procedure is undesirable.

The choice of antagonist and its desired action is dependent on two factors: species and location. Black rhinoceroses are reversed to load into a crate with nalbuphine or butorphanol (Kock et al. 2006; Radcliffe & Morkel 2007; Tables 47.1 and 47.2). In the boma, *Diceros bicornis* are reversed with naltrexone, although very nervous or aggressive individuals may benefit from reversal with diprenorphine for its sedative properties. Naltrexone is used for complete antagonism in the field.

In marked contrast to black rhinoceroses, white rhinoceroses are reversed into a crate using diprenorphine with perhaps 1 or 2 mg of naltrexone. In the boma and in the field, *Ceratotherium simum* are similarly reversed with naltrexone. Diprenorphine is often used for translocation of white rhinoceroses since its partial agonist-antagonist actions provide significant narcosis during travel. However, diprenorphine has minimal agonist effects in *Diceros bicornis* and therefore should be used judiciously for transport in this species. For any partial antagonism in a crate situation it is critical that the rhinoceros be monitored very carefully to prevent excessive head pressing and occlusion of the airway or damage to the neck and limbs. A cattle prodder is a vital piece of equipment in managing sedated rhinoceroses during travel.

Rhinoceros Anesthesia Complications

With opioid-induced cardiopulmonary compromise common in anesthetized rhinoceroses, the need may arise to assist respiration. For emergency respiratory support for apnea (after having reversed the opioid with pure opioid antagonist), the animal is first pushed onto its side. A large person forces the knee and lower leg (with foot placed firmly on the ground) into the abdomen to vigorously force the abdomen diagonally upward and forward against the

diaphragm. This moves the diaphragm, forcing air into and out of the lungs and keeps the animal alive while the IV opioid antagonist takes effect. When one leg is tired use the other leg and recruit additional people to assist. Jumping on the ribs or back of the rhinoceros is ineffective and does nothing but fracture ribs and inflict unnecessary trauma. Mechanical positive pressure ventilation can be used, but few field practitioners have such equipment routinely at hand (Pohlin et al. 2019).

Myopathies are common in rhinoceroses that experience excessive chase periods or hyperthermia during capture. An especially critical period occurs at the time of crate loading and initial transport during field translocation of rhinoceroses. If stimulated to rise too early after partial reversal, animals may enter the crate and assume a rigid, semi-squatting position with their hind legs. This is undesirable and must be resolved quickly before the muscles are irreversibly damaged (Fig. 47.12). Use of the electric prodder on the head can often stimulate the animal to rise and stand, but avoid prodding the hindquarters as this can exacerbate the problem. If this does not work consider prompt IV administration of diprenorphine. A sling can also be placed under the belly of the animal, just in front of the rear legs to lift the hindquarters (using the crane on the recovery truck) until the strength has returned to the hind limbs.

A very small percentage of black rhinoceroses develop an adverse reaction that the author refers to as the "fat nose syndrome" (Radcliffe & Morkel 2007). Essentially the nostrils close up and appear edematous with a much-reduced opening to the nares. The anesthetist is often forced to hold open or pull the nostrils apart. This unusual response may indicate a hypersensitivity (anaphylactic) reaction; morphine is known to cause histamine release in humans and perhaps etorphine – derived from the same group of opium alkaloids – can produce the same uncommon effect in susceptible rhinoceroses.

New Field Anesthesia Techniques

Today's understanding of Rhinocerotidae anesthesia is truly the embodiment of many courageous pioneers who have led by exciting experimentation and hard-won experience (Harthoorn & Lock 1960; Player 1972; Young 1973; Kock et al. 2006). Yet with the immense challenges inherent in practical anesthesia of these complex mammals, innovative procedures are welcome. The newest ideas for rhinoceros anesthesia are arising from a combination of practical experience and a desire to explore the depths of pharmacology. Nowhere are such explorations more exciting than the emerging science of mixed opioid receptor action on central nervous system activity (Chindalore et al. 2005). Various opioid receptor affinities and their pharmacologic actions are well described in humans but remain little understood in animals, including the rhinoceros, which is certain to be unique in many respects. Indeed, the most exciting of these novel investigations is, at least for rhinoceros capture specialists, the incorporation of mixed agonist-antagonist opioid cocktails as part of routine field capture methodologies for the African rhinoceros (Bush et al. 2005).

Recent work by Bush and colleagues in white rhinoceroses combines a mixture of concentrated butorphanol (40–90 mg, 50 mg/mL solution) with etorphine and midazolam (2–3.5 and 25–50 mg, respectively; Table 47.1) (Bush et al. 2005, 2011). The addition of butorphanol to the anesthetic combination of etorphine and midazolam produces enhanced muscle relaxation with improved physiological parameters compared to the standard protocol of etorphine and azaperone in the white rhinoceros. Butorphanol is a mixed opioid agonist-antagonist; its agonist κ receptor produces analgesia and marked sedation while the high affinity at the μ receptor displaces etorphine and acts as a partial agonist, thereby producing catatonic effects while simultaneously reducing respiratory compromise, tremors, and rigidity. Etorphine is a μ agonist causing respiratory compromise, tremors, and muscle rigidity – these adverse μ agonist actions are partially antagonized by butorphanol and significantly reduce tremors and the cardiopulmonary depression typical of the pure opioids alone. In white rhinoceroses, practitioners now routinely give 40–60 mg butorphanol as soon as they reach the animal to improve respiratory function (C. Moueix, pers. comm., 2019). In black rhinoceroses, the butorphanol antagonism of μ-opiate actions will result in a lively rhinoceros not suitable for handling without additional sedation.

Etorphine produces an increase in sympathetic activation that produces profound impacts on cardiopulmonary physiology, including elevations in heart rate and cardiac output; these effects are partially antagonized by butorphanol (Boesch et al. 2018). Following butorphanol administration blood gas values reveal a more normal pH and partial pressure of arterial carbon dioxide ($PaCO_2$) while blood pressures remain lower than with the standard pure opioid agonist protocols. Administering diprenorphine, a μ antagonist, intravenously 12 minutes into the anesthetic episode reverses etorphine but not butorphanol, further counteracting adverse μ effects of etorphine while preserving butorphanol sedation effects, therefore if inadvertent opioid overdosage should occur, compromised physiological parameters can be rapidly corrected without losing control of the animal. These discoveries may help to bring field rhinoceros capture into the realm of safety

realized with captive animals where butorphanol-based protocols are now standard replacements for more potent opioids (Radcliffe et al. 2000a; Portas 2004).

Suspension of Black Rhinoceroses for Air Lifting

Aerial translocation of captured black rhinoceroses living in rugged environments in Namibia has been accomplished by suspending them by their feet (Fig. 47.13). To study black rhinoceroses in the hanging posture, a preliminary study was conducted by slinging immobilized animals under a crane to simulate aerial transport (Radcliffe et al. 2020). It was anticipated that suspension would compromise respiratory gas exchange more than lateral recumbency. Twelve wild black rhinoceroses were immobilized with etorphine and azaperone; half were positioned in lateral recumbency first and then suspended by their feet from a crane second, while an equal number were suspended first and then moved into lateral recumbency. All animals were hypoxemic and hypercapnic in both postures. When suspended by the feet, PaO_2 and partial pressure of alveolar oxygen (PAO_2) were 4 mmHg greater and $PaCO_2$ was 3 mmHg less than in lateral recumbency. Tidal volume and minute ventilation were similar between postures.

Although suspension by the feet for 10 minutes impaired pulmonary function to a similar degree as that imposed by lateral recumbency, PaO_2 was higher and $PaCO_2$ lower during suspension than during lateral recumbency. These findings suggest that airlifting immobilized black rhinoceroses compromised their cardiopulmonary system to a similar degree as lying in lateral recumbency. Arterial blood gas partial pressures might be marginally improved in the hanging posture, but the profound hypoxemia and hypercapnia remains clinically important.

Rhinoceros Calf Anesthesia

Captive Calf Protocols

Anesthesia of captive white and black rhinoceros calves is safely accomplished with butorphanol alone or in combination with detomidine (Radcliffe et al. 2000c; Langan et al. 2001; Gandolf et al. 2006). Due to high sensitivity to opioid agents, rhinoceros calves respond very well to sedation and anesthesia with mixed agonist-antagonists, precluding many of the adverse cardiopulmonary depressant effects observed with more potent pure agonists of this class. Furthermore, a rapid onset of action is attained by IV delivery or a slower induction by IM administration, with both methods proving safe and effective for serial anesthesia (Gandolf et al. 2006; Table 47.5). The combination of the alpha-2 agonist detomidine along with butorphanol was thought to enhance muscle relaxation and depth of anesthesia with IM use in white rhinoceros calves. Complete reversal is achieved using naltrexone at four to five times the butorphanol milligram dose and yohimbine HCl (Yobine) or atipamezole at 0.125 mg/kg for antagonism of the alpha-2 agent.

Cow and Calf Field Capture

Field immobilization of juvenile rhinoceroses is not without inherent risk as calves may separate from their dams after darting or become recumbent at different times despite



Figure 47.13 Hanging posture of a black rhinoceros (*Diceros bicornis*) using a crane on a flatbed truck to simulate aerial suspension (left). Helicopter-assisted aerial slinging of a black rhinoceros by its feet during translocation operations in northwest Namibia (right).



Figure 47.14 Anesthesia of rhinoceros calves is challenging, particularly under field conditions, where darting of the cow–calf pair must be well coordinated to limit stress on both parent and offspring.

concurrent drug delivery (Fig. 47.14). Additionally, calves are more susceptible to capture stress, hyperthermia, and post-capture morbidity and mortality in boma situations (Kock et al. 1995). Translocation of cows with calves less than 18 months of age can be traumatic and is best avoided while movement of very young calves 2–3 months old is particularly high risk. Even with successful translocation, it can be difficult to reunite the cow and calf as the stress of capture and confinement often results in adult aggression directed toward the calf or the cow drying-up. Methods for opioid sedation (0.2 and 0.05 mg of etorphine for a cow and calf, respectively) have been used to facilitate boma reintroduction of cow–calf combinations (Kock et al. 2006). The wild black rhinoceros cow is solitary by nature and usually retreats to a quiet spot to calve and will stay there for the first month afterwards. Therefore, if a black rhinoceros gives birth in a boma she rarely manages to raise the calf.

Opioid doses lower than those reported for adult animals are utilized for juvenile rhinoceroses, with subadults receiving approximately one-half the adult dose. For example, when combined with a tranquilizer subadult African rhinoceros (age ~2.5 years) should receive 1.75–2 mg of etorphine while very young calves (age 2–3 months) can be immobilized with as little as 0.5–1 mg of etorphine (Rogers 1993a,b; Morkel & Nel 2019; Table 47.5). A marked difference is observed in the escape behavior of African rhinoceros cow–calf pairs and should be anticipated during the chase and capture. White rhinoceros calves run ahead of their mothers, while black rhinoceros calves run close at their mothers' heels (Kock et al. 2006).

When darting a cow with a calf from a helicopter, a fixed-wing aircraft is desirable to circle the capture site to assist with spotting. As a general rule, the cow is darted first and about a minute later the calf is darted (Kock et al. 2006). If the timing and darting are good, the pair will often go down together. Should the pair split up, the fixed-wing aircraft can stay with one animal. In open country where visibility is good, the calf can be darted once the cow shows early signs of narcosis. In more thickly vegetated country where it is difficult to observe two separated animals, it is better to wait until the cow shows marked effects or is even recumbent before darting the calf. If the calf splits from its mother, the position of the immobilized mother can be taken by GPS or marked with a smoke grenade or toilet paper and the calf followed. Losing sight of a darted rhinoceros must be avoided and it is therefore mandatory to have experienced trackers as part of the ground team. When darting a cow–calf pair on foot, the calf will usually stay close to its immobilized mother. If approached carefully, the calf can be darted and will generally become recumbent close to its mother; note that black rhinoceros calves are skittish and run off more easily than white rhinoceros calves.

Wild subadult greater one-horned rhinoceroses have been immobilized using the same dosage as adult animals (2–2.5 mg of etorphine plus 10 mg of acepromazine; Dinerstein et al. 1990). However, subadult animals proved more difficult to capture and often evaded darting attempts by outrunning the trained elephants that are commonly utilized for field immobilization of greater one-horned rhinoceroses in the tall grassland habitats of India and Nepal. Rhinoceros calves were immobilized with 0.5–1 mg of etorphine and 5 mg of acepromazine using shorter 2.5-cm Cap-Chur needles. As with capture of African rhinoceros cow–calf pairs, it is recommended that greater one-horned cows be immobilized before their calves. Calves did not run away and were easier to capture if the mother was immobilized first to avoid trampling risk to calves or aggression toward the ground crew (Dinerstein et al. 1990).

Conclusion

During the Indian Mutiny a British soldier fired a bullet into the regiment's cherished mascot, a rhinoceros. In a spirit of scientific inquiry the soldier tested the long-held belief – a conviction still strongly held by many since Dürer's famous rhinoceros – that its skin was held together with rivets like a knights armor and impenetrable to any volley man could throw its way. To the surprise of royalty and commoners alike the rhinoceros quickly expired.

The future of the world's rhinoceroses will remain tenuous as human conflicts over shared resources escalate

and rhinoceros horn continues to be cherished by traditional Asian societies for supposed unicorn-like mythical properties. Nevertheless, it is comforting to know that man – while solely responsible for the current crisis – is also simultaneously making strides to save the relic rhinocerotoids from their greatest enemy, ourselves. Safe anesthesia of wild and captive rhinoceroses alike will help scientists realize these conservation goals. Let us not make the same mistake as the British soldier and believe, naïvely, that the armored rhinoceros is invincible to the actions of our kind.

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48

Suids

Luis R. Padilla and Jeff C. Ko

Introduction

A large amount of information has been published on anesthesia and immobilization techniques in domestic swine. In contrast, studies pertaining to the anesthesia of free-ranging or nondomestic suid species are limited in the documentation of physiological responses to anesthetic drugs, focusing instead on efficacy, induction, and recovery times, and subjective descriptions of anesthetic quality. The domestic pig is still the most appropriate physiological model for anesthesia of other species, but readers seeking protocols for the anesthesia of captive domestic pigs are referred to specific literature reviews on the subject (Swindle 1998; Thurmon & Smith 2007). We have included specific comments on Vietnamese potbellied pigs, since these are common exhibit animals in zoological institutions.

Taxonomy

The suborder Suiformes includes the families Suidae and Tayassuidae, which encompass all pigs, hogs, babirussa, and peccaries. The generic term "suid" is commonly used to refer to members of both families. Table 48.1 is a list of known suid species, and adult weight ranges have been listed where available. The family Suidae includes pigs, hogs, and babirussa, totaling 14 species in five genera. The Eurasian wild boar (*Sus scrofa*) is the wild ancestor of the domestic pig. Numerous breeds of the domestic pig (*Sus scrofa*) exist, and in many places feral populations have been established in a free-ranging state, blurring the distinction between wild boar and domestic pig. The family Tayassuidae includes the peccaries or javelinas, currently found in three genera with one species each. A third family in the suborder Suiformes, Hippopotamidae, is the subject of a separate chapter in this book.

The main anatomical differences between the Tayassuidae and Suidae families are in dentition, tail length, hind limb anatomy, and the presence of a scent gland dorsally in the lumbosacral region in peccaries. Sexual size dimorphism is more prominent in the Suidae than the Tayassuidae. The babirussa (*Babyrousa babyrussa*) has distinct features from the other members of the Suidae family, including a complex, sacculated stomach suggestive of foregut fermentation (Leus et al. 1999), and remarkable canines in the males.

General Considerations of Suid Biology and Physiology

All suids can be dangerous animals when approached. Most species have powerful jaws with sharp dentition, and individuals can be extremely fast and capable of inflicting severe wounds on humans. Canines grow as sharp tusks in many species, which is accentuated in males of the Suidae family. In addition, the short, strong limbs and a muscular neck limit the possibility of physical restraint to juveniles or very small individuals. Many individuals will fight aggressively when cornered or restrained, and sows can be very protective of their offspring. Suids can be capable climbers and agile jumpers that can escape from many situations or evade restraint.

Physiological or social stress should be minimized prior to anesthetic induction to achieve the desired results. Gregarious, social individuals are likely to be highly stressed if isolated prior to anesthesia. If prolonged isolation is necessary, stress can be decreased by allowing visual contact between group mates. During anesthetic induction, it is preferable to isolate the target animal from the rest of a group to minimize the risk of inadvertent trauma or misdirected aggression from companions.

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Table 48.1 Species of suids by family and weight range.

Species	Adult Weight (kg)	Common Name	Comments
Family Suidae			"True" pigs
Sus scrofa	40–300	Eurasian wild boar	Domesticated into farmed pigs, many wild "races" exist
	32–100	Vietnamese potbellied pig	Breed of domestic pig, commonly seen in zoos
Sus salvanius	6–10	Pygmy hog	
Sus bucculentus		Vietnamese warty pig	
Sus verrucosus	35–185	Javan warty pig	
Sus barbatus	100–200	Bearded pig	
Sus philippensis		Philippine warty pig	Three subspecies are recognized, although at least one may be a full species
Sus cebifrons	20–80	Visayan warty pig	
Sus celebensis	40–70	Sulawesi warty pig	
Potamochoerus porcus	45–120	Red river hog	
Potamochoerus larvatus	50–115	African bush pig	
Hylochoerus meinertzhageni	100–275	Giant forest hog	
Phacochoerus africanus	50–150	Common warthog	
Phacochoerus aethiopicus	45–140	Desert warthog	
Babyrousa babyrussa	40–100	Babirusa	
Family Tayassuidae			Peccaries or Javelinas
Catagonus wagneri	30–45	Chacoan peccary	
Tayassu (Pecari) tajacu	15–35	Collared peccary	
Tayassu pecari	25–40	White-lipped peccary	

Domestic pigs should be fasted for 24 hours (Moon & Smith 1996) and nondomestic suids should be fasted for 12–18 hours (Calle & Morris 1999) or longer. In addition to being at risk for vomiting and aspiration, inadequately fasted pigs are prone to gastric distension, which may physically compromise ventilation by altering pleural pressure and chest wall mechanics (Mutoh et al. 1991). When food is withheld, suids may consume other things accessible to them, including shavings, bedding material, or ground and wall substrates.

Suid skin is tough, tight, and not very pliable, and contains a significant subcutaneous adipose tissue layer. Areas with thick fat deposits are less desirable for reliable injections, as administration into the adipose tissue layers will result in variable or altered responses when compared to true intramuscular (IM) injections, which should not be mistaken for decreased drug efficacy or variable species susceptibility. The amount and distribution of fat varies with age and between species, subspecies, and breeds. Injection into leaner muscle masses, such as the semimembranosus, semitendinosus, or the dorsal prescapular muscle mass (Calle & Morris 1999), will result in more predictable effects. The choice of needle length is crucial to obtaining deep muscle injections, and a minimum length of 1.5 inches (3.8 cm) is suggested to assure IM placement in adult animals.

Suids are prone to hyperthermia. All species have a relatively low surface area in a proportionately large-volume body with a significant layer of subcutaneous body fat and limited sweating capabilities for heat dissipation. Physical excitement or increased exertional activity prior to successful immobilization may result in muscular heat generation and elevations in core body temperature. Severe elevations in body temperature can be treated by cooling the skin surface with alcohol baths or placing ice packs around large vessels (Moon & Smith 1996), using cool intravenous (IV) fluids, or, in extreme cases, using cold water enemas. Close temperature monitoring and good clinical judgment must be used to prevent overtly aggressive rapid cooling and hypothermia.

Although hyperthermia can occur in any suid species, the syndrome known as malignant hyperthermia only occurs in domestic swine. The malignant hyperthermia

syndrome of swine is a well-documented, autosomal recessive condition of domestic pigs resulting in abnormal skeletal muscle function due to defective calcium handling (Moon & Smith 1996). Large white breeds of domestic swine are considered most susceptible, but it can occur in any breed or mixed-breed individual, including miniature pot-bellied pigs (Claxton-Gill et al. 1993). Manifestations of hyperthermia and muscle rigidity can be induced by stress, elevated ambient temperatures, inhalant and injectable anesthetics, paralytic agents, and other drugs. The body temperature of affected pigs can increase as high as 110°F (43.3°C) (Moon & Smith 1996), and muscle rigidity, tachycardia, tachypnea, hypoxemia, and cardiac arrhythmias can develop. Serum chemistries may show elevations in potassium, ionized calcium, myoglobin, and creatine kinase. Clinicians suspecting this condition should immediately institute supportive symptomatic therapy and discontinue inhalant anesthetics. Dantrolene is an effective treatment for this condition (Gronert 1980) and can be used prophylactically in pigs considered at risk. Azumolene, a dantrolene analog, has greater water solubility, and may be a more practical treatment option (Dershwitz & Sréter 1990). Other drugs that cause muscle relaxation might be used in managing hyperthermia by reducing continued muscle activity.

Neonatal suids are prone to hypothermia during the first few days after birth. Managers should provide supplemental heat sources and protection from environmental temperature fluctuations. Sows, in particular inexperienced ones, should be monitored to ensure adequate maternal care is provided and that denning sites are safe for the piglets.

Trapping and Physical Restraint

Manual restraint of nondomestic suids should be reserved for juveniles or small domesticated individuals. Juvenile suids and small pigs can be restrained with one hand under the sternum and one hand over the back. The handler should anticipate that loud vocalizations may occur in response to physical restraint and manipulations. Prolonged or rough handling should be avoided, especially during hot weather, as it can result in hyperthermia. Juvenile and neonates may vocalize and struggle to the point of exhaustion and collapse during prolonged or strenuous restraint.

The use of snares, ropes, and similar physical restraint devices used in domestic swine production is not generally recommended in nondomestic suid species due to the high probability of injury to restrainer or animal, but can be done by experienced personnel. A description of translocations of collared peccaries detailed the use of a pole snare loop placed behind the upper canines and drawn tight while a second person physically restrained the hind legs (Porter 2006). This restraint was sufficient for placing ear tags and loading onto a trailer for relocation.

A variety of net restraint devices have been designed for domestic swine restraint and modified for the capture of free-ranging suids. Warthogs have been captured using a funnel-shaped net set at the entrance of their sleeping burrows, occasionally resulting in the capture of multiple individuals as they emerge (Cumming 1975). Modified deer traps, "box traps," and corral traps have been used for capturing free-ranging suids with variable rates of success.

Vascular Access

The subcutaneous adipose tissue layer and the tight skin of most suids can make vascular access a challenging task. Sedation or anesthesia should be used to facilitate blood collection in nondomestic species, except in very small individuals. Blood can be collected from the jugular, femoral, cephalic, saphenous, tail (coccygeal), and auricular veins. Catheter placement is possible in the cephalic, saphenous, and auricular veins. Although other sites are described in this section, they are not recommended in most situations due to inherent technique risks.

Blood collection from the femoral vein can be done in most species, although the amount of adipose tissue and thick muscle mass can make it difficult in certain individuals. Caution must be taken to avoid lacerating the femoral artery. The femoral vein can be accessed with the animal on dorsal recumbency and slightly extending the hind leg caudally. The clinician palpates between the muscle bellies to find the femoral groove and a long needle (1 inch or longer, depending on the size and body condition of the animal) is advanced with slight negative pressure. After successful collection, pressure should be applied to minimize hematoma formation. Venipuncture on this site can be painful and some individuals may show some lameness after recovery, associated with deep hematoma formation or soft tissue trauma. With aggressive repositioning of the needle, there is also a risk of creating an iatrogenic arteriovenous fistulation.

The cephalic and lateral saphenous veins can sometimes be palpated under the skin. In individuals of some species, such as warthogs and red-river hogs, these veins are easily palpated and accessible, but in others the veins can roll under the skin. A clinician familiar with the orientation of these veins might be able to blindly advance a small needle and obtain a blood sample. Blind catheterization of these veins is possible, although it is recommended that a scalpel

blade be used to puncture the thick skin and avoid damaging the catheter stylette, or that a true "cut down" procedure be used for optimum visualization and securing an IV catheter in place.

The coccygeal or tail vein is a marginally adequate venipuncture site for collecting small volumes of blood in most species. In peccaries, the tail is relatively shorter, and venipuncture is more challenging, but small volume samples (1–3 mL) can still be collected if the needle is heparinized. The vein is located on the ventral mid-point of the tail. An individual can be placed on lateral recumbency and the vein is approached ventrally at the base of the tail using a 21- to 23-gauge needle. If too much negative pressure is used, the vein can be easily collapsed.

Suids have thick, muscular necks and the jugular vein is not palpable or externally visible. Redundant folds of skin around the neck, or extensive adipose tissue stores, may limit access to the jugular vein. However, if accessed, the jugular vein is large in all species. A long needle advanced cranially in the direction of the jugular furrow, with a slightly medial orientation while applying negative pressure, can be successful at venipuncture.

Anterior vena cava puncture is widely used for blood collection in domestic pig production, but is not without potentially detrimental effects, and its application should be judiciously employed by clinicians on a case-by-case basis. Risks of improper anterior vena cava puncture include blood vessel laceration and cardiac tamponade (Moon & Smith 1996). In small pigs, or with improper restraint, an overtly aggressive clinician may accidentally induce a pneumothorax, hemothorax, or other intrathoracic laceration if using an improper length needle. A technique has been described for chemically restrained collared peccaries and has been used in large numbers of anesthetized collared peccaries (*T. tajacu*) to obtain large (>20 mL) volumes of blood, with no fatalities (Lochmiller et al. 1984). After placing a peccary in dorsal recumbency in a V-shaped trough, the head is extended slightly to stretch the sternocephalicus musculature. The site of needle entry is found by placing a thumb against the anterior portion of the manubrium of the sternum. The needle is inserted at a point equal to the width of the thumb anterior and lateral to the edge of the sternocephalicus muscle. The needle is directed caudally and angled dorsomedially at a 30–40° angle formed by the point of the sternum. In an adult peccary, the authors preferred a 21-gauge, 1.5-inch-long needle.

The auricular veins on the ears of domestic pigs are a common site for IV access, catheter placement, and blood collection. The veins are present on the dorsolateral aspect of the ear. Their usefulness in exotic suid species varies, but should be considered for quick vascular access or when injecting small volumes. Large-eared species, such as red river hogs and warthogs, may have prominent veins, but they are of negligible size in other species (babirussa, warty pigs, and peccaries). Using a warm compress or topical alcohol may induce superficial vasodilation, and applying pressure at the base of the ear may help identify the veins. A butterfly catheter can be secured around the flat (posterior) part of the ear, or a short catheter can be glued in place with the inside of the ear rolled around gauze to provide rigidity and support in securing the catheter. A clinician should keep in mind that most suid species have very sensitive ears, and even seemingly minor manipulations have resulted in auricular discomfort (abnormal ear posture and rubbing ear on surfaces) for days after a procedure.

Orbital sinus puncture is used in some research laboratories for blood collection in domestic pigs, and a variation has been used and described for anesthetized collared peccaries (Lochmiller et al. 1984). A peccary is placed in dorsal recumbency, with the head extended and stabilized by holding the snout. A 16-gauge, 1-inch-long needle without a syringe is placed at the medial canthus of the eye, medial to the nictitating membrane. The needle is advanced approximately 2 cm at a slightly ventral, posterior angle through the conjunctiva until the orbital sinus is reached. Blood will flow through the needle and can be freely collected in a tube placed under the hub. When collection is completed, the needle is removed and pressure is applied to the closed eyelid to stop blood flow. As described, this technique may have value in research settings, but is not likely to be popular with zoo staff or pet owners, and potential complications exist. Orbital sinus puncture is not recommended for venipuncture in most situations, since more readily accessible sites exist.

Endotracheal Intubation and Anesthetic Monitoring and Support

Sternal recumbency is recommended for ease of endotracheal intubation, but lateral recumbency is more practical for very large individuals, animals with large tusks, and obese and brachycephalic animals. Some clinicians may prefer positioning individuals with large abdominal girth in lateral or dorsal recumbency. In these cases, suspending the head slightly at the end of an elevated table or platform may facilitate positional manipulation. A common hurdle to successful endotracheal intubation is the difficulty in opening the mouth sufficiently to visualize and advance an endotracheal tube. This might be facilitated with a deeper plane of anesthesia or different drug combinations, but one must consider that the mouth does not open widely in some species, even in extremely relaxed individuals. In addition, the larynx of most suids is difficult to reach due to

the elongated shape of the head and distal location in most species.

Using soft gauze strips behind the upper and lower canines, an assistant can open the mouth and simultaneously position and extend the head slightly. Anatomical idiosyncrasies in suids make endotracheal intubation challenging, but familiarization with the anatomy and visualization of the tortuous route to the airway will facilitate success. A long laryngoscope blade can be used to push the epiglottis and expose the larynx. A long stylette can be passed into the larynx and the endotracheal tube can be threaded over the stylette or guided through the eye of Murphy while rotating at the point of contact with the larynx. If advanced too aggressively, a stylette can damage the laryngeal mucosa, resulting in edema and subsequent airway obstruction. A stylette that is advanced too far into the trachea may damage the peribronchial tissues, causing a pneumothorax (Thurmon et al. 1996). If the larynx is physically stimulated, laryngospasms, apnea, and subsequent cardiovascular collapse may occur as part of the laryngochemical reflex (Ko et al. 1993a). The reflex occurs commonly in domestic pigs, but the response can be ameliorated with a topical anesthetic, such as lidocaine or cetacaine, applied on the larynx prior to attempts at intubation.

The endotracheal tube can be advanced into the larynx with the normal curvature of the tip pointing ventrally. The tube will encounter resistance as it reaches the posterior floor of the larynx, and rotating the tube slightly at this point facilitates advancement. Suids are obligate nasal breathers, and caution should be used when securing the endotracheal tube. Tying a tube too tightly around the nose or muzzle may cause significant congestion of upper respiratory passages, leading to difficulty breathing during and after recovery. This consideration should be emphasized in brachycephalic individuals, such as potbellied pigs (Fig. 48.1).

When endotracheal intubation is not feasible, the intranasal route is an easy and practical way to administer supplemental oxygen or anesthetic gas to suids, but should not be used for positive ventilation. Attempts at ventilating domestic pigs through nasal intubation have resulted in significant gastric distension, anterior displacement of the diaphragm, and decreased functional lung capacity (Thurmon et al. 1996). Improper intubation (i.e., esophageal instead of endotracheal) may result in similar complications.

The same monitoring equipment used in other mammalian species can be used in anesthetized suids (Fig. 48.2). However, the clinician should not rely on monitoring equipment alone, and visual or palpable assessment of respirations, pulse or heart rate, and mucous membrane coloration and capillary reflex times should not be ignored.

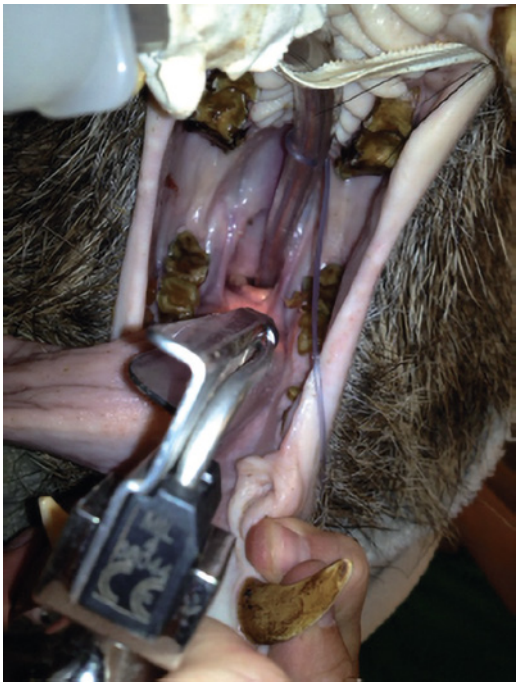


Figure 48.1 Intubation of a Chacoan peccary (*Catagonus wagneri*) utilizing a Miller laryngoscope blade (photo by Gary West).



Figure 48.2 An anesthetized Chacoan peccary (*Catagonus wagneri*) being monitored with mainstream capnography and pulse oximetry. An intravenous catheter had been placed in acephalic vein (photo by Gary West).

Ocular positioning is not an adequate indicator of anesthetic depth in suids due to the shallowness of the orbital socket.

A pulse oximetry probe can be placed on the tongue, ear, or vulvar or preputial folds. A rectal probe can be used, but mucosal contact must be confirmed by removal of feces. Interpretation of pulse oximetry values is more accurately done if respiration and ventilations are

concurrently monitored. Capnography is a useful indicator of the physiologic state of anesthetized suids. In domestic pigs, elevations in end-tidal CO_2 are seen early in the onset of malignant hyperthermia before other signs appear (Moon & Smith 1996), and early recognition of elevations in end-tidal CO_2 may help identify other physiological derangements that are significant to anesthetic management. Capnography trends can be monitored nasally in nonintubated animals by tightly fitting a tube inside the nostril and attaching the reading device to the end. Most suids tend to hypoventilate under anesthesia, which may be a reflection of the most popular anesthetic protocols used, a large (possibly full) stomach, obesity in most captive animals, or a combination of these. End-tidal CO_2 readings higher than 45 mmHg warrant ventilatory support and possibly oxygen supplementation. Positive pressure mechanical ventilation should not exceed what is necessary for minimal visible chest expansion, and caution should be used to avoid exceeding 20 cm H_2O, which has been seen to cause spontaneous pneumothorax in healthy pot-bellied pigs (Lukasik & Moon 1996).

Indirect blood pressure monitoring is recommended. Placing direct, invasive blood pressure monitors in anesthetized suids is impractical and time-consuming for most nondomestic species, mostly due to difficulties in arterial catheterization. Although no specific studies have been done in any exotic suid species, a close correlation between oscillometric methods of blood pressure monitoring and direct arterial blood pressure methods have been shown in domestic pigs, and trends seen in indirect blood pressure readings are more useful than absolute numbers recorded (Moon & Smith 1996). If a commercially available indirect blood pressure monitor is not available, a simple method is to use a Doppler flow probe on the second digit to locate a pulse and place a cuff with a sphyngomanometer proximally over the metatarsus. A study done on domestic sows showed that similar cuff placement with a pulse oximetry probe positioned distally on the second digit (instead of a Doppler flow probe) correlated closely with direct arterial blood pressure (Caulkett et al. 1994). Cuffs placed on the legs should be of a width between 40% and 60% of the limb circumference (Moon & Smith 1996). Cuff placement on the legs can be above or below the carpus or tarsus, but the cuff bladder should be over the medial aspect of the leg. If the cuff is placed on the tail, the bladder should face ventrally (Moon & Smith 1996).

Traditional electrocardiography "alligator" clips may be difficult to attach to the tight suid skin. Instead, 25-gauge needle electrodes can be inserted subcutaneously or patch electrodes can be adhered to the skin after degreasing with acetone, as has been described for domestic swine (Moon & Smith 1996). Temperature can be measured easily rectally or with an esophageal probe.

Anesthetic Combinations

General Principles

The majority of immobilization scenarios for nondomestic suids will be to facilitate routine, minimally invasive procedures (such as relocation, physical examination, hoof trimming, blood collection, and placement of radio collars), where a light plane of anesthesia or deep sedation will suffice. After induction, deeper planes of anesthesia can be achieved with inhalant anesthetics or supplemental doses of injectable anesthetics.

Many injectable anesthetic protocols have been reported and are summarized in Table 48.2. Most balanced combination protocols have fewer side effects than any single-drug protocol, since the different drugs may potentiate anesthetic effects and decrease the effective necessary dose of any single drug. In choosing a balanced anesthetic combination, it has been suggested that suids may be relatively more resistant to opioids and alpha-2 adrenergic agonists than other species, but relatively more sensitive to the effects of benzodiazepines (Moon & Smith 1996). However, this assumption should be taken with caution when extrapolating to different suid species as significant species and individual variation exists and there have been reports of individuals with profound sensitivity to opioids.

Sedatives and Preanesthetic Medications

Preanesthetic sedatives can be used to decrease anesthetic drug doses, facilitate administration of the induction agent, or ease preanesthetic anxiety. Oral diazepam or midazolam has been given to suids prior to anesthetic induction, resulting in calmer individuals prior to immobilization, facilitating darting, and minimizing complications (such as hyperthermia) associated with preanesthetic excitement.

Oral alpha-chloralose was historically used to capture feral pigs in the United States. The sites would be prebaited with food for several days to attract pigs to the area before adding drug-laced bait for the capture. Different mixtures are used to enhance the adherence of alpha-chloralose to bait, such as corn. The minimum effective dosage for hog capture has been reported as 2.2 g/40 kg of body weight and the maximum safe dosage for feral hog capture has been reported as 2.2 g/10 kg of body weight (Carpenter & Brunson 2007).

The use of xylazine (1.1–2.1 mg/kg IM) prior to anesthetic induction with tiletamine-zolazepam has been

Table 48.2 Common immobilization protocols used in nondomestic suids.

Drug Combination	Dose (mg/kg)	Species Documented	Comments	References
Ketamine	20 K	Collared peccaries	Not recommended Induction and recoveries are prolonged and violent, and high mortality possible	Gallagher et al. (1985); Hellgren et al. (1985)
Ketamine/xylazine	7.7 K/4.3 X	White-lipped peccaries	Field use for radio-collaring 17 free-ranging animals, but no physiologic parameters reported Recoveries were prolonged (1–3 hours) with no mention of antagonism	Reyna-Hurtado et al. (2009
Ketamine/tiletamine-zolazepam/medetomidine	3.9 K/0.63 TZ/0.03 M	Chacoan peccaries	Prolonged recoveries despite atipamezole antagonism, residual ataxia	Sutherland-Smith et al. (2004)
Tiletamine-zolazepam	2–5 TZ	Multiple species	Smooth induction, poor muscle relaxation, prolonged recoveries might be rough Duration of recovery is dose dependent, not induction	Allen (1992); Calle & Morris (1999)
	2.18 TZ	Chacoan peccaries	Prolonged recoveries, poor relaxation	
Tiletamine-zolazepam/xylazine	2.35 TZ/2.35 X	Collared peccaries	Prolonged recoveries, but study did not antagonize X; fatality associated with a double dose	Gabor et al. (1997)
	1.23 TZ/1.23 X	White-lipped peccaries	Dose of 1.51 TZ and 1.51 X not successful in collared peccaries	Selmi et al. (2003)
	1.2–2.1 X/1.8–3.3 TZ	Babirussa	X administered as a premedicant, followed by TZ 20 minutes later Antagonism with 0.14 mg/kg yohimbine and 1 mg flumazenil for every 20 mg zolazepam Bradycardia seen in some cases Concurrent administration of TZ and X can be used at similar doses with same effects	James et al. (1999)
	3 TZ/0.5 X	Warthogs	Recoveries >90 minutes	Sonntag et al. (2004)
	3.3 TZ/1.6 X	Feral pigs		Sweitzer et al. (1997)
Tiletamine-zolazepam/romifidine	3–6 TZ/0.1 R	Wild pigs		Siemon et al. (1992)
Tiletamine-zolazepam/butorphanol	1.46 TZ/0.14 B	White-lipped peccaries	Similar doses ineffective for collared peccaries	Selmi et al. (2003)
	1.26 TZ/0.36 B	Babirussa	Reverse with naltrexone, poor overall relaxation	Padilla (2004)
Medetomidine/butorphanol/ketamine	0.06–0.1 M/0.3–0.4 B/0.6–1.1 K	Bearded pigs		

(*Continued*)

Table 48.2 (Continued)

Drug Combination	Dose (mg/kg)	Species Documented	Comments	References
Medetomidine/ butorphanol/midazolam	0.04–0.07 M/0.15–0.3 B/0.08–0.3 Mz	Multiple species	*Preferred combination can be used in all suid species* Antagonize M with atipamezole, B with naltrexone. Lower dose range used in calm, captive individuals. Mz or M can be administered as a premedicant 10–15 minutes prior to rest of anesthetic cocktail, or all can be administered concurrently Dexmedetomidine can be used as a substitute for M (see text)	Morris & Shima (2003) (upper range of doses)
Detomidine/butorphanol/ midazolam	0.06–0.125 D/0.3–0.4 B/0.2–0.4 Mz	Multiple species	Antagonize detomidine with atipamezole or yohimbine, and naltrexone Detomidine or Mz can be administered as a premedicant or concurrently Animals may resedate within hours after antagonism	Morris et al. (1999)
Xylazine/butorphanol/ midazolam	2–3 X/0.3–0.4 B/0.3–0.4 Mz	Multiple species	Antagonize with atipamezole or yohimbine, and naltrexone X or Mz can be administered as a premedicant or concurrently	Morris et al. (1999)
Detomidine/butorphanol/ tiletamine-zolazepam	0.06–0.125 D/0.3–0.4 B/0.6 TZ	Multiple species		Morris et al. (1999)
Xylazine/butorphanol/ tiletamine-zolazepam	2–3 X/0.3–0.4 B/0.6 TZ	Multiple species		Morris et al. (1999)

B, butorphanol; D, detomidine; K, ketamine; M, medetomidine; Mz, midazolam; R, romifidine; TZ, tiletamine-zolazepam; X, xylazine.

reported in babirussa (James et al. 1999), and midazolam (0.15 mg/kg IM) and medetomidine (0.02– 0.07 mg/kg IM) have been similarly used prior to induction of anesthesia with other agents. However, the use of preanesthetic drugs is impractical in animals that cannot be confined or where the anxiety of multiple injections clearly outweighs the practicality of a single darting event.

The use of anticholinergics as adjunct premedications with a sedative before anesthesia has been advocated in domestic pigs (Moon & Smith 1996) and should be considered in Vietnamese potbellied pigs. Anticholinergics decrease the likelihood of bradycardia, avoid bronchoconstriction, minimize airway secretions, and decrease salivation. Atropine (0.04 mg/kg) or glycopyrrolate (0.005–0.02 mg/kg) can be administered intramuscularly as part of premedicants. Glycopyrrolate is a more potent antisialogogue than atropine, but is also longer acting. Caution should be used when administering anticholinergics in conjunction with drugs that can cause peripheral hypertension, such as alpha-2 adrenergic agonists.

Anesthetic and Sedation Protocols

Butyrophenones and Phenothiazines

Azaperone is a short-acting butyrophenone neuroleptic designed for IM injection with a wide safety margin in domestic swine. Although its main use has been to decrease aggression in domestic swine, azaperone can be used alone as a reliable sedative or as an anesthetic adjunct with dose-dependent effects. Doses of 0.25–0.5 mg/kg produce mild sedation without ataxia in domestic pigs (Braun 1993). Doses of 0.5–2.0 mg/kg reduce intraspecies aggression and cause mild ataxia, while doses of 2–4 mg/kg result in

significant sedation and possible recumbency in adult pigs (Braun 1993). However, doses exceeding 2 mg/kg are also more likely to cause negative drug effects, which are similar to those caused by phenothiazines, including hypotension, bradycardia, and decreased cardiac output and contractility. Priaprism has been reported in adult boars (Moon & Smith 1996).

Although the use of azaperone in exotic suid immobilization protocols has not extensively documented, it has a lot of potential as an anesthetic adjunct in nondomestic species and has been used reliably in Vietnamese potbellied pigs. The recommended dose for potbellied pig sedation is 0.25–2.0 mg/kg IM, and doses of 2.0–8.0 mg/kg are suggested for anesthesia (Calle & Morris 1999). Caution should be used at the higher range of the suggested dose, as prolonged recoveries may be seen.

Acepromazine is a phenothiazine compound used as a sedative adjunct in domestic pigs, but considered an inadequate sedative when used by itself (Moon & Smith 1996). Its negative side effects are dose dependent and can be severe, including hypotension, decreased heart rate, hypothermia, and decreased respiratory rate. However, acepromazine can be used to manage hyperthermia (Moon & Smith 1996) and hypertension, or as a mild sedative adjunct.

Ketamine Combinations

Ketamine has been used extensively in suid immobilizations. Ketamine should not be used as a sole anesthetic agent due to the poor quality of anesthesia, extreme muscle rigidity, and rough recoveries, but is the base for balanced anesthetic protocols and understanding its effects is important for the formulation of these combinations. To produce immobilization, ketamine alone requires relatively high doses (15–25 mg/kg), and the muscle rigidity precludes endotracheal intubation. Despite a relatively minor cardiorespiratory depressant effect (Tranquilli et al. 1983), ketamine can increase systemic and pulmonary arterial blood pressure, cause tachycardia, and increase in cardiac output and myocardial oxygen consumption. Recoveries are rough, including hypersensitivity to stimulus and increased activity of the limbs (paddling), which may lead to hyperthermia, predisposing suids to self-trauma, pulmonary edema, and even death.

Domestic pigs absorb ketamine rapidly, and almost completely, after IM injection (Loscher et al. 1990). Anesthetic recovery in pigs occurs as ketamine is redistributed from the brain to other tissues, with drug excretion and metabolism being less critical for anesthetic duration. This is a significant consideration when choosing drugs for individuals with compromised organ function, since prolonged excretion is unlikely to affect duration of anesthesia. The elimination half-life of ketamine in healthy pigs is approximately 2 hours after IM or intravascular administration.

Ketamine has been used safely as a sole anesthetic agent in numerous peccary immobilizations (Hellgren et al. 1985). In collared peccaries (*Tayassu tajacu*), ketamine was used without detrimental permanent effects at 20 mg/kg (Hellgren et al. 1985) administered intramuscularly. Prolonged recoveries (>120 minutes) should be expected when peccaries are immobilized with 15–25 mg/kg ketamine administered intramuscularly and heat stress may be seen in relation to ambient weather (Gallagher et al. 1985).

Some of the negative effects of ketamine anesthesia can be ameliorated with anesthetic adjuncts, which also decrease the ketamine dose required to achieve effective immobilization. Alpha-2 adrenergic agonists, such as xylazine, detomidine, medetomidine, or dexmedetomidine, are popular adjuncts to ketamine as a suid anesthetic. These combinations offer the advantage of being reversible to result in faster recoveries, but the reversal of the alpha-2 adrenergic agonists is independent of the patient's ability to metabolize and clear ketamine. If the alpha-2 adrenergic agonist is reversed before ketamine is fully metabolized, recoveries can be undesirable, characterized by hyperkinesia of all limbs while recumbent, severe and prolonged ataxia, and distress vocalizations. It has been shown cardiac output decreased significantly for 30 minutes after administration of a ketamine (10 mg/kg) and xylazine (1 mg/kg) combination in domestic pigs, and arterial PO_2 decreased for 10 minutes while total vascular resistance was significantly increased (Trim & Gilroy 1985). It is likely that other alpha-2 adrenergic agonists in combination with ketamine have similar effects in exotic suids and should be used with caution, but the more specific receptor affinity of the newer generation drugs is likely to result in less undesirable effects.

The wide availability of ketamine and xylazine has made this combination a popular choice used by field biologists studying wild or feral suids. Xylazine decreases the induction dose of ketamine, and can be antagonized with atipamezole or yohimbine (Montenegro et al. 2018). Although the effects of anesthetic monitoring were not reported, Reyna-Hurtado et al. (2009) reported safely immobilizing 17 white-lipped peccaries (*Tayassu pecari*) using a combination of ketamine (7.7 mg/kg) and xylazine (4.3 mg/kg) delivered by dart rifle. The animals recovered in 1–3 hours, and the authors did not report administering any antagonists.

Ketamine used in conjunction with benzodiazepines (diazepam, climazolam, or midazolam) offers better relaxation and smoother recoveries than ketamine alone. Midazolam is a more reliable IM sedative than diazepam because it is water soluble. Recoveries after

ketamine-benzodiazepine combinations can be prolonged, usually taking several hours. Recovery times can be shortened by the administration of flumazenil.

Tiletamine-Zolazepam Combination

A commercially available 1:1 formulated ratio of tiletamine-zolazepam combination has been used extensively in exotic suids (Calle & Morris 1999) and can be used safely in any species if the recovery effects are anticipated and properly managed. Kumar et al. (2006) reported the half-lives for tiletamine and zolazepam in the terminal elimination phase in domestic pigs anesthetized with a 10 mg/kg combined dose as 3.7 and 8.4 hours, respectively. These half-lives are significantly prolonged when compared with other domestic species (Lin et al. 1993). The authors also commented on the observation of a secondary peak in a concentration–time profile of zolazepam, which could be attributed to enterohepatic recycling or differential absorption rates from the injection site.

Despite the prolonged recovery times and possible undesirable effects, the combination of tiletamine-zolazepam offers the advantages of relatively low cost, wide availability, and a relatively wide margin of safety. Commercially available formulations can be reconstituted to different concentrations, allowing for smaller volumes of induction. Induction times are rarely affected by increasing dose, but recovery times can be prolonged at higher doses. The dissociative anesthetic portion of this combination, tiletamine, is considered more potent than ketamine. Zolazepam, the benzodiazepine part of the combination, is likely responsible for prolonged recoveries. The use of flumazenil (1 mg flumazenil for 20 mg zolazepam IV or IM; Calle & Morris 1999) as a benzodiazepine antagonist may shorten recovery times, but the effects may be of short duration and animals may relapse into a more sedate state as the flumazenil is metabolized.

Tiletamine-zolazepam anesthesia is characterized by relatively fast inductions, moderate muscle relaxation that is inadequate for endotracheal intubation, and prolonged, sometimes violent, recoveries. Most suids retain some degree of hyperresponsive reflexes, such as exaggerated limb withdrawal when stimulated. Heart rate and arterial blood pressure may increase. Respiration rate may decrease initially, but minute ventilation is well maintained. Recoveries may show repetitive motion of the legs (paddling) prior to standing, excessive salivation, altered thermoregulation, increased vocalizations, and prolonged ataxia (Moon & Smith 1996). Deaths have been occasionally reported after using tiletamine-zolazepam due to complications of rough recoveries (Morris & Shima 2003).

Chacoan peccaries (*Catagonus wagneri*) were immobilized reliably and safely with tiletamine-zolazepam at a mean dose of 2.18 mg/kg IM (Allen 1992). Anesthesia was induced in 7.6 minutes, but recoveries were prolonged (90–240 minutes) and some animals retained a dull mentation for up to 8 hours after immobilization. A more recent study (Sutherland-Smith et al. 2004) mentions that Chacoan peccaries anesthetized with 3.2 mg/kg tiletamine-zolazepam took longer than 8 hours to recover, which may be a function of higher doses resulting in prolonged recoveries, as has been previously suggested (Allen 1992).

Tiletamine-Zolazepam/Alpha-2 Adrenergic Agonist Combinations

The addition of alpha-2 adrenergic agonists adjuncts to tiletamine-zolazepam anesthetic protocols allows the usage of lower doses of tiletamine-zolazepam to achieve desired effects while improving overall muscular relaxation. The negative cardiovascular side effects involved with this addition are offset by the benefits of faster, smooth recoveries and better relaxation, often allowing for endotracheal intubation.

Xylazine has been a popular, inexpensive, and widely used adjunct to tiletamine-zolazepam immobilization protocols in nondomestic suid immobilizations. Commercially available formulations of tiletamine-zolazepam can be reconstituted with xylazine (Gabor et al. 1997), and immobilization protocols can be predetermined by volume per weight to simplify dose calculations in the field. In domestic pigs, it has been shown that the addition of xylazine to tiletamine-zolazepam-based immobilization protocols increases relaxation to facilitate intubation (Ko et al. 1993b). Increasing the xylazine dose in xylazine-tiletamine-zolazepam anesthesia of domestic pigs enhances the quality of anesthesia, sedation, and muscle relaxation without prolonging recovery times (Ko et al. 1995).

Wild feral pigs (*Sus scrofa*) in North America have been reliably immobilized with a xylazine (1.6 mg/kg) and tiletamine-zolazepam (3.3 mg/kg) IM combination delivered to trapped pigs by blowdart (Sweitzer et al. 1997). Animals recovered and were released within 120 minutes of initial injection. Authors reported slight decreases in heart rates and body temperatures, but adequate respiration rates and blood oxygen saturation levels. Immobilization of a large number ($n = 107$) of collared peccaries (*Tayassu tajacu*) has been described using a tiletamine/zolazepam (2.35 mg/kg) and xylazine (2.35 mg/kg) combination, although the authors reported it as a combined average dose of 4.7 ± 0.9 mg/kg (Gabor et al. 1997). One fatality was reported in a peccary receiving an overdose (9.78 mg/kg combined dose). Recovery times in peccaries were prolonged, being described as conscious at 64 ± 29 minutes and first standing at 92 ± 33 minutes from injection, but xylazine was not antagonized in the study.

Selmi et al. (2003) used IM tiletamine-zolazepam (1.23 ± 0.26 mg/kg) in combination with xylazine (1.23 ± 0.26 mg/kg) successfully in white-lipped peccaries, but similar doses (1.51 ± 0.29 mg/kg tiletamine-zolazepam and 1.51 ± 0.29 mg/kg of xylazine) were unsuccessful at providing immobilization in collared peccaries, undermining that species-specific differences must be taken into account.

A combination of 3.9mg/kg ketamine, 0.63 mg/kg tiletamine-zolazepam, and 0.03 mg/kg medetomidine was used to immobilize captive Chacoan peccaries (*Catagonus wagneri*) (Sutherland-Smith et al. 2004). Sufficient immobilization for handling was achieved at 12.6 ± 3.7 minutes, and good muscle relaxation was produced, although animals that were approached too soon after recumbency would be aroused and stumble away. Heart and respiratory rates declined, but oxygen saturation increased during anesthesia. Atipamezole was used to antagonize the medetomidine, but recoveries were still very prolonged (55–455 minutes) and showed residual ataxia.

In babirussa, xylazine (1.2–2.1 mg/kg IM) premedication followed by tiletamine and zolazepam (1.8–3.3 mg/kg) produced good relaxation, smooth inductions, and sufficient immobilization for minimally invasive procedures, although additional drugs were necessary to deepen or prolong anesthesia (James et al. 1999). The authors report bradycardia in some animals (range of 35–111 beats per minute) while maintaining good oxygen saturation and stable respiratory rates (James et al. 1999). Female babirussa required slightly higher induction doses to reach similar effects. A small study (Sonntag et al. 2004) showed that warthogs can be immobilized safely with tiletamine-zolazepam (3.0 mg/kg) and xylazine (0.5 mg/kg), although recoveries were prolonged (>90 minutes).

Romifidine has not been used extensively in suids, but one report describes its use (0.1 mg/kg) as an anesthetic adjunct to tiletamine-zolazepam (3–6 mg/kg) in wild boars (Siemon et al. 1992). Since these doses of tiletamine-zolazepam alone may be sufficient to sedate swine, the benefits of romifidine are likely to be supplemental and improve overall relaxation.

Tiletamine–Zolazepam/Butorphanol

Tiletamine-zolazepam (1.46 mg/kg) has been used successfully in conjunction with butorphanol (0.14 mg/kg) to immobilize white-lipped peccaries (*Tayassu pecari*), but similar doses are ineffective to immobilize collared peccaries (Selmi et al. 2003). However, similar doses of tiletamine-zolazepam (1.26 mg/kg IM) combined with higher doses of butorphanol (0.36 mg/kg) resulted in adequate immobilization of babirussa for elective procedures (Padilla 2004), and similar doses can be used in peccaries and warthogs, although relaxation is inadequate for intubation. Caution is prudent when using higher doses of butorphanol, as some practitioners have reported profound sensitivity and characteristic opiod effects (respiratory depression and muscle tremors) in certain individuals, notably babirussa. Antagonism of opioid effects with naltrexone or naloxone may shorten recoveries.

Medetomidine- and Dexmedetomidine-based Anesthesia

Medetomidine has been shown to induce deeper planes of sedation than xylazine in domestic pigs (Sakaguchi et al. 1992a), making it a useful and more complete anesthetic agent for suid immobilization. At higher doses of medetomidine (>0.08 mg/kg), depth of sedation does not seem to increase significantly in domestic pigs, but the duration of sedation does. The study also showed better analgesia with medetomidine when compared with xylazine. The anesthetic properties of medetomidine can be potentiated in domestic pigs by administering butorphanol concurrently at 0.2 mg/kg (Sakaguchi et al. 1992b), and the combination is safe when administered to atropinized pigs (Sakaguchi et al. 1993). Medetomidine effects in domestic pigs can be antagonized with atipamezole at two to four times the medetomidine dose (Nishimura et al. 1992), although most clinicians prefer to use a 5:1 atipamezole:medetomidine ratio for antagonism (Morris & Shima 2003).

Medetomidine effects can also be potentiated when used in combination with midazolam (Nishimura et al. 1993). The cardiopulmonary effects of a medetomidine (0.04 mg/kg) and midazolam (0.2 mg/kg) combination in swine include a rapid increase in arterial and pulmonary arterial pressure due to peripheral vasoconstriction (Nishimura et al. 1994). The antagonism of medetomidine with atipamezole resulted in a decrease in peripheral vascular resistance, decrease in blood pressure, and increased cardiac output and heart rate (Nishimura et al. 1994).

The ability to potentiate medetomidine with both butorphanol and midazolam has made the combination of the three a very popular anesthetic choice in nondomestic suids. A 0.07 mg/kg medetomidine, 0.3 mg/kg butorphanol, and 0.3 mg/kg midazolam protocol has been extensively used in captive suids of multiple species (Morris & Shima 2003) and is the preferred protocol across suid species at most captive zoological institutions (Morris et al. 1999). Medetomidine can be administered 5–15 minutes prior to the rest of the drugs, having a premedicant effect. This protocol offers the advantages of being almost entirely reversible and producing consistently good results across species (Morris & Shima 2003). However, at the doses published, significant bradycardia and hypoxemia are common side effects, and unexplained severe hypoglycemia has been seen in fasted and unfasted

suids at one institution (Morris & Shima 2003). Lingering sedation from which suids can be aroused is often seen at high doses using this drug combination for immobilization. Lower doses, as low as 0.04 mg/kg medetomidine, 0.08 mg/kg midazolam, and 0.15 mg/kg butorphanol, have been used successfully in babirussa, red river hogs, and warthogs, and might be used in other species. These lower ranges were derived from the domestic swine literature (Nishimura et al. 1994; Sakaguchi et al. 1992b) and may reflect variations in individual temperament and species susceptibility. For most animals, a large volume of induction drugs is needed, although the recent availability of highly concentrated or compounded formulations of medetomidine, midazolam, and butorphanol allows smaller volumes of induction. Clinicians have also reported sudden arousals when suids are approached too soon after recumbency or when stimulated, and recently there have been anecdotal reports of profound sedation within hours after initial antagonism. These anecdotal reports may be due to a recycling of the medetomidine when used at higher doses.

Dexmedetomidine is a dextroisomer of medetomidine and responsible for the anesthetic effects seen with medetomidine. When compared to medetomidine, dexmedetomidine has not been available for as long for veterinary usage. In addition, because it is only commercially available as a 0.5 mg/mL formulation in the United States, its application to nondomestic suid anesthesia has been limited by volume. Medetomidine (which is available in more concentrated, often compounded, formulations) is still more widely used and practical in the anesthesia of nondomestic suid species. Dexmedetomidine can replace medetomidine in balanced anesthetic combinations at a dose range of 0.02–0.04 mg/kg (which is roughly 50% of the mg/kg dosage used for medetomidine) in most species. The manufacturer of 0.5 mg/mL dexmedetomidine recommends antagonism with 5 mg/mL atipamezole at a 1:1 volume (or 10:1 atipamezole to dexmedetomidine on a mg:mg basis). When compared with medetomidine, dexmedetomidine produces similar anesthetic effects, although controlled comparisons are limited and primarily anecdotal in nondomestic suid species. In a recent study done in propofol-sedated domestic swine, dexmedetomidine administered intravenously at rates of 0.2, 0.4, and 0.7 mg/kg/h resulted in decreased bispectral index, mean arterial pressure, heart rate cardiac output, and mixed venous oxygen saturation, although the effects were dose dependent (Sano et al. 2010). This study suggests that relatively low doses of dexmedetomidine may be adequate as an adjunct in balanced anesthetic protocols. Due to limited reports of its use in nondomestic suid species, dexmedetomidine-based protocols are not included in Table 48.2.

Variations of the medetomidine-based protocols have been described. A combination of butorphanol (0.3–0.4 mg/kg), detomidine (0.06–0.125 mg/kg), or xylazine (2–3 mg/kg) and midazolam (0.3–0.4 mg/kg) has been used in Vietnamese potbellied pigs, Eurasian wild boar, red river hogs, warthogs, bearded pigs, and babirussa (Calle & Morris 1999). This protocol is characterized by rapid, smooth induction with excellent relaxation. In these combinations, medetomidine has been replaced by xylazine or detomidine, and it is likely that the other two drugs (midazolam and butorphanol) result in similar potentiation of the alpha-2 agonist effects. Another variation has been the substitution of tiletamine-zolazepam (0.6 mg/kg) for midazolam, used in some species with similar results (Calle & Morris 1999) and having the distinct advantage of smaller induction volumes. The authors suggest that some species are more sensitive to this drug combination based on temperament (red river hogs, babirussa, and potbellied pigs) and lower dosages of butorphanol can be used. Bearded pigs, warthogs, and Eurasian boars may require the higher end of the suggested dosage range. Free-ranging warthogs were successfully immobilized with tiletamine-zolazepam, butorphanol, medetomidine, and ketamine in combination (Hewlett et al. 2019).

Propofol

Because propofol must be administered intravenously, it is an impractical choice for induction of anesthesia in exotic suids, but some individuals could be potentially conditioned to tolerate IV injections and anesthetic induction with propofol. More commonly, propofol has been used as an anesthetic supplement to reach a deeper plane of anesthesia after induction with different agents, or used for maintenance of anesthesia as a continuous IV infusion. At higher infusion rates, heart rate and cardiac index decrease in domestic pigs (Moon & Smith 1996). Propofol can be a significant respiratory depressant if administered rapidly or if high doses are used.

Inhalant Anesthetics

The use of inhalant anesthetic gases as induction agents is impractical in most exotic suid species. However, inhalant anesthetics can be used in small or severely debilitated animals for supplementation or maintenance of anesthesia after induction with an injectable agent. Sevoflurane is the safest inhalant anesthetic agent currently available. Minimum alveolar concentrations for domestic pigs are estimated at 0.9–1.25 for halothane, 1.5–2.0 for isoflurane, and 2.0–2.7 for sevoflurane (Thurmon et al. 1996). A study done on newborn swine comparing halothane, isoflurane, and sevoflurane showed that mean systemic arterial pressure and heart rate decreased the least with sevoflurane

when compared with awake piglets, but heart rate decreased the least with isoflurane (Lerman et al. 1990). Mean measurements of systemic arterial pressure were also lower in isoflurane- and halothane-anesthetized piglets than when sevoflurane was used. Sevoflurane is associated with faster recoveries than other inhalants. Caution should be used with domestic pigs known to be susceptible to malignant hyperthermia, as this condition can be triggered by inhalants and is traditionally associated with halothane usage.

Long-acting Tranquilizers

Limited objective information is available on the use of long-acting tranquilizers in suids. Perphenazine, a long-acting phenothiazine, has been used at 30–50 mg per warthog prior to translocations (Ebedes 1993). Two young warthogs overdosed with perphenazine at 5 mg/kg died 3 days later. Although it is unclear if the animals died directly from the overdose, the warthogs were anorexic after drug administration (Ebedes 1993).

Conclusions

Balanced anesthetic protocols using multiple drug combinations allow for fewer detrimental side effects with better anesthetic qualities. Although the combination of butorphanol-medetomidine and midazolam is reliable and safe for inducing anesthesia in most captive nondomestic suids, it is not applicable or practical in all situations. Clinicians should choose an anesthetic protocol that is likely to achieve the desired level of anesthesia while balancing this against the detrimental effects most likely to be significant for an individual patient.

As newer monitoring equipment becomes available and is applied to document the physiological effects in nondomestic suid anesthetic episodes, the literature should evolve into more scientific and objective descriptions of different anesthetic protocols. Ultimately, this will help in refining techniques applicable to the captive and free-ranging management of these species.

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49

Hippopotamidae

Michele A. Miller, David V. Cooper, and Peter E. Buss

Introduction

Both species of hippopotamus, the Nile or common hippopotamus (*Hippopotamus amphibious*) and the pygmy hippopotamus (*Choeropsis liberiensis*), remain challenging to immobilize or anesthetize due to their physical size, physiology, aquatic nature, and potential danger to staff. As new techniques become available, as well as more concentrated injectable drugs, the feasibility and safety of performing procedures on hippopotamuses increases. This chapter will provide updated as well as historical information on techniques available for captive and free-ranging common and pygmy hippopotamus sedation, immobilization, and anesthesia.

Taxonomy and Anatomy Related to Immobilization

There are two existing species of hippopotamus, the Nile or common hippopotamus (*Hippopotamus amphibious*) and the pygmy hippopotamus (*Choeropsis liberiensis*). These species are in different genera and free-ranging populations are found only on the African continent. The common hippopotamus is widely distributed in sub-Saharan Africa, while the pygmy hippopotamus is restricted to West Africa. *Hippopotamus amphibious* weigh approximately 1179–2500 kg, with adult males typically larger than females (Miller 2003). Length along the back ranges from 119 to 302 cm, with an average of 270 cm. Hippopotamuses in captivity are often much heavier than free-ranging counterparts, and this may increase complications during immobilization, including respiratory compromise by pressure on the diaphragm and delivery of intravenous (IV) or intramuscular (IM) drugs. Ideally, if a scale is available, drug doses should be based on accurate weights when feasible.

Common hippopotamuses have prominent eyes and nostrils set on the dorsal aspect of the head, which allows them to see and breathe without lifting their head out of water. The nares are adapted for an aquatic environment by having a valve-like closure that activates when submerged and opens on surfacing, even when sleeping. This reflex is also present in immobilized animals, depending on the drugs used.

The pygmy hippopotamus, *Choeropsis liberiensis*, is significantly smaller than the common hippopotamus, with weights ranging between 160 and 350 kg. They are approximately 70–80 cm high at the shoulder and 140–160 cm in length (Eltringham 1999), with males only slightly larger than females. Eyes are placed laterally on the head, which may make them more susceptible to trauma if placed in lateral recumbency during immobilization. Both hippopotamus species have opening jaw angles of greater than 90°, which allows easy access to dental structures and glottis for intubation. However, the powerful masseter muscles and weight of the skull may make opening the mouth difficult. Having equipment available to open and prop the jaw is important if oral access is required. Otherwise, their ability to rapidly bite if stimulated should be minimized by using a strap around the jaws to keep the mouth closed.

Both species have a four-compartment stomach and are considered "pseudo-ruminants". Food may be present in the stomach representing up to two nights of feeding (Eltringham 1999). Along with the normally slow gastrointestinal transit time, gastrointestinal tract contents may result in significantly increased pressure on the diaphragm and lungs during recumbency in immobilized hippopotamuses, therefore a minimum of 12–24 hours of fasting is recommended for captive hippopotamuses, with overnight water restriction to reduce abdominal content prior to immobilization when feasible (Ramsay et al. 1998; Loomis & Ramsay 1999).

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Typically, both common and pygmy hippopotamuses remain in or near water during the day and come out to feed between dusk and dawn. Common hippopotamuses are social, living in pods that may include a few to over 100 animals. Typically, the pod is led by a dominant bull with a harem of cows and their offspring. Adult bulls will engage in territorial fights.

Pygmy hippopotamuses are solitary by nature and often aggressive even to other individuals, especially if housed together in captivity. They also spend days in or near water, although they may spend more time on land than the common hippopotamus.



Figure 49.1 Blood collection from the hub of a needle using a digital vein on the forelimb of a Nile hippopotamus.

Physiology Related to Capture and Immobilization

Skin and Thermoregulation

Hippopotamus skin is uniquely designed to assist in the control of temperature and water loss. Although it appears thick, the epidermal layer is thin with a thick dermis containing blood vessels and subdermal glands which secrete frothy white or reddish viscous material (Eltringham 1999). The role of the secretions is incompletely understood but is speculated to assist in evaporative cooling and wound healing. Increased secretions are often observed during times of excitement. These secretions, along with body shape and weight, increase the difficulty of handling a recumbent hippopotamus.

Vascular Access Sites for Blood Collection and Catheterization

The pigmented epidermis and thick dermal connective tissue surrounding peripheral blood vessels make visualization difficult. In young or some free-ranging animals, veins may be visible due to lean body condition, or increased blood pressure after exertion or as a drug effect (i.e., opioids). Other methods for locating blood vessels include Doppler and ultrasound probes or blind approximation. Most peripheral veins on hippopotamuses are relatively thin-walled and can easily collapse with negative pressure from a syringe or vacutainer (Fig. 49.1).

One technique to collect blood is to allow it to drip from the hub of a needle into an open tube containing the appropriate anticoagulant. If there is good blood flow, use of an extension set may assist with collection into multiple tubes without disturbing the needle position. Due to often slow blood collection, clotting is a potential problem and pretreatment of tubing or syringes with anticoagulant is recommended. Samples should be prioritized due to the potentially limited volume associated with collection difficulties. Ideally, dedicated personnel should be assigned to acquire the most essential samples to minimize the time required during the immobilization.

Peripheral veins that can be accessed include cephalic, lateral, and medial saphenous, palmar and plantar digital (located on the caudal aspect of the distal limb), ventral abdominal, ventral tail, interdigital (located midway between the toes just proximal to the webbing on the dorsal aspect), and sublingual (Miller 2007; Stalder et al. 2012; McCurdy et al. 2014; Franklinos et al. 2017). Auricular veins tend to collapse, yield minimal blood volume, and are very sensitive, even under anesthesia. The ventral tail artery, on the midline at the base of the tail, lies very close to the ventral tail vein. Both the artery and vein are sensitive to movement of the needle and can constrict with repeated attempts, preventing any further blood collection.

IV catheterization has been accomplished but often with difficulty. In one study, the sublingual paramedian veins were found to be the most consistent site for rapid vascular access in adult common hippopotamuses (Stalder et al. 2012). Isotonic saline was administered at 1–2 mL/kg/h through this catheter. Others have reported catheterization of the palmar medial digital vein and auricular veins (Stalder et al. 2012; Hernandez et al. 2015). In a pygmy hippopotamus, 16-gauge catheters were placed in cephalic and lateral saphenous veins for fluid administration (McCurdy et al. 2014). However, caution should be exercised since the vessels are thin-walled and prone to extravasation of drugs and fluids. Intraosseous catheters can be used in juvenile or small hippopotamuses as an alternative to IV fluid or drug administration. Spinal needles or intraosseous biopsy needles placed in the greater trochanter of the femur were used successfully in one case of a juvenile common hippopotamus (Miller, unpubl. data). Fluid replacement therapy alternatives include nasogastric tube, rectal enema, or intra-peritoneal fluids.

Respiratory Responses during Immobilization

One of the obstacles to hippopotamus immobilization is the severe, often fatal, respiratory depression associated with potent opioid administration (Ramsay et al. 1998). Even with other immobilizing drug combinations, hippopotamuses exhibit temporary apnea, which mimics the physiologic "dive reflex" (Parker 1935). The respiratory pattern observed in hippopotamuses taking several breaths in short succession then breath-holding (Stalder et al. 2012) and they may even lift their head. This may result in erratic minute respiratory rates, oxygen saturation, and end-tidal CO_2 values during monitoring (Fleming et al. 2010). Hippopotamuses anesthetized with potent opioids are often apneic and tend not to show this dive response. In a report of 10 captive common hippopotamuses immobilized with medetomidine and ketamine, half of the animals showed self-limiting apnea (Stalder et al. 2012). Apneic periods lasted 1–9 minutes; although peripheral oxygen saturation (SpO_2) values declined significantly, they immediately returned to pre-apneic levels once the hippopotamus started breathing (Stalder et al. 2012). It is therefore critical to visually monitor respiratory cycles over several minutes and assess trends since apnea, hypoxemia, and hypercapnia are common complications.

Nasal Insufflation

When feasible, nasal insufflation with oxygen using a 12-mm endotracheal tube for a common hippopotamus (smaller for a pygmy hippopotamus) can increase both dead space and alveolar oxygen partial pressures, which may result in increased arterial oxygen (Ramsay et al. 1998; Stalder et al. 2012). Supplemental inhalant anesthetics can also be administered by nasal insufflation (Dumonceaux et al. 2000) (Fig. 49.2). This may reduce the need for additional injectable anesthetic drugs during prolonged procedures. Typically, 0.5–2.5% isoflurane administered through a nasal tube can provide sufficient analgesia and restraint for most procedures.

Intubation

For extended procedures or when using inhalant agents for supplemental or maintenance anesthesia, intubation is recommended. The necessary equipment and personnel should be available to assist in repositioning the animal to open the jaws, although some drug combinations provide adequate muscle relaxation for manual opening.



Figure 49.2 Oxygen insufflation.

Propofol (200 mg intravenously) has been used in a young (120 kg) common hippopotamus to facilitate intubation (Hernandez et al. 2015). An inflated tire inner tube from a small vehicle may be used under the head to keep the head in line with the body and keep the airway straight. Ropes or straps placed behind the canines can be used to open the mouth and different size wooden wedges between the upper and lower molar arcades used to keep the mouth open. This technique allows for easier access to the oral cavity. Rope handles, or pulls, should be attached to each block for ease of removal. Other equipment may be needed, including poles with nooses ("rabies poles"), ropes, duct tape, ratchet straps, and headlamps or flashlights for visualizing tube placement. Due to the redundant folds of buccal and oropharyngeal tissue, fleshy tongue, and long soft palate, it is easier to place an endotracheal tube in an adult hippopotamus by blind manual insertion than using a laryngoscope, which are typically too short. An adult common hippopotamus usually requires a 24–30-mm endotracheal tube and a 14–16-mm endotracheal tube is used for pygmy hippopotamuses. The smaller narrow oral cavity of the pygmy hippopotamus makes intubation slightly more difficult but can be accomplished by manual palpation of the glottis and insertion of the tube in a similar manner. A large animal anesthesia machine should be used with the flow rate set at approximately 5–10 mL/kg/min. For nonemergency procedures, ensure that there are adequate supplies of oxygen cylinders and inhalant anesthetics during the planning phase. If a large animal anesthetic machine is not available, a high-pressure demand valve may be used to insufflate the lungs. Demand valve systems for assisted ventilation, developed for elephant anesthesia, could also be used for hippopotamuses (Horne et al. 2001; Rubio-Martínez et al. 2014).

Monitoring Immobilized Hippopotamuses

Cardiovascular System

Auscultation and palpation of pulses are difficult due to size and anatomical features in most adult hippopotamuses. Using an electronic stethoscope can enhance audible detection of heart sounds as well as positioning the animal leaning slightly left to place the heart closer to the thoracic wall. The stethoscope should be placed near the left elbow in the axilla when the animal is in sternal recumbency. Pulses can sometimes be palpated interdigitally or occasionally near the cephalic, medial saphenous, and sublingual vessels. Heart rates vary significantly depending on the level of exertion and excitement prior to anesthesia, drugs, and dosages administered. Typical heart rates in immobilized animals are 20–60 beats per minute, but trends are more critical than actual numbers. Mean heart rate was 43 (±15, range 17–100) beats per minute in a hippopotamus immobilized with medetomidine-ketamine (Stalder et al. 2012). Typically, pulse oximeters or Doppler probes, placed directly on the cornea using copious amounts of gel, are used to monitor heart rates in immobilized hippopotamuses (Stalder et al. 2012; Miller, unpubl. data).

Respiratory System

Respiratory monitoring is one of the most important components of hippopotamus anesthesia since it is the area where complications most commonly occur (Ramsay et al. 1998; Miller 2007). The most common method of monitoring is visualization of thoracic excursions or anesthetic bag movements, although air flow through the nares can also provide information on depth as well as rate of breaths. Respiratory rates are influenced by the drugs administered but ideal ranges are 4–20 breaths per minute, although apneustic breathing patterns may make a rate less reliable. It is therefore recommended that an average is taken over a 5-minute monitoring period. In a study of 10 hippopotamuses immobilized with medetomidine and ketamine, the mean respiratory rate was 3 (±3) breaths per minute, with a range of 0–15 (Stalder et al. 2012). Importantly, trends in breathing rate and depth should be used rather than actual values.

Respiratory complications include apnea, hypoventilation, hypoxemia, hypercapnia, and respiratory acidosis (Flach et al. 1998; Loomis & Ramsay 1999; Miller 2003; Fleming et al. 2010). Administration of doxapram or supplemental oxygen, or partial or complete reversal should be considered depending on the degree of other physiological impairments (Ramsay et al. 1998; Dumonceaux et al. 2000). Lack of response to interventions should be quickly determined and reversal drugs administered IM in these cases, while ensuring the safety of personnel.

Body Temperature

Due to their large volume to surface area ratio, thermoregulation is an important function in hippopotamuses and should be carefully monitored during an immobilization. This is especially critical when a hippopotamus is out of water for a prolonged period. Water, ice, a hose for enema, methods to provide evaporative cooling (e.g., fans), and shade should be available to control temperature and cool the animal if necessary. Expected body temperatures of anesthetized hippopotamuses are 35–38°C (using a thermometer inserted 6 inches into the rectum). A hippopotamus undergoing castration had a mean temperature of 36.1°C (±1.6°C) (Stalder et al. 2012). However due to the large mass of the hippopotamus, this may not reflect core temperature. Readings over 39°C should be considered hyperthermic and cause for immediate concern and intervention (Stalder et al. 2012).

Specific use of Anesthetic Monitoring Equipment on Hippopotamus

As mentioned above, commonly used anesthetic monitoring equipment can be adapted for immobilized hippopotamuses but may be limited to certain locations or placement due to anatomy. This section describes techniques to improve accuracy and success.

Pulse Oximetry

Pulse oximetry can be used to measure heart rates but should not be the sole method due to the unreliability associated with probe placement (difficult to keep in place), possible vasoconstriction due to drugs or cool temperatures, poor reflectance through the dense dermal connective tissue, and interference by skin secretions. Auricular pulse oximetry may be attempted by using a blade to scrape the skin of the ear and then applying the pulse oximeter probe; however, oozing blood from the scraped skin may result in an inaccurate reading. A reflectance probe can also be used on the well-lubricated conjunctiva/nictitating membrane.

Other sites that have been used to obtain pulse oximeter readings in hippopotamuses include oral mucous membrane, vulva, prepuce, and rectal mucosa (Morris et al. 2001; Miller 2007). Trends should be monitored and interpreted in conjunction with other observations such as the color of mucous membranes, capillary refill time, etc.

In one report, mean SpO_2 was 79.2 ± 12.4% in immobilized hippopotamuses, although the range was 4–99% (Stalder et al. 2012). Therefore, oxygen saturation readings above 90% can be achieved in anesthetized hippopotamuses, especially if provided with supplemental oxygen (Dumonceaux et al. 2000; Stalder et al. 2012). The temporary apnea often observed can cause a significant decrease in SpO_2, but the values after breathing resumes should be used for monitoring trends. For example, the mean SpO_2 in common hippopotamuses immobilized with medetomidine and ketamine declined to 41% (±22%), with a range of 4–69% during apneic periods (Stalder et al. 2012).

Capnography

Capnography can be useful for measuring both respiratory rate and end-tidal CO_2 ($ETCO_2$) in hippopotamuses. The capnograph can be attached to a small (9–12 mm) endotracheal tube or the sensor can be directly placed into one of the nares (Fig. 49.3). After breath-holding, the first $ETCO_2$ reading may be 70–80 mmHg, which usually decreases to levels around 40–50 mmHg after a few breaths (Stalder et al. 2012). Hippopotamuses that do not exhibit the apneic pattern usually have values ranging from 35 to 55 mmHg when breathing air (Mortola & Seguin 2009; Miller, unpubl. data).



Figure 49.3 Use of capnograph.

Thermometers

A constant-reading digital thermometer with a long flexible probe placed rectally may provide the most accurate readings in hippopotamuses. Small digital thermometers, if used, should be placed in direct contact with the rectal mucosa to improve accuracy.

Blood Gas Analysis

Portable blood gas analyzers are becoming more available and can provide a more complete picture of cardiorespiratory function. Access to arterial samples may be difficult in hippopotamuses since this is usually performed blindly from the ventral tail artery, which is located close to the ventral tail vein. Sampling should be done with a preheparinized 1-mL syringe, which should fill by arterial pressure unless the animal is hypotensive. The color and filling pressure can be helpful in determining that the sample is arterial and not venous. Repeated samples from the ventral tail artery are possible.

Although normal values for blood gases in hippopotamuses have not been established, reference ranges for other large ungulates can be extrapolated to these species. Both venous and arterial samples have been reported in the common hippopotamus. Morris et al. (2001) reported average venous blood values from an immobilized juvenile common hippopotamus as follows: pH = 7.4 ± 0.1, partial venous pressure of carbon dioxide (PCO_2) = 61.5 ± 8.1 mmHg, partial venous pressure of oxygen (PO_2) = 71 ± 30 mmHg. Values in a common hippopotamus that received supplemental oxygen with three sequential arterial samples were SpO_2 = 96.7 ± 4.0% and arterial partial pressure of oxygen (PaO_2) = 122.3 ± 44.6 mmHg (Stalder et al. 2012). Venous blood samples from hippopotamuses in this same study had mean pH = 7.32 ± 0.05, PCO_2 = 67.5 ± 13.9 mmHg, lactate = 2.8 ± 1.4 mmol/L, and HCO_3- = 35.0 ± 6.8 mmol/L.

Planning for a Hippopotamus Immobilization

Any procedure requiring extensive equipment, supplies, and personnel should be planned well in advance to increase the chances of a successful outcome. It is important that all involved staff have clearly defined roles and responsibilities. Regular communication and checklists can be helpful to determine progress. Defined priorities and contingency plans should be discussed prior to the procedure. Safety considerations and contingencies for animals and personnel must be included in the planning.

Drug Administration and Induction

Drug administration to hippopotamuses is generally performed using darts, although options for confined hippopotamuses can include pole-syringe, hand-injection, or oral administration (Weston et al. 1996; Clyde et al. 1998; Dumonceaux et al. 2000; Stalder et al. 2012; McCurdy et al. 2014). Preferred injection sites (due to thinner skin thickness) are just caudal to the ear, caudal thigh, and biceps area. In the common hippopotamus, a 60–100-mm needle is used and must be at right angles to the skin to ensure an IM injection. A 38–40-mm needle should be adequate for adult pygmy hippopotamuses. Spinal needles have been used for hand-injections (William et al. 2010). Administration in crates, chutes, or from remote locations may limit the choice of injection sites. Intradermal injection of drugs will result in a slower or incomplete induction, which can lead to sudden arousal if stimulated too early, or the requirement for supplemental drug administration (Stalder et al. 2012; Miller, unpubl. data). Signs of induction usually include head lowering, sweating, salivation, ataxia, "dog-sitting", and recumbency (Loomis & Ramsay 1999; Stalder et al. 2012).

Adequate time after recumbency should be allowed before approaching since stimulation and arousal are possible, especially with nonpotent opioid combinations (Clyde et al. 1998; Morris et al. 2001). The mean induction time for 10 hippopotamuses immobilized with medetomidine (60–80 μg/kg) and ketamine (1 mg/kg) IM was 27 ± 12 minutes (range 14–44 minutes), with four animals requiring supplement medetomidine and ketamine to achieve recumbency and a safe plane of anesthesia (Stalder et al. 2012). In juvenile hippopotamuses administered detomidine (0.05 mg/kg) and butorphanol (0.15 mg/kg) IM, the mean time to recumbency was 13 ± 3 minutes (Morris et al. 2001). Even with administration of potent opioids such as etorphine, induction times can vary widely but may take 30 minutes for the animal to become recumbent (Loomis & Ramsay 1999). Hippopotamuses should be assessed remotely before approaching; there should be no response to noise or physical stimulation before starting to handle the animal. Placing a blindfold and ear plugs can minimize stimulation during the procedure.

Positioning

Hippopotamuses should be left in their initial position until they reach an adequate plane of immobilization since movement can also stimulate arousal. Their short limbs and barrel-shaped body can make positioning and transport difficult during immobilization. Sternal recumbency should be avoided for prolonged procedures since there is a greater risk of neuropathy, compromised tissue perfusion, and myopathy in the limbs. In addition, abdominal contents may put pressure on the diaphragm, resulting in compromised ventilation (Ramsay et al. 1998; Morris et al. 2001). However, rolling a hippopotamus into lateral recumbency may not be feasible and often depends on the drugs administered. Adult hippopotamuses immobilized with medetomidine-butorphanol may require ketamine or additional anesthetic drugs to tolerate being rolled into lateral recumbency (Miller, unpubl. data).

Maintenance

This is discussed in other sections but plans for maintaining or extending immobilization should be part of the planning process, and appropriate drugs and equipment should be available.

Recovery

Once the procedure is completed, all personnel and equipment should be removed to a safe distance. The hippopotamus can be left in either sternal or lateral recumbency for recovery (Morris et al. 2001; Miller 2007). Reversal drugs should be administered intramuscularly by inserting a 3-inch spinal needle into thin-skinned areas to ensure a deep IM injection. The tongue muscle has been used for IM injection of reversal drugs (Fleming et al. 2010). However, care must be taken if large drug volumes are injected (e.g., atipamezole) due to swelling and trauma. Drugs may be administered IV if venous access has been established but may be split between IV and IM administration to avoid excitation and rapid reversal (Stalder et al. 2012). Recovery times depend on the drugs used but are often rapid and uneventful. In common hippopotamuses immobilized with medetomidine-ketamine, mean recovery time was 5 ± 3 minutes after atipamezole administration (Stalder et al. 2012). Immediate short-term ataxia may be observed, but rapidly resolves and unless otherwise indicated (based on the procedure) animals can have access to water within few hours (Morris et al. 2001).

Anesthetic Records

Detailed records are critical for reviewing both successful and unsuccessful immobilization techniques for hippopotamuses. Minimum data should include animal information, date, weight (or estimate), drugs administered (dose, route, time), time to initial effect, time to recumbency, heart rates, respiratory rates, temperatures, other monitoring parameters, any complications, antagonists administered (dose, route, time), and recovery time and effect. Standardized

forms are available through many computerized medical records programs and can be modified for field use.

Safety

Both hippopotamus species are extremely dangerous and can inflect mortal wounds to humans if charged or trapped in a pen. If the hippopotamus is to be moved or handled without immobilization, then this must occur from a protected position. Under field conditions, a heavy caliber rifle (.375 or bigger) must be on hand to deal with emergency situations. If there is any concern regarding the level of immobilization, supplemental drugs should be administered remotely (using a dart or pole-syringe) before handling the animal. Other safety measures include placement of a strap around the jaw, using a blindfold and earplugs to reduce audible stimulus, and minimizing physical stimulation. Most drug combinations will provide 45–60 minutes of immobilization before supplemental drugs are required. However, continuous monitoring of anesthetic depth should be part of the safety procedures and staff must be made aware of any changes.

Review of Hippopotamus Immobilization

Common Hippopotamus

Historically, immobilizations of common hippopotamuses employed potent narcotics (etorphine) with or without xylazine or acepromazine (Loomis & Ramsay 1999). Frequent complications included apnea, cyanosis, bradycardia, and death. In one review, 6/16 (37.5%) immobilizations resulted in complications (Ramsay et al. 1998). However, successful immobilization with etorphine at 0.001–0.005 mg/kg (total dose 2–6 mg) with or without xylazine (0.061–0.083 mg/kg, total dose 100–150 mg) intramuscularly has been performed in captive hippopotamuses (Ramsay et al. 1998). Reversal was achieved with 100 mg of naltrexone to 1 mg of etorphine IM and yohimbine 0.1–0.3 mg/kg IM. The use of potent opioids requires close monitoring for adverse signs and prompt reversal if complications occur.

In more recent years, the use of restraint devices and husbandry training has facilitated medical procedures with captive hippopotamuses so that only restraint or minor sedation can be used (Krueger et al. 1996). Azaperone and acepromazine provide mild sedation but no analgesia (Loomis & Ramsay 1999). Tusk trims have been accomplished in a standing common hippopotamus using detomidine at 20 μg/kg IM (William et al. 2010).

Currently various combinations of alpha-2 agonists (detomidine, medetomidine), butorphanol, azaperone, and ketamine have been used for immobilization and procedures requiring analgesia, such as surgical procedures (Table 49.1). In a study using juvenile hippopotamuses, detomidine (0.02–0.026 mg/kg) was combined with butorphanol (0.06–0.20 mg/kg) IM (Morris et al. 2001). Another immobilizing combination that has been used in both wild and captive common hippopotamuses consists of medetomidine (0.04–0.05 mg/kg), butorphanol (0.05–0.10 mg/kg), and azaperone (0.05 mg/kg, to a maximum of 125 mg total) (Fleming et al. 2010). More recently, medetomidine (60–80 μg/kg)-ketamine (1 mg/kg) and detomidine (0.5 mg/kg)-ketamine (0.5 mg/kg)-butorphanol (0.15 mg/kg) combinations have been successfully used in common hippopotamuses undergoing castration and ovariectomy, respectively (Stalder et al. 2012; Hernandez et al. 2015).

Although time to initial effects and recumbency varies, initial sedation may occur in 10–20 minutes, with recumbency taking 20–30 minutes or longer. An additional dose of 1–2 mg/kg of ketamine in a second dart may provide some additional anesthesia and provide a higher level of safety if the hippopotamus is still responsive to stimulus. Supplemental drugs such as isoflurane/sevoflurane, ketamine (0.1–1 mg/kg IM), propofol (0.5 mg/kg IV as a bolus or 50–100 μg/kg/minute as an infusion), remifentanil (0.25 μg/kg/h as an infusion), low-dose etorphine, or supplemental detomidine/medetomidine and butorphanol may be required to extend or deepen the level of immobilization or provide additional analgesia (Morris et al. 2001; Miller 2007; Stalder et al. 2012; Hernandez et al. 2015).

Inhalant anesthetics (isoflurane and sevoflurane) have been used by both nasal insufflation and intubation to provide general anesthesia for surgical and other procedures (Dumonceaux et al. 2000; McCurdy et al. 2014; Hernandez et al. 2015; Franklinos et al. 2017). When administering inhalant anesthetics by nasal insufflation, staff and environmental safety should be considered. Procedures on captive hippopotamus lasting up to3 hours have been achieved using butorphanol-alpha-2 agonist induction with isoflurane supplementation (Miller, unpubl. data).

The choice of reversal drugs will depend on the drugs used for immobilization and maintenance of anesthesia. Naltrexone at three to 20 times the butorphanol dose in milligrams administered intramuscularly, atipamazole at three to five times the alpha-2 agonist dose in milligrams administered intramuscularly or intravenously, or yohimbine 0.1–0.3 mg/kg IM or IV have been used to reverse butorphanol-medetomidine/detomidine combinations (Clyde et al. 1998; Morris et al. 2001; Miller 2007; Stalder et al. 2012). Arousal is relatively rapid, usually within 5–20 minutes, unless the hippopotamus has received supplemental drugs. In captive hippopotamuses, if the animal is not standing in 45–60 minutes, it is advisable to give

Table 49.1 Immobilizing drug combination dosages for common hippopotamus (*free-ranging).

Immobilizing Drug	Dose	Reversal	Reference
Detomidine	0.026 mg/kg	Atipamezole (5× detomidine total dose) or yohimbine 0.1–0.3 mg/kg	Clyde et al. (1998)
Butorphanol	0.04 mg/kg	Atipamezole (3–5× detomidine total dose) or yohimbine 0.3 mg/kg	Morris et al. (2001)
Detomidine	0.05 mg/kg		
Butorphanol	0.15 mg/kg	Naltrexone 0.5 mg/kg	
Detomidine	0.02–0.026 mg/kg	Atipamezole (3–5× detomidine total dose)	Morris et al. (2001)
Butorphanol	0.06–0.20 mg/kg	Naltrexone (3–5× butorphanol total dose)	
Medetomidine	0.06–0.08 mg/kg	Atipamezole (3–5× medetomidine total dose)	Stalder et al. (2012)
Ketamine	1 mg/kg		
Detomidine	0.5 mg/kg		Hernandez et al. (2015)
Butorphanol	0.15 mg/kg		
Ketamine	0.5 mg/kg		
*Medetomidine	0.04–0.05 mg/kg	Atipamezole (5× medetomidine total dose)	Fleming et al. (2010)
*Butorphanol	0.05–0.10 mg/kg	Naltrexone (5× butorphanol total dose)	
*Azaperone	0.05 mg/kg to max 125 mg		
*Ketamine top-up	100–500 mg total dose		
*Medetomidine	0.03–0.075 mg/kg	Atipamezole (5× medetomidine total dose)	Cooper (pers. comm.)
*Butorphanol	0.10–0.20 mg/kg	Naltrexone (5× butorphanol total dose)	
*Azaperone	0.10–0.125 mg/kg		
*Ketamine	0.625 mg/kg		
Standing sedation			
Detomidine	0.02 mg/kg		William et al. (2010)

an additional dose of naltrexone and atipamezole by dart. Yohimbine (0.1 mg/kg) can also be used but does not appear to be as effective as atipamezole in reversing medetomidine.

Capture and Immobilization of Free-ranging Common Hippopotamuses

Wild hippopotamuses frequently use trails from the water to feeding sites that can be used for camera trapping and capture (D. Cooper, pers. comm.). Knowledge of these locations provides potential capture sites. When possible, small bodies of water are targeted. Hippopotamuses are then restricted from grazing areas with electrification and thereby forced to go into the feeding pen (Fig. 49.4). This may result in animals that become compromised and in poor body condition, therefore trapping is usually done during the winter or dry periods when they are more likely to enter the trap. The trap design must appear to form a passage that gives the animals access to both land and water. Hippopotamuses are then enticed with alfalfa hay to walk over the pop-up doors to be captured. This method is time-consuming but usually the only way in which large numbers of common hippopotamuses are captured safely and cost effectively in Africa.

Free-ranging hippopotamuses create another level of complexity due to their tendency to be in or near water and other hippopotamuses during daytime hours when capture is usually planned. Immobilization of free-ranging common hippopotamuses can be accomplished by darting at night when the animal is at least 1 km from the water. A combination of medetomidine (0.04–0.05 mg/kg), butorphanol (0.05–0.10 mg/kg), and azaperone (0.05 mg/kg, to a maximum of 125 mg) with hyaluronidase is utilized. If darted and left alone, undisturbed hippopotamuses usually will only run 10–30 m and then resume grazing. Free-ranging hippopotamuses should only be darted in or close to water, if they are on their own, or can be separated from the pod. Once in the pod, the animal can become lost or



Figure 49.4 Passive capture pen for free-ranging hippopotamuses.

pushed under water when the drugs take effect. Helicopter darting is an effective way to dart a single hippopotamus or individuals that have broken away from the pod, especially in those animals that are habituated to boats, since the group may move away from the disturbance. From a helicopter, the dorsal hindquarters or the muscles along the spine are ideal targets for perpendicular darts. Longer needles are required due to the thicker skin over the dorsum; recommended dimensions are 75–100 mm in length and 3-mm diameter. The capture of free-ranging hippopotamuses by darting from a helicopter can be attempted during the winter months in southern African when water levels in river systems are low. Suitable animals for this technique are usually subordinate bulls which occupy shallower pools on the periphery of the main pod. On the approach of a helicopter, these animals will frequently leave the water and can be herded away from deep water bodies to an area suitable for darting. Hippopotamuses in the main pod are usually located in large deeper pools and will submerge and not move out of the water in the presence of a helicopter. Hippopotamuses, especially adults, are susceptible to hyperthermia-associated mortalities and immobilization should only be attempted when environmental temperatures are low, and the herding of a selected individual prior to darting should be for short distances and at walking speed.

Historically, free-ranging hippopotamuses have been darted with potent opioids, including etorphine and thiafentanil, but the use of these drugs is associated with high mortality rates (Maritz 1993). More recently, a combination of butorphanol (0.1–0.2 mg/kg), medetomidine (0.03–0.075 mg/kg), and azaperone (0.1–0.125 mg/kg) with ketamine (0.625 mg/kg; D. Cooper, pers. comm.) or without ketamine (Burroughs et al. 2012) has been used with some success. Even with drugs formulated at high concentrations (e.g., 50 mg/mL butorphanol + 25 mg/mL medetomidine), this combination requires the use of large-volume darts with long needles (≥75 mm), which can be difficult to use when darting from a helicopter.

The hippopotamus to be darted should be approached from behind and the dart placed in the dorsal rump area. It is essential that the dart is placed perpendicular to the skin surface to ensure a deep IM delivery of the immobilizing drugs. Drugs administered by additional darts following an initial subcutaneous or partial drug delivery tend to have a reduced effect; this may be caused by an alpha-2 agonist-induced peripheral vasoconstriction or a sympathetic response associated with the darting procedure. Once the dart has been placed, the helicopter should back off immediately to minimize further disturbance to the darted hippopotamus. Observation of the darted animal during induction must be from a distance to limit auditory or visual stimulation. Most hippopotamuses, if left undisturbed following darting, will initially run a short distance before walking slowly or becoming stationary. However, it is essential that darting takes place at least 200 m from any pool of water that is deep enough for a hippopotamus to completely submerge itself. A darted hippopotamus may start moving towards such a pool as the drugs take effect and it is almost impossible to stop this from happening using a helicopter or by personnel that might be on the ground. Should a darted hippopotamus reach deep water, it may drown once fully affected by the immobilizing drugs. Access to the immobilized hippopotamus to monitor vital functions and administer drug antidotes will not only be hampered by the animal being underwater but also the possible presence of other hippopotamuses and crocodiles.

Induction following darting takes 10–20 minutes depending on dart placement and the drug dose administered. If the drug administration is subcutaneous, induction can take as long as 45 minutes and require supplemental doses for safe handling. The darted hippopotamus initially slows, then becomes stationary with its chin on the ground and may become sternally recumbent; at this stage, it does not respond to the close proximity of a helicopter. Great care should be taken in approaching an apparently immobilized hippopotamus on foot and the presence of a suitably qualified and experienced marksman with an appropriate caliber rifle is advised. A hippopotamus that is not fully immobilized may react to the proximity of humans by charging rather than trying to flee. Removing a hippopotamus from a water body can be problematic as the darted animal may only show its nares when breathing. Monitoring bubbles released due exhalation will allow positioning to attempt to place a noose around the head or neck. Often attempts to move the hippopotamus can stimulate the animal, which should be avoided whenever possible.

The depth of immobilization is assessed by the hippopotamus' response to noxious noise or tactile stimulation. The immobilized hippopotamus is secured with a blindfold and the mouth closed with a broad strap placed around the jaws caudal to the nostrils. These precautionary procedures are to protect personnel should the hippopotamus be aroused by procedures or it spontaneously wakes up. The immobilized hippopotamus can remain in sternal recumbency, especially if lying on loose river sand, without adversely affecting circulation to the limbs, or be rolled into lateral recumbency. Respiratory and cardiovascular functions should be regularly monitored as previously described and depth of immobilization assessed, which is done through administering tactile stimuli.

Depending on the initial drug dose and combination, a hippopotamus will remain immobilized for 45–60 minutes. If required, ketamine (100–500 mg) can be used to deepen the level of immobilization; however, as access to superficial veins is limited, it is usually given intralingual, intrabuccal, or IM, with the associated delays in reaching full effect. Once all procedures have been completed, both naltrexone (five times the butorphanol dose in milligrams) and atipamezole (five times the medetomidine dose in milligrams) are administered. It is usually not possible to administer these antidotes intravenously and they are given into the tissues of the mouth or via IM sites; however, the large volumes of both drugs must be divided over multiple sites to avoid tissue damage. The blindfold and strap around the mouth are immediately removed, and personnel retreat to a safe distance. The hippopotamus should be observed until fully recovered; it may be partially tranquillized from residual azaperone if used in the immobilizing combination.

Several free-ranging hippopotamuses immobilized with the medetomidine, butorphanol, and azaperone combination (Fleming et al. 2010) had transient apnea and exhibited breath-holding behavior for approximately 20–30 minutes post darting. With regular respirations, SpO_2 values were in the high 90s and $ETCO_2$ was 30–50 mmHg. Higher $ETCO_2$ and lower SpO_2 values were initially recorded during the initial breath-holding phase. Other physiologic values followed a similar trend suggestive of acidosis (PCO_2 35–70 mmHg, PO_2 35–75 mmHg, SO_2 82–95%, pH 7.15–7.35, and rectal temperature 35–38°C). Procedure length was variable but averaged about 80 minutes in the field without any supplemental drug administration.

Recovering hippopotamuses in field conditions may face additional challenges such as water or other topographical issues that should be considered. A large rubber mat can be slid under the hippopotamus and used to move the animal prior to reversal. Straps attached to the legs above the hock may allow the hippopotamus to be hoisted or slid into a crate on a rubber mat.

Pygmy Hippopotamuses

Although there are fewer anesthetic reports in pygmy hippopotamuses, they nonetheless present the same types of challenges as their larger counterparts. To minimize the need for immobilization, many facilities have instituted training programs and modified structures to permit minor medical procedures, such as wound treatment and tusk trims, to be performed.

There have been a few anesthetic events using narcotics in pygmy hippopotamuses combining etorphine or carfentanil with xylazine, or etorphine and acepromazine (Miller 2003). However, anesthetic complications were observed in pygmy hippopotamuses and the use of potent opioids has fallen out of favor.

For minor sedation or as an adjunct for initial induction, oral premedication with midazolam (0.1 mg/kg), diazepam (0.5 mg/kg), or detomidine (0.045 mg/kg) has been used prior to immobilization with alpha-2 agonist-butorphanol combinations (with or without ketamine) (Weston et al. 1996; J. Napier, Z. Gyimesi, E. Baitman, K. Mehren, pers. comm.). In general, no obvious drug effect was reported, although some synergistic effects may have occurred since overall ratings for the procedures were good

Table 49.2 Immobilizing drug combination dosages for pygmy hippopotamus.

Immobilizing Drug	Dose	Reversal	Reference
Ketamine	1 mg/kg		Morris et al. (2001)
Medetomidine	0.036 mg/kg	Atipamezole (3–5× medetomidine total dose)	Morris (pers. comm.)
Butorphanol	0.20 mg/kg	Naltrexone (3–5× butorphanol total dose)	
Detomidine	0.07 mg/kg	Yohimbine 0.11 mg/kg	Weston et al. (1996)
Butorphanol	0.15mg/kg		
Ketamine	0.88 mg/kg		
Medetomidine	0.08 mg/kg		McCurdy et al. (2014)
Ketamine	1.2 mg/kg		Franklinos et al. (2017)
Medetomidine/detomidine	0.04–0.06 mg/kg		Morris (pers. comm.)
Butorphanol	0.1–0.2 mg/kg		
Oral premedications			
Midazolam	0.1 mg/kg PO		Mehran (pers. comm.)
Diazepam	0.5 mg/kg PO		Weston et al. (1996)
Detomidine	0.045 mg/kg PO		Weston et al. (1996)

PO, per os.

to excellent. Drug combinations for immobilizing pygmy hippopotamuses are similar to those used in the common hippopotamus (Table 49.2). The use of butorphanol-detomidine or medetomidine for immobilization of pygmy hippopotamuses has shown good results. The ratio of alpha-2 agonist to butorphanol is approximately 1:5, which is different than that used in the common hippopotamus (Miller 2007). This results in dosages of 0.04–0.06 mg/kg medetomidine or detomidine and 0.1–0.2 mg/kg butorphanol IM (P. Morris, pers. comm.). Ranges for IM detomidine-butorphanol-ketamine combinations were as follows: detomidine (0.07–0.08 mg/kg), butorphanol (0.15–0.20 mg/kg), and ketamine (0.8–2.0 mg/kg). Other successfully used drugs for pygmy hippopotamuses are medetomidine (0.035 mg/kg) and butorphanol (0.2 mg/kg) given IM (Z. Gyimesi, pers. comm.).

Medetomidine (0.08 mg/kg) and ketamine (1.2 mg/kg) administered IM has been used to immobilize pygmy hippopotamuses in zoos for diagnostic procedures (McCurdy et al. 2014; Franklinos et al. 2017). Like common hippopotamuses, supplemental doses of ketamine or inhalant anesthetics will provide additional analgesia or extend the immobilization time. Reversal agents are similar to those used in the common hippopotamus. Alpha-2 agonists are reversed with atipamezole at five times the dose (in milligrams) of medetomidine or detomidine administered IM. Naltrexone was typically used to reverse butorphanol at a ratio of five to 16 times the dose (in milligrams) of the opioid. Recovery times were reported as mild sedation at 2–17 minutes after administration of the reversal agents.

Capture and Immobilization of Free-ranging Pygmy Hippopotamuses

Due to the location and habitat of free-ranging pygmy hippopotamuses, there have been few attempts to capture these animals. Successful capture of a pygmy hippopotamus in Sierra Leone was accomplished using a pit trap system (A. Conway, pers. comm.). Pit traps are dug along trails with dimensions of 2 m deep, 2 m long, and 1 m wide. Rice bags containing dirt are placed at the bottom to prevent injury and a series of small branches is used to support a reed mat to cover the entrance of the pit, which is then covered by leaves. When the hippopotamus steps on the mat, the branches collapse, which results in the animal falling into the trap. Although immobilization of captured pygmy hippopotamuses has not occurred, it may be feasible to dart an animal in the pit trap with immobilizing drugs used for captive pygmy hippopotamuses. However, the availability of darting equipment and drugs may present a challenge in range countries.

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Camelids

Khursheed R. Mama and Chris Walzer

Introduction

Anesthesia may be required for diagnostic and corrective procedures in veterinary hospitals, in zoological parks, in the field, or in the animal's natural habitat. This chapter will attempt to provide information relevant to the anesthetic management of camelids so as to maximize chances of a favorable outcome.

It is important to recognize that camelids are native to very different geographical areas, ranging from the high altitude of the Andes to the deserts of India, Africa, and the Middle East. As such, even though they are all camelids, their physiological adaptations differ. For example, camels are well adapted to drought conditions and may store and draw on water reserves. Llamas and alpacas have a left-shifted oxygen hemoglobin dissociation curve (Chiodi 1970), and their red blood cell configuration and hemoglobin content differ from those of many other mammalian species (Fowler & Zinkl 1989; Van Houten et al. 1992). These are likely adaptations for survival at high altitudes, where the oxygen tension is low.

Patient Restraint and Handling

Fasting prior to general anesthesia is recommended to minimize regurgitation, aspiration, and bloating. Depending on the nature of the procedure and anticipated duration of recumbency, a 12- to 18-hour fasting period is recommended in adult llamas and alpacas; a 24- to 36-hour fast has been recommended for camels. Many recommend withholding water in addition to feed for at least a portion of that time. Fasting of nursing juveniles is not necessary and may increase their stress and likelihood of metabolic derangement.

Camelids may be trained to a halter and led using this. A towel may be hung loosely over the nostrils and mouth in the event that an animal attempts to spit at the handler. A small corral may be used to facilitate catching an individual animal from a herd. An arm placed around the neck of llamas and alpacas will help restrain the patient until a halter can be placed. Chutes designed especially for llamas and alpacas greatly facilitate restraint for procedures such as catheter placement. Domesticated camels may be restrained in stocks designed for horses or eased to sternal recumbency using a rope placed around the forelimb. They may also be trained to a seated ("cushed") position by their handler.

Instrumentation

Intravenous catheterization and endotracheal intubation have historically been considered challenging in camelids. Success can be maximized with proper knowledge of the anatomy and availability of appropriate equipment.

The most common site for venous access in camelids is the jugular vein. The greatest challenge in placing a jugular catheter in adult camelids is lack of animal compliance. Many patients will "cush" and rise during the procedure, making for a moving target. Restraint in an appropriate chute or stanchion can help significantly. The other difficulty faced when placing a jugular catheter is locating the vein. Many camelids, especially males, have thick (up to 1 inch) skin in the proximal portion of their neck and balloting the vein can prove challenging, especially as the vein is fairly deeply located. Knowledge of the anatomical landmarks is therefore important. In the proximal neck, the jugular vein is located at the bisection of a line drawn

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caudally from the lower jaw with a line drawn ventrally from the base of the ear (Davis et al. 1996). Despite difficulty palpating the vessel in the proximal portion of the neck, many prefer this site for catheter placement due to better separation between the jugular vein and carotid artery (Davis et al. 1996; Riebold et al. 1989). This approach should also be considered when performing venipuncture for administration of drugs as cerebral injury has been reported following inadvertent intracarotid injection of anesthetic drugs (Valentine et al. 2009), and it can be difficult to differentiate arterial from venous blood in South American camelids due to the brightness of venous blood (Grint & Dugdale 2009). Distention of the vein is best accomplished by holding off behind the palpable ventral projection of the C6 vertebra. If one is still unable to palpate the vein, a narrow gauge (25 or 23), inch to inch and a half needle may be used to locate the same prior to catheter placement.

Once the vein is located and the site appropriately prepared, an incision through all the layers of the skin is recommended in the adult camelid. This incision is best made with a scalpel blade after subcutaneous local anesthetic (1–2 mL of 2% lidocaine) is infiltrated at the site (Heath 1989). In order not to accidentally lacerate the vessel, do not distend the vein while making this incision through which the catheter may then be placed. Continue to distend the vein while the catheter is advanced to minimize the chances of it getting caught on valves within the same. Valves have been anecdotally reported to impede threading the jugular catheter. Secure the catheter so that it does not "kink" at the point of entry through the skin.

Alternate sites for catheter placement include the lateral thoracic vein in adult camels and the cephalic or saphenous vein in juvenile patients. Auricular vessels may be used in anesthetized patients. The size of the catheter used should be appropriate for the size of the animal, with consideration given to the reason for its placement. For example, a large-gauge catheter similar to that placed in adult patients is generally unnecessary in a 10-kg cria. Alternatively, if significant hypotension is expected in an adult patient due to the disease process or because of anticipated hemorrhage, at least one large-gauge catheter is recommended.

The technique for endotracheal intubation varies with the camelid species in question. For llamas and alpacas, visual orotracheal intubation is facilitated by appropriate equipment and positioning. Ideally, the animal should be placed in sternal recumbency with the head extended. A ruminant mouth gag or strips of tape/gauze may be used to spread the jaws and facilitate visualization using a long, but narrow laryngoscope blade. Intubation may be performed directly using an endotracheal tube or either directly or retro grade by first placing a flexible guide to help direct the endotracheal tube into the trachea (Sanchez et al. 1993). Topical local anesthetic (lidocaine) is used to facilitate intubation in the lightly anesthetized patient. The tube is generally secured behind the ears after the cuff is inflated. Passage of the tube via the nasal passage (nasotracheal intubation) may also be performed in llamas and alpacas (Riebold et al. 1994). The tube is passed into the trachea via the ventral medial nasal meatus after proper lubrication. While this usually necessitates a smaller tube (e.g., 8- or 9-mm internal diameter vs. 12- or 14-mm internal diameter in an adult llama) than via the oral route and there is a potential for hemorrhage during placement, the tube may be left in place until the animal is fully recovered without fear of the patient chewing it. Vasoconstrictors, such as phenylephrine, may be administered topically to minimize hemorrhage during nasotracheal tube placement. Since camelids are nasal breathers, this method helps minimize the risk of upper airway obstruction in the recovery period. This technique may also be utilized to minimize the need to work around the endotracheal tube during procedures involving the oral cavity.

In adult camels, intubation is usually performed blindly or by manual palpation of the arytenoid cartilages. After the patient is adequately anesthetized, a large animal mouth gag may be used to facilitate introduction of the arm into the oral cavity. If the oral cavity is too narrow, a guide tube may first be inserted into the trachea. Caution must be exercised to prevent laceration of the endotracheal tube on the rear teeth. Depending on the size of the patient, a range of tubes from 16- to 26-mm internal diameter may be necessary (Alsobayil & Mama 1999) (Fig. 50.1).



Figure 50.1 Direct manual intubation of a dromedary camel. Photo courtesy of Gary West.

Anesthetic Techniques

Regional and general anesthetic techniques may be used in camelids. General anesthesia may be achieved with injectable agents, inhaled agents, or a combination of these. For the reader who wishes to pursue this further, detailed reviews of anesthetic drugs and techniques for camelids are available (Ali 1988; Alsobayil & Mama 1999; Fowler 1989; Mama 2000). Regardless of the drugs selected, keep in mind that the range of body weights is very broad among camelids, ranging from an 8- to 10-kg newborn cria to a 500-kg camel. Hence, it is important to try to get an accurate weight and calculate dosage based on this. Fiber in adult llamas and alpacas can be very misleading, and when a scale is not available, palpation of the patient may assist in determining weight. Typically, adult alpacas weigh 40–60 kg, whereas body weight in adult llamas may range from 120 to 300 kg. Body weight also influences equipment requirements, ranging from endotracheal tubes and the anesthetic machine to the type of padding used.

Regional Anesthesia

Regional administration of local anesthetics can facilitate surgical intervention and minimize the need for administration of drugs with systemic effects. Local anesthetics may be used to facilitate a host of procedures. Blocking individual nerves, for example the mandibular nerve, for dental procedures involving the lower jaw is commonly utilized in awake or sedated patients and as an adjunct to general anesthesia. The anatomy and location of the mandibular and mental foramina to facilitate regional anesthesia at these nerves has been well described (Zhu et al. 2009). Paravertebral blocks similar to those described in both horses and cattle have been used in camelids (Fowler 1989; Said 1964) as have epidural techniques.

Caudal epidural administration of 12–15 mL of 2% lidocaine in a sternally recumbent adult camel provides anesthesia of the perineum and udder or scrotum for 1–2 hours without influencing motor control (White 1986). Lidocaine (0.22 mg/kg) and xylazine (0.17 mg/kg) have been used to facilitate diagnostic and surgical procedures involving the rectum, vagina, and perineum in llamas (Grubb et al. 1993). The onset of anesthesia was 3–4 minutes following either lidocaine or xylazine and lidocaine, but the duration varied significantly, lasting about 1 hour in the lidocaine group and 6 hours in the group receiving both drugs. Analgesia following xylazine alone was evident after about 20 minutes and lasted 3 hours. Mild sedation is reported in animals receiving xylazine. Clinical evaluation of the efficacy of caudal epidural analgesia with lidocaine, or a combination of lidocaine and xylazine in alpacas undergoing castration, revealed that while a combination or epidural xylazine and lidocaine had the best efficacy, incomplete blockade of the spermatic cord was observed in many animals (Padula 2005). Epidural morphine at doses similar to those used in other species may provide longer-term analgesia and may have value for postoperative analgesia for procedures involving the hindlimbs or caudal abdomen and perineum.

Drugs for Sedation and Field Anesthesia in Domesticated Camelids

Many techniques and drugs for sedation and anesthesia have been used in camelids and for detailed information on the same and individual drug effects, the reader is referred to more comprehensive reviews and references therein. (Ali 1988; Alsobayil & Mama 1999; Fowler 1989; Mama 2000). This section of the manuscript will highlight commonly used techniques for domesticated animals.

Intramuscular (IM) and intravenous (IV) administration of xylazine or xylazine and ketamine has been extensively described for use in llamas, alpacas, and camels (Bolbol 1991; DuBois et al. 2004; Fowler 1989; Gavier et al. 1988; Prado et al. 2008a; White et al. 1987). While these drugs alone and in combination do provide effects ranging from sedation to short-term anesthesia, the degree (level of sedation or anesthesia) and duration (may range from 10 to 60 minutes) of response in individual animals is variable. The addition of butorphanol to an IM combination of xylazine and ketamine has also been evaluated in llamas and alpacas. Xylazine (0.03 or 0.04 mg/kg IM), butorphanol (0.3 or 0.4 mg/kg IM), and ketamine (3 or 4 mg/kg IM) was administered to seven male llamas and seven male alpacas based on dose recommendations from Dr. LaRue Johnson (Mama et al. 2000). Most animals became recumbent in an average of 4.3 (llamas) and 6.7 (alpacas) minutes. Induction quality was good, with animals generally showing some degree of ataxia before assuming a sternal or lateral position. Despite receiving lower drug doses, llamas appeared more deeply anesthetized and remained recumbent for a longer duration (mean time to standing 63 minutes) than did alpacas (mean time to standing 22 minutes). All animals recovered without apparent complications, but hypoxemia (average partial pressure of oxygen arterial blood [PaO_2] of 45–55 mmHg, barometric pressure 640 mmHg) and mild hypoventilation (average $PaCO_2$ was 46–49 mmHg), associated with recumbency, were commonly seen in this study. Direct mean auricular arterial blood pressure was well maintained, averaging 131 mmHg in llamas and 144 mmHg in alpacas; heart rate ranged from 29 to 37 beats per minute (bpm) in llamas and 37 to 49 bpm in alpacas.

Other alpha-2/dissociative and/or benzodiazepine combinations include xylazine or dexmedetomidine and tiletamine/zolazepam or medetomidine and ketamine (DuBois et al. 2004; Hammer et al. 1999; Seddighi et al. 2016; Waldridge et al. 1997) and medetomidine, butorphanol, and ketamine (Georoff et al. 2010). Selection of a specific alpha-2 or dissociative agent is in large part based on drug availability, circumstance, and familiarity on the part of the veterinarian. Effects may vary in duration and magnitude but tend to be qualitatively similar between the different agents.

Butorphanol (0.1 mg/kg IM) has also been used in combination with intratesticular lidocaine (2%, 2–5 mL/testicle) for chemical restraint to facilitate standing castration in over 100 llamas (Barrington et al. 1993). The authors' impression was that the animals receiving butorphanol appeared less stressed than those receiving only intratesticular lidocaine.

Similar drug combinations are utilized for anesthesia in field conditions for camels. White et al. (1987) describe the use of intramuscular xylazine and ketamine individually and in combination. Behavioral responses and measured cardiovascular parameters of the combination were thought to be improved over individually administered drugs. Detomidine and medetomidine have also been used alone to provide sedation or in combination with ketamine for anesthesia. Recently, sedative effects of intravaginal and intravenous detomidine administration were compared and while onset following IV administration was more rapid, both routes provided moderate sedation of an equivalent duration (Chow et al. 2020). In studies evaluating the effect of these drugs on platelet function and coagulation, xylazine, but not detomidine or ketamine, was shown to decrease platelet numbers, which might be of relevance for procedures in which bleeding is anticipated (Almubarak 2007). The effects of the alpha-2 drugs may be reversed with yohimbine or atipamezole at the conclusion of the procedure to facilitate a more rapid recovery (Riebold et al. 1986; Waldridge et al. 1997). While tolazoline has also been used successfully in the research environment for reversal of alpha-2 effects (DuBois et al. 2004; Prado et al. 2008a), there have been anecdotal reports suggesting complications following its administration is possible in camelids.

The phenothiazine tranquilizers are a class of drug that seem to be more widely used in camels than in llamas and alpacas. While acepromazine is the tranquilizer most veterinarians are familiar with, other drugs in this class include proprionyl promazine, chlorpromazine and triflupromazine. These drugs tend to have prolonged effects and are not reversible, but in many circumstances, camels are quieted and seem generally less responsive to their surroundings (Alsobayil & Mama 1999). Prado et al. (2008b) report no sedation with acepromazine or acepromazine and butorphanol in young llamas. However, they did demonstrate a longer period of antinociception during anesthesia maintained with Telazol following these treatments.

Drugs for Sedation and Field Anesthesia in Nondomesticated Camelids

Conservation efforts often require capture and handling of animals. Wildlife capture and anesthesia is a complex operation that can cause significant injury or death. Although skill, experience, and appropriate veterinary training can minimize the risk, it is necessary to evaluate whether the procedure is necessary and whether the potential gains in knowledge for conservation of the species outweigh the risks (Osofsky & Hirsch 2000). Many of the aforementioned techniques may be used at modified dosages to provide chemical restraint for nondomesticated camelids. Additional suggestions are provided in the subsequent text.

Wild South American Camelids

Traditionally, South American camelids are physically restrained for fiber (wool) harvest using various herding techniques (Bonacic et al. 2006). There are very few reports in the literature detailing the capture and field anesthesia of wild South American camelids for conservation purposes. One describes the use of tiletamine and zolazepam for immobilization of guanacos in a Chilean national park, but results of this combination were thought to be largely unsatisfactory (Karesh et al. 1998; Sarno et al. 1996). Recently, Georoff et al. (2010) described use of a combination of IM medetomidine, butorphanol, and ketamine followed by reversal with atipamezole and naltrexone in captive (zoological park) guanacos. They report a reliable onset of anesthesia and effective reversal with no noted behavioral side effects. Due to these favorable qualitative aspects, further evaluation in the field situation is warranted. However, bradycardia, hypertension, and hypoxemia as reported by authors will need to be managed during drug-induced recumbency.

As with guanacos, descriptions of field anesthesia for the smallest South American camelid, the vicuna (*Vicugna vicugna*) are extremely limited. Ketamine (7.8 mg/kg) and xylazine (1.2 mg/kg) sometimes in combination with midazolam (0.35 mg/kg) and atropine (0.07 mg/kg) has been used successfully in the field setting to collect semen via electroejaculation (Hoyos 2009; Urquieta et al. 1992).

Wild Bactrian Camel (*Camelus ferus*)

The range of the wild Bactrian camel has been reduced to only three locations worldwide: two in China (Lop Nuur

and Taklamakan Desert) and one in Mongolia (Great Gobi A Strictly Protected Area). The population is listed by IUCN as critically endangered and there remain an estimated ~600 animals in China and between 350 and 1950 in the Great Gobi A Strictly Protected Area (Walzer et al. 2008).

Potent opioids, such as etorphine, have been used in camels either alone or in combination with acepromazine, ketamine, xylazine, detomidine, butorphanol and tiletamine, and zolazepam (Blumer et al. 1999; deMaar et al. 1998; Walzer & Kaczensky 2005). Pacing is commonly described prior to recumbency when potent opioids are used without a tranquilizer. Significant respiratory depression is a potential complication. Availability of a mechanical breathing device and oxygen supplementation are therefore highly recommended when potent opioids are utilized. Alpha-2 agents, when used, and potent opioids may be reversed at the conclusion of the procedure.

As has been described for other species, such as the Asiatic wild ass (*Equus hemionus*) and Przewalski's horse (*Equus ferus prezwalskii*), a chase method (in this instance the animal was darted from a moving jeep) was used to capture a single wild Bactrian camel for radio collaring. This method is similar to that traditionally employed by poachers (Blumer et al. 1999; Walzer 2003). However, whereas poachers use a shot gun, veterinary and conservation personnel typically use a CO_2-powered dart gun (Daninject JM, TM Dan-Inject ApS, Børkop, Denmark) often with a short (4-cm) barrel to facilitate mobility in the confines of the chase vehicle (jeep). When using the chase technique personnel must be sensitive to ambient conditions and to limiting chase time to 15 minutes (or less) to prevent hyperthermia. Additionally, when tracking the animal post injection in the rump, caution must be exercised so it is not disturbed until fully immobilized. Animals are then typically approached from the rear.

Walzer and Kaczensky (2005) describe using the chase technique to induce anesthesia in one male and two female camels with etorphine (4.4 mg), butorphanol (10 mg), detomidine (13 mg), and tiletamine-zolazepam (160 mg). Because ambient temperature varied between −15 and −30°C during the day, all drug combinations were supplemented with propylene glycol to prevent freezing. Anesthesia was reversed with naltrexone (200 mg IV), a long-acting opioid antagonist, and atipamezole (25 mg IV).

During subsequent expeditions, 10 additional camels were immobilized using the method described above. In nine of 10 camels, anesthesia and subsequent recovery was uneventful, but one animal, an old bull (>15 years), died during capture. While the cause is unknown, the animal was extremely bloated and appeared to have regurgitated when located approximately 40 minutes post injection (Walzer et al. 2008).

Based on these experiences, the author (Walzer) currently recommends a combination of etorphine (4.4 mg IM), butorphanol (10 mg IM), and detomidine (15 mg IM) for the immobilization of wild adult camels. Butorphanol is used in this combination to a potentially alleviate the marked respiratory depression induced by the etorphine at the μ receptor while potentiating sedation at the κ and σ opioid receptors. This combination can be varied as necessary for the circumstance. For example, the addition of tiletamine-zolazepam provides a more rapid transition to sternal recumbency. Alternatively, by decreasing the etorphine dose by 1 mg and omitting tiletamine and zolazepam, the animal appears sedated but often remains standing or in sternal recumbency. This can be helpful when locating the animal in the steppe landscape, but can also lead to prolonged pacing phase in which the animal can cover a greater distance and potentially injure itself.

While not specific to anesthesia management, a unique drug that has received some consideration for handling and transportation of camels is reserpine, an indole alkaloid that irreversibly blocks uptake of norepinephrine and dopamine (Al-Ani 2004). Its availability in many developed nations, however, is limited, due to significant side effects (Figs 50.2 to 50.6).

Anesthetic Techniques for a Hospital Environment

Anesthetic Induction and Short-term Maintenance

The hospital setting provides a more controlled environment and allows one to better titrate drugs to achieve sedation, short-term anesthesia, or to transition a patient to inhalation anesthesia. The placement of an intravenous catheter facilitates this titration of the drugs to a given endpoint for an individual patient.



Figure 50.2 Pursuing a herd of wild Bactrian camels in the Great Gobi A Strictly Protected Area in Mongolia in order to place a dart. Photo courtesy of Petra Kaczensky.



Figure 50.3 Applying a dart to the hindquarters of a wild Bactrian camel from a jeep in the Great Gobi A Strictly Protected Area. Photo courtesy of Petra Kaczensky.

Most induction combinations include either ketamine (2–5 mg/kg titrated to effect) or propofol (2 mg/kg titrated to effect) in conjunction with a centrally acting muscle relaxant, such as guaifenesin (25–75 mg/kg), diazepam, or midazolam (0.02–0.1 mg/kg). Use of chloral hydrate alone or with magnesium sulfate has also been described for induction and short-term anesthesia maintenance in camels (Ali 1988). Alpha-2 agonists, such as xylazine and medetomidine, may also be used, especially in larger and more unruly animals. These may be administered IM to facilitate catheterization or IV prior to ketamine or propofol. Keep in mind that the dose for xylazine in camelids is in between that reported for cattle (0.03–0.1 mg/kg) and horses (0.3–1.0 mg/kg).

Ketamine combinations have been routinely used for anesthetic induction in camelids. Typically, animals become recumbent about 45 seconds following IV



Figure 50.4 Applying a supplemental anesthetic dose to an immobile but not approachable wild Bactrian camel in the Great Gobi A Strictly Protected Area in Mongolia. Photo courtesy of Petra Kaczensky.



Figure 50.5 Team working in subzero conditions collecting biological samples and placing a satellite radio collar on a wild Bactrian camel. Photo courtesy of Petra Kaczensky.



Figure 50.6 A satellite radio-collared, wild Bactrian camel, shakily rising to its feet some 30 seconds after anesthesia reversal with intravenous naltrexone and atipamezole. Photo courtesy of Chris Walzer.

administration, and intubation conditions are good in most circumstances if one is fairly efficient. Additional drugs may be safely administered if the patient maintains pharyngeal tone or is swallowing. A retrospective study has described successful anesthesia maintenance in dromedary camels for a variety of surgical procedures with repeated doses of xylazine and ketamine (Al-Mubarak et al. 2008).

While propofol combinations are not used as frequently, studies do report its safety and efficacy in camelids. For example, propofol was used in camels premedicated with xylazine and diazepam to induce and maintain short-term anesthesia (Fahmy et al. 1995). The same dose has also been used for induction in llamas (Duke et al. 1997). Alfaxalone, a newer injectable anesthetic agent, was assessed for use in alpacas and while anesthesia induction to intubation was readily accomplished with a dose of 2.1 mg/kg, recovery quality with its sole use was not favorable (del Alamo et al. 2015).

Inhalation anesthetic induction has been successfully used in llamas and alpacas on occasions where intravenous catheterization prior to anesthetic induction has proved challenging. While regurgitation and aspiration concerns are valid, fasted animals are less likely to manifest these complications. However, this process can be quite time consuming; anesthetic induction was reported to take an average of 17–19 minutes from time of first isoflurane breath to orotracheal intubation in unpremedicated healthy adult llamas (Mama et al. 1999, 2001). This time may be significantly reduced in debilitated patients and in those receiving premedication.

Anesthetic Maintenance

When available, inhalation anesthetic techniques are used to maintain anesthesia in patients undergoing highly invasive surgical procedures (e.g., celiotomy and fracture repair). Halothane, isoflurane, sevoflurane, and desflurane have all been used been used to maintain anesthesia in camelids, but studies are limited. One report provides the minimum alveolar concentration (MAC) of isoflurane in llamas as $1.05 \pm 0.17\%$ (Mama et al. 1999), whereas another provides the same information for sevoflurane in both llamas ($2.29 \pm 0.14\%$) and alpacas ($2.33 \pm 0.09\%$) (Grubb et al. 2003). Desflurane MAC (7.99 ± 0.58 in llamas and $7.84 \pm 0.51\%$ in alpacas) has also been reported (Grubb et al. 2006). These values are similar to those reported in other species and one presumes that adult camels would be similar. A small animal anesthetic machine and breathing circuit is appropriate for llamas and alpacas, whereas a large animal breathing circuit is necessary for adult camels.

Cardiopulmonary and behavioral responses are described with inhalation agents in anesthetized camelids. In adult llamas, a decrease in mean arterial blood pressure and an increase in heart rate were observed with increasing isoflurane dose during both spontaneous and controlled ventilation. Cardiac output and $PaCO_2$ were higher during spontaneous ventilation than during controlled ventilation (Mama et al. 2001). The broadest base of experience in camels is with halothane. Following anesthetic induction with injectable agents, anesthesia has been successfully maintained with halothane vaporizer settings between 1% and 3% (Singh et al. 1994; White et al. 1986). Blood pressure is reported to be in the same range as for other domestic species, but with a tendency toward higher values, much like those observed in cattle. Rapid shallow breaths and rising $PaCO_2$ values are also described. During inhalation-induced recumbency, spontaneous behaviors (e.g., swallowing and limb movement) decreased with increasing anesthetic depth. Jaw tone and palpebral reflex activity also decreased as isoflurane dose increased. Recovery from anesthesia was also reported to be uneventful (Mama et al. 1999, 2001; Singh et al. 1994; White et al. 1986).

Inhalation anesthetics are the mainstay for anesthetic maintenance, but the need for specialized delivery equipment generally limits the use of this technique to the hospital environment. While expensive, the advent of short-acting, rapidly cleared IV drugs, such as propofol, provides veterinarians with the option of maintaining general anesthesia using continuous infusions. Two intravenous infusion doses of propofol (0.2 and 0.4 mg/kg/min) used for anesthetic maintenance in llamas have been assessed after a 2 mg/kg induction dose (Duke et al. 1997). The infusions were maintained for 60 minutes, during which time llamas receiving the higher dose appeared adequately anesthetized and generally unresponsive to external stimuli, whereas llamas receiving the lower dose were

noise sensitive and made some weak attempts to raise their head. Animals stood an average of 13–22 minutes following termination of the low and high dose infusion, respectively, and showed little to no ataxia.

During anesthetic maintenance with both infusions of propofol the heart rate was increased (to approximately 90 bpm) over predrug values (of approximately 55 bpm). Mean carotid arterial pressure was similar to predrug values and ranged from an average of 103 to 147 mmHg during drug-induced recumbency. The $PaCO_2$ increased and PaO_2 decreased in recumbent animals but were felt to be within a clinically acceptable range. Three llamas did, however, become dyspneic and required placement of a nasopharyngeal tube to ensure a patent airway.

Combinations of inhalation agents and injectable drugs may also be of benefit in managing general anesthesia. In one study, authors describe a mean reduction in isoflurane dose requirement of 37% when receiving 40 mg/kg/min of ketamine by IV infusion (Schlipf et al. 2005). Another report describes a small but not statistically significant decrease in bispectral index values following 0.1 mg/kg IV of butorphanol in isoflurane-anesthetized alpacas, indicating a potential benefit (Garcia-Pereira et al. 2007). Except for a decrease in systemic vascular resistance, cardiovascular parameters were largely unchanged after butorphanol; as animals were ventilated, effects on respiration could not be assessed. Larenza et al. (2008) described the successful use of a more complex protocol using fentanyl s-ketamine, midazolam, and isoflurane in an alpaca with increased anesthetic risk. Respiratory function was, however, negatively affected.

Muscle Relaxation during General Anesthesia

When muscle relaxation provided by the anesthetic agents alone is not adequate (e.g., intraocular surgery and reduction/repair of a displaced long bone fracture), drugs that block the neuromuscular junction (peripherally acting muscle relaxants) are used as adjuncts during general anesthesia. The efficacy of atracurium, administered via intermittent IV bolus (0.15 mg/kg initial dose, followed by 0.08 mg/kg) or IV infusion (0.15 mg/kg initial dose, followed by 0.4 mg/kg/h), has been evaluated in halothane anesthetized, mechanically ventilated llamas (Hildebrand & Hill 1993). More recently the successful use of rocuronium was described for ophthalmological surgery in an alpaca (Yamaoka & Auckburally 2015). Another report suggests that both succinylcholine and gallamine may be used successfully to supplement relaxation during general anesthesia in camels (Held & Paddleford 1982). While these agents can be very useful in facilitating other interventions, it is essential to be aware that they provide no analgesic or sedative properties, and that ventilation will be significantly depressed and must be supported.

Anesthetic Recovery

Although the occasional patient may have a violent recovery, in general, camelids recover well from anesthesia. When possible, it is ideal to place the camelid in a sternal posture with the head elevated. This both allows for eructation and helps minimize any nasal edema. Oxygen insufflation during this period is also beneficial. If the patient is orotracheally intubated, the endotracheal tube should be protected so it does not get lacerated by the molars. In the alpaca and llama this is relatively easy to do with a partially used 2-inch roll of tape, which can be placed over the tube in the mouth with a tab hanging out. It is important not to remove the endotracheal tube until one is sure that the patient can control their airway. Camelids frequently show early arousal and chew their tube and raise their head briefly and then seemingly "fall asleep" again. Removal of the tube in this early period therefore can result in airway obstruction. Often, this is silent and only evident when observing the chest move inward (as opposed to outward) during inspiration. Intervention is critical and may be as simple as extending the head, trying to get the patient to swallow, and providing oxygen; in extreme cases, reintubation is necessary.

Analgesic Techniques

While efficacy of local and regional anesthetic techniques is reported in camelids (Barrington et al. 1993; Grubb et al. 1993), there is very little published regarding benefits or side effects of systemically administered analgesics in these animals. Hence, much of the use is based on personal preference and extrapolation from other species. Evaluation is further confounded by difficulty in assessing clinical signs of and hence resolution of pain. While no animal should suffer because of pain, one should continue to obtain evidence for the efficacy of analgesic drugs to ensure appropriate therapy for the patient.

Nonsteroidal anti-inflammatory drugs and opioids have been used and studied to a limited extent in South American camelids (llamas). The pharmacokinetics of ketoprofen, phenylbutazone, and flunixin meglumine are described in llamas (Navarre et al. 2001a–c). However, as the authors state, the determination of serum or plasma concentrations associated with analgesia are only extrapolated from other species; serum concentrations between 0.4 and 0.6 μg/mL of ketoprofen are considered effective in humans, and a target of 5–15 μg/mL is suggested for phenylbutazone in horses. As plasma or serum concentrations may not truly represent therapeutic effects at the site of the lesion within the tissue, relating kinetic data to clinical

efficacy is further confounded. However, these drugs continue to be used in camelids with apparent clinical success.

Use of the opioids in the clinical environment is perhaps more controversial. While potent opioids have been used to provide immobilization, information on the use of these drugs as analgesics is limited. There is one report suggesting use of intramuscular butorphanol (0.1 mg/kg) is of some benefit in animals experiencing somatic pain; the short half-life following intravenous butorphanol was thought to limit its clinical usefulness (Carroll et al. 2001). Mixed results were described by authors assessing analgesia produced by morphine in healthy llamas. A dose of 0.25 mg/kg IV produced the most consistent increase in tolerance to a cutaneous electrical stimulus in this report (Uhrig et al. 2007). While studies such as these may not represent the true clinical condition, the variability in response when compared with the effects of these drugs in studies conducted in other species (e.g., dog) suggest the need for further evaluation.

Other analgesic drug classes have not been commonly used, but some clinicians describe the successful use of oral gabapentin to treat presumed neuropathic pain in a Bactrian camel.

Monitoring during Anesthetic-induced Recumbency

Monitoring anesthetic depth in camelids can be challenging as they maintain ocular reflexes at seemingly all planes of anesthesia. In addition to a brisk palpebral, the globe also tends to rotate periodically during anesthesia and to the inexperienced individual this is quite disconcerting, but seems to bear little correlation with movement in response to a noxious stimulus. Eyelid aperture (or the distance between eyelids) has been correlated and widens with increasing inhalant anesthetic depth in llamas (Mama et al. 2001). Jaw tone is another useful method for monitoring anesthetic depth in the smaller camelids. Assessment of prepucial and rectal tone, drooping of the lower lip, relaxation of neck, and abdominal and tail musculature have been advocated by some as another means to assess depth of anesthesia and muscle relaxation (Alsobayil & Mama 1999).

Guidelines for monitoring physiologic responses during drug-induced recumbency are much the same as for any other species. The degree of monitoring should be appropriate for the patient's health status and with regard to the procedure; monitoring a young animal undergoing a castration will differ significantly from a patient needing abdominal exploratory surgery.

Monitoring for short-term chemical restraint in a field situation may include auscultation of the heart and lungs, palpation of the pulse, and evaluation of mucous membrane color and refill time. Changes in muscle tone or gross movement are commonly used to assess anesthetic depth. For longer procedures or those in which the animal may be at more risk, noninvasive battery-powered monitors, such as a pulse oximeter and Doppler or oscillometric blood pressure monitor, may easily be placed. The reader should be aware, however, that oscillometric blood pressure has not been shown to be reliably corelated with direct blood pressure (Aarnes et al. 2012). A rectal thermometer is used to monitor body temperature if deemed necessary. While it is recommended that record notations be made at 5-minute intervals, it is ideal to observe the patient continuously.

In a referral hospital setting, monitoring is generally more extensive as patients are often significantly compromised. Typically, in addition to pulse palpation and observation of mucous membranes, the cardiovascular system is evaluated using an electrocardiogram (ECG) to assess heart rate and rhythm, and an arterial catheter is placed for direct (invasive) blood pressure monitoring. ECG leads function best when clips are placed in areas with less fiber (axilla and flank or upper lip/base of the ear). Depending on the procedure, leads should be placed on either side of the heart or cranial and caudal to the heart. Arterial catheters (20- or 22-gauge, 3–5 cm) are commonly placed in the auricular or medial saphenous artery, but the carpal, cranial tibial, or middle coccygeal artery may also be used in camels. Heart rate ranges from 60 to 120 bpm in llamas and alpacas during inhalation anesthesia but may be significantly lower if alpha-2 agonists are used. In camels, heart rate is more typically 40–50 bpm, but bradycardia and second-degree AV block may be observed with use of alpha-2 agonists (White et al. 1987). Blood pressure in llamas and alpacas seems to be quite labile and may vary from a mean pressure of 50–60 mmHg to 100 mmHg for seemingly no apparent reason. Despite this, studies have shown that there is a trend and blood pressure decreases with increasing inhalation anesthetic depth, as has been shown for other species (Mama et al. 2001).

A thermistor probe is placed nasally or rectally for evaluation of body temperature and either a pulse oximeter (SpO_2) and capnograph or arterial blood gases ($PaCO_2$, PaO_2) are used to evaluate pulmonary function. Values are similar to those observed in other domestic species or in the range of 95–100% for SpO_2 and 40–50 mmHg for end-tidal and $PaCO_2$. PaO_2 values are influenced by the inspired oxygen and may range from 80 to 100 mmHg at sea level for a patient breathing room air to 500 mmHg for a patient breathing 100% oxygen. Keep in mind that altitude will significantly decrease these values.



Figure 50.7 Placement of an arterial catheter in the medial saphenous artery. Photo courtesy of Gary West.

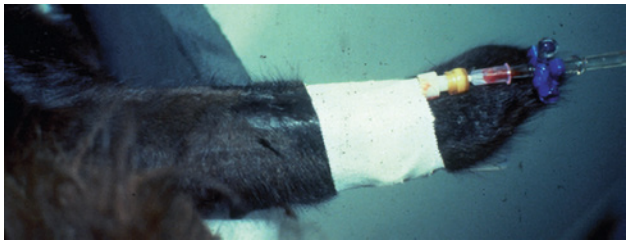


Figure 50.8 Placement of an arterial catheter in the auricular artery of a llama.

For critically ill patients, glucose, electrolyte, and acid–base monitoring, and measurement of packed cell volume and total protein can add useful information. Note that unlike most other species, apparently healthy llamas and alpacas frequently have a packed cell volume ranging upwards from the mid-20s.

Monitoring abdominal distention and for the presence (and volume) or absence of regurgitation, and for degree of nasal edema during drug-induced recumbency is also important as these factors may indicate the need for intervention to ensure a favorable outcome (Figs 50.7 and 50.8).

Support during Anesthetic-induced Recumbency

As with monitoring, supportive care should also be related to the patient's needs, with some exceptions. For example, the eye should always be protected and lubricated in camelids as they tend to protrude from the head and are easily traumatized. Attention should always be given to patient positioning so as not to cause neural or muscle damage; lower forelimb pulled forward in lateral recumbency and upper limbs supported in a natural position (not hanging). In dorsal recumbency, the limbs should be flexed. For longer procedures or larger patients, padding becomes increasingly important. Air or foam mattresses and water beds have all been utilized successfully.

In cool environments or in young and small patients, external heat should be provided, whereas active cooling may be necessary in warm environments. Circulating air or water blankets or radiant heat lamps may be used for warmth, whereas providing shade or using a fan or simply hosing the patient with water will help keep the patient cool.

A balanced electrolyte solution should be administered intravenously to patients undergoing inhalation anesthesia or those in whom recumbency is expected to last more than 1 hour. An administration rate of 5 mL/kg/h is suggested for most patients. Dehydrated patients should receive a fluid volume appropriate for the perceived level (e.g., 5% of a 100-kg animal is equivalent to 5 L). If heart rate or blood pressure values fall out of the normal range, additional intervention may be necessary. This may include anticholinergics, such as atropine, and inotropes/vasopressors, such as ephedrine, dobutamine, or phenylephrine. A recent study describes the use of both dobutamine (4 and 8 mg/kg/min) and norepinephrine (0.3 and 1 mg/kg/min) in isoflurane-anesthetized alpacas. Both drugs increased cardiac output and appeared safe and effective at the lower dose studied for each drug. At higher doses, increased arrhythmogenicity was observed for dobutamine, and excessive vasoconstriction was a noted side effect for norepinephrine (Vincent et al. 2009).

In critically ill patients, electrolytes may need to be adjusted and acid–base balance corrected. In very young patients, glucose supplementation may be necessary. Methods for calculating and adjusting these values are available.

While oxygen is routinely used in patients during inhalation anesthesia, this is less common when using injectable techniques. Since llamas and alpacas have been shown to become hypoxic during injectable anesthetics, oxygen supplementation is highly recommended, especially for patients at altitude. Camels are also prone to hypoxemia due to their body mass, and oxygen supplementation should always be considered during recumbency. The availability of lightweight aluminum tanks and flow meters has made this easier to achieve in field conditions. The flow meter is connected to a small flexible hose placed in the ventromedial nasal meatus up to the medial canthus of the eye. An ambu bag should be available in case of a need to ventilate a patient in the field. For a patient connected to a breathing circuit, manual or mechanical ventilation is easily accomplished.

While uncommon in llamas and alpacas, recumbent camels may bloat, and placement of a "bloat" tube may be necessary to help relieve this and minimize the influence on venous return and pulmonary function. Because these animals are obligate nasal breathers, nasal edema

can be problematic following extubation. When possible, the head should be positioned to allow drainage of regurgitant fluid while still minimizing edema. Alternatively, vasoconstrictors, such as phenylephrine, may be diluted and gently placed in the nasal passages prior to extubation. If food material is observed from the nose, gentle lavage (after ensuring the endotracheal tube cuff is sealed) is recommended.

Summary

The chances of a favorable outcome are increased with an understanding of basic physiological differences between camelids and other species, and the selection of appropriate drug, monitoring, and supportive techniques (Tables 50.1 and 50.2).

Table 50.1 Drug protocols for sedation and anesthesia in domesticated healthy adult camelids.[a]

Drug or Drug Combination	Dose (mg/kg) and Route of Administration	Approximate Onset of Action and Anticipated End Point	Approximate Duration of Anesthetic Action	Anticipated Recovery for Drugs Resulting in General Anesthesia
Sedation				
Acepromazine	0.05–0.1 IM	5–15 minutes, tranquilization	1–4 hours	N/A
Xylazine	0.25 IM	15 minutes, sedation	1–4 hours	N/A
	0.1–0.2 IV	5 minutes, sedation	1–4 hours	N/A
Anesthesia				
Xylazine	0.1–0.2 IM	5–10 minutes, recumbency	10–20 minutes	45 minutes to2 hours
Ketamine	2–3 IM			
Xylazine	0.03–0.05 IM	5–10 minutes, recumbency	10–20 minutes	20 minutes to 1 hour
Butorphanol	0.3–0.5 IM			
Ketamine	2–4 IM			
Xylazine	0.1–0.2 IM	45 seconds after guaifenesin and ketamine, recumbency	10–20 minutes	45 minutes to 2 hours
Guaifenesin	50–100 IV			
Ketamine	1–2 IV			
Xylazine	0.1–0.2 IM	45 seconds after diazepam and ketamine, recumbency	10–20 minutes	45 minutes to 2 hours
Diazepam	0.1–0.25 IV			
Ketamine	1–2 IV			
Xylazine	0.1–0.25 IV	1 minute after propofol, recumbency	10–20 minutes	45 minutes to 2 hours
Diazepam	0.25 IV			
Propofol	2 IV			
Maintenance				
Halothane	Vaporizer set between 0.8% and 1.5%	Administered to effect	Administered to effect	30–90 minutes following discontinuation
Isoflurane	Vaporizer set between 1% and 2%	Administered to effect	Administered to effect	20–60 minutes following discontinuation
Sevoflurane	Vaporizer set between 2% and 3%	Administered to effect	Administered to effect	20–60 minutes following discontinuation

IM, intramuscular; IV, intravenous; N/A, not available.
[a] Dosages are approximate and may need adjustment for the individual patient and scenario.

Table 50.2 Drug protocols for sedation and anesthesia in domesticated neonatal camelids.[a]

Drug or Drug Combination	Dose (mg/kg) and Route of Administration	Approximate Onset of Action and Anticipated End Point	Approximate Duration of Anesthetic Action	Anticipated Recovery for Drugs Resulting in General Anesthesia
Sedation				
Butorphanol	0.05–0.1 IV	30 seconds–1 minute	10–20 minutes	N/A
Diazepam	0.05–0.2 IV	30 seconds–1 minute	10–20 minutes	N/A
Anesthesia				
Isoflurane	1–3% by mask, to recumbency	Variable but within 5 minutes	While being administered	15–30 minutes after discontinuation
Sevoflurane	2–4% by mask, to recumbency	Variable but within 5 minutes	While being administered	15–30 minutes after discontinuation
Diazepam	0.05–0.1 IV	30–45 seconds after	10–20 minutes	30 minutes
Ketamine	1–2 IV	administration		
Diazepam	0.05–0.1 IV	30–45 seconds after	5–15 minutes	20–30 minutes
Propofol	1–2 IV	administration		

IM, intramuscular; IV, intravenous; N/A, not available.
[a] Dosages are approximate and may need adjustment for the individual patient and scenario.

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Giraffidae

Scott B. Citino and Mitchell Bush

Taxonomy and Biology

Giraffids were once very diverse and widespread throughout Africa, Asia, and Europe. Presently, only two genera with one species per genera are extant within the family *Giraffidae*, the giraffe, *Giraffa camelopardalis*, and the okapi, *Okapia johnstoni*. Historically, nine subspecies of giraffe have been described based on body size, color, coat pattern, and geographic distribution (Dagg & Foster 1976; Nowak & Paradiso 1983). Recent mitochondrial DNA and nuclear microsatellite analysis show that there are at least six genealogically distinct lineages of giraffe with little evidence of interbreeding between them, and five of the six lineages also contain genetically discrete populations, yielding at least 11 genetically distinct populations (Brown et al. 2007). Shared characteristics of giraffids include long legs with forelegs longer than rear legs, elongated necks, large eyes and ears, long, dark, prehensile tongues, lack of a gallbladder in most animals, thick skin with coat patterns that provide camouflage, and the presence of skin-covered ossicones that arise over the parietal bones in the giraffe and the frontal bones in okapi (Bush 2003; Dagg & Foster 1976; Nowak & Paradiso 1983). Giraffids are browsing ruminants that are highly selective feeders. Their stature allows them to exploit feeding niches unavailable to other terrestrial herbivores. Giraffes dwell primarily in *Acacia*-, *Commiphora*- and *Terminalia*-dominated savannahs and semi-arid, open woodlands, while the okapi lives in the mid-elevation, equatorial hardwood forests of northeast Democratic Republic of the Congo (Dagg & Foster 1976; Nowak & Paradiso 1983). Okapi live relatively secretive, solitary lives while giraffes are more social, living in loosely organized female herds and subadult male bachelor groupings with solitary adult males.

Anatomy and Physiology Related to Anesthesia

The art and science of giraffe anesthesia remains a challenge due to their unique anatomy and physiology, which present inherent risks during chemical restraint and, consequently, can result in unacceptable morbidity or mortality. Their large size and cumbersome shape limits physical control during critical times of induction and recovery, and limits manipulation once the giraffe is down. Adult giraffes range from 4.5 to 5.5 m tall and can weigh from 500 to 1950 kg, with males being larger (Bush 2003; Dagg & Foster 1976; Nowak & Paradiso 1983). Even weighing giraffes during anesthetic procedures can be difficult due to their size and shape. Formulas have been published to estimate weight from body measurements (Hall-Martin 1977). Adult okapi range in weight from 240 to 350 kg and have shoulder heights of 1.5–1.8 m, with females being larger (S. Citino, pers. obs. and unpubl. data, 2011; Nowak & Paradiso 1983). Giraffes have a characteristic long neck, which, if not controlled, acts as a lever arm during inductions and recoveries, creating a danger to the giraffe and/or the support staff. Malpositioning of the neck can lead to airway obstruction and/or cramping or focal myopathies of neck muscles, which can produce fatalities (Bush et al. 2002; S. Citino, pers. obs. and unpubl. data, 2011). The giraffe's long neck also presents unique problems in regard to regulation of systemic arterial blood pressure, maintenance of cerebral circulation, and generation of respiratory dead space (Bush 1993, 2003; Bush et al. 2002; Hargens 1988; Hargens et al. 1987; Hugh-Jones et al. 1978; Langman 1973; Mitchell & Skinner 1993; Pedley et al. 1996; Warren 1974). To maintain cerebral circulation, giraffes maintain the highest mean arterial pressure at the level of

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the heart of any animal thus far studied (~200 mmHg) (Hargens 1988; Hargens et al. 1987). In dependent areas such as the legs and feet, the mean arterial pressure may exceed 400 mmHg (Hargens 1988; Hargens et al. 1987). To prevent edema and pooling of fluids in dependent areas, giraffe have capillaries that are highly impermeable to plasma proteins, precapillary sphincters, and pronounced arterial and arteriolar wall hypertrophy, a prominent lymphatic system, one-way valves in lymphatics and veins, and tight skin and fascial layers that provide a functional "anti-gravity suit" and pumping mechanism during movement (Hargens 1988; Hargens et al. 1987). Because of the giraffe's unique cardiovascular physiology, the giraffe heart may be more prone to injury from oxygen debt during periods of hypoxemia (Linton et al. 1999). Giraffe are speculated to have a large respiratory dead space generated by their long trachea, which appears to be compensated for by a smaller than expected tracheal diameter, slow deep respirations, and a large tidal volume (Bush 2003; Hugh-Jones et al. 1978; Langman et al. 1982). The long legs of giraffes make them prone to stumbling and splaying during induction and recovery, which can lead to fractures, luxations, muscle and ligament tears, and/or nerve damage. Recumbent giraffes require good footing and sufficient room to be able to rock forward with their long neck to get their long legs underneath them to stand. Giraffes and okapi have elongated skulls (elongated diastema) with narrow interdental spaces, which can make endotracheal intubation challenging, and the posterior position of the larynx impedes drainage of pharyngeal fluids and enhances the potential for aspiration (Bush et al. 2002; Dagg & Foster 1976; Nowak & Paradiso 1983). Giraffes and okapi have a tendency to regurgitate while under the influence of certain chemical restraint agents, which can lead to morbidity and mortality from aspiration pneumonia (Bush 1993, 2003; Bush et al. 2002). The thick skin of giraffids requires the use of long, robust needles to assure good intramuscular injections. Giraffes can alter their body temperature to minimize water loss and help with heat regulation (Bush 2003; Langman et al. 1982). Besides having a tendency toward hyperthermia from overexertion during field capture, giraffes are reported to sometimes suffer from a malignant hyperthermia-like syndrome during anesthesia (Citino et al. 1984). Conversely, if ambient temperatures are low, giraffes and okapi tend to lose body temperature rapidly during anesthesia and can become hypothermic (S. Citino, pers. obs. and unpubl. data, 2011).

The most commonly used vascular access site in giraffids is the jugular vein. Due to thick cervical skin, the jugular vein may not always be visible but can usually be palpated and is generally more accessible closer to the head. Auricular and facial veins are also very accessible during anesthetic procedures. Through-the-needle catheters are more effective for jugular catheterization in these species. If over-the-needle catheters are used for jugular catheterization, a stab incision or partial cut-down is generally required. The auricular artery on the dorsal ridge of the ear is most often used for arterial blood collection and for arterial catheterization for invasive blood pressure measurements. Pulse oximetry transmission sensor placement is generally most effective across a scraped ear or across vulvar, mammary, prepucial, or scrotal skin. End-tidal CO_2 adapters can be attached to an endotracheal tube or to a small tube placed in a nostril. Tail cuffs appear to work best for noninvasive blood pressure measurement (see Fig. 51.1). Lead placement for electrocardiography is best accomplished with needles placed through the thick skin of giraffids.

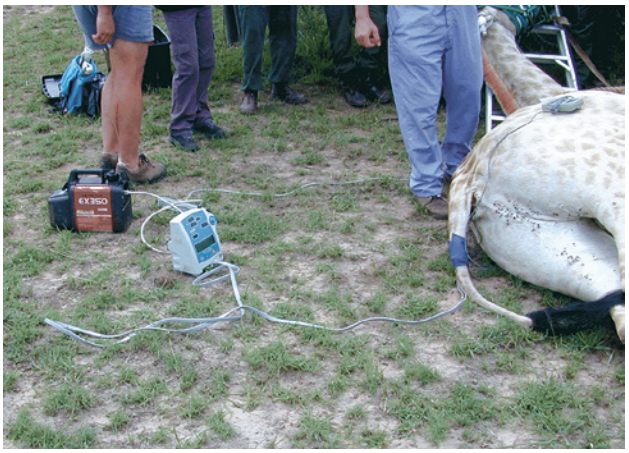


Figure 51.1 Indirect blood pressure monitoring utilizing an oscillometric blood pressure monitor and cuff on the tail of an immobilized giraffe.

Analgesia

The most commonly used drugs for analgesia in giraffids are nonsteroidal anti-inflammatory agents (NSAIDS) (Teare 2000). Flunixin meglumine (1.0–2.0 mg/kg intravenous [IV], intramuscular [IM], or per os [PO], once daily [SID]), phenylbutazone (1.0–3.0 mg/kg PO, SID to twice daily [BID]), and ketoprofen (0.5–2.0 mg/kg IV or IM, SID) have been used most often (S. Citino, pers. obs. and unpubl. data, 2011; Teare 2000). Other NSAIDS used in giraffids include etodolac (2.5–5.0 mg/kg PO, SID to BID), carprofen (2.0 mg/kg, PO SID to BID), and meloxicam (0.10 mg/kg, PO SID) (S. Citino, pers. obs. and unpubl. data, 2011). Gabapentin (2.0–5.0 mg/kg PO, SID), a GABA analogue, has shown promise as an analgesic for neuropathic and orthopedic pain in giraffids (S. Citino, pers. obs. and

unpubl. data, 2011). Low doses of butorphanol may also be effective for some types of pain.

Physical and Mechanical Restraint

Only very young giraffe and okapi calves can be safely restrained manually. Mattresses or flexible padding can be wrapped around older calves, or they can be pushed into a padded corner with push boards to safely restrain them for minor procedures.

Mechanical restraint of giraffes is appropriate for minimally invasive procedures such as blood sampling, tuberculin testing, rectal examinations, and minor hoof trimming, but giraffes can present dangers to handlers and themselves during such procedures. Giraffes have powerful kicks, can strike outward with their forelegs, and can swing and bash with their neck and head. If the ground is slippery, they can fall and injure themselves or ground support staff. Giraffe restraint devices vary from crates and walk-through chutes to small stalls or hallways with moveable walls to innovative mechanical or hydraulic squeeze chutes (Calle & Bormann 1988). All restraint devices should be designed to prevent entrapment of the neck or legs and to allow easy removal of a giraffe that goes down in the device. Successful mechanical restraint of giraffes is dependent on facility design, the training and conditioning of the giraffe, plus a well-trained staff. A well-designed chute, with a side that opens, can also be a valuable giraffe anesthesia induction device that allows close confinement, head control, and controlled progression to sternal recumbency. Mechanical restraint has been infrequently used on okapi; however, okapi have been conditioned to a special crate for venipuncture and other minor procedures (Mehrdadfar et al. 2003). Okapi are excellent kickers and the head and ossicones of males are formidable weapons.

For more extensive or invasive procedures on standing giraffes, such as hoof trims, obstetrics, minor surgeries, percutaneous biopsies, etc., chemically assisted mechanical restraint can sometimes be used. This generally involves the use of an alpha-2 adrenergic agonist alone or alpha-2 adrenergic agonist-azaperone combination given just prior to placing a giraffe into a mechanical restraint device. Xylazine (0.10–0.2 mg/kg IM), detomidine (15–40 μg/kg IM), xylazine-azaperone (0.10–0.12 mg/kg IM to 0.20–0.50 mg/kg IM), and detomidine-azaperone (15–30 μg/kg IM to 0.25–0.35 mg/kg IM) have been most commonly used for this purpose (Bush 2003; Bush et al. 2002; S. Citino, pers. obs. and unpubl. data, 2011). To increase sedation and analgesia, low doses of butorphanol (10–20 mg IV total) can be given to adult giraffes (S. Citino, pers. obs. and unpubl. data, 2011). Giraffes given these drugs in a restraint device can potentially become ataxic and go down, so handlers should always be prepared for this. Xylazine and detomidine can be partially reversed with yohimbine (0.10–0.20 mg/kg IV or IM) or atipamezole (0.10–0.20 mg/kg IV or IM), and butorphanol can be reversed with naltrexone (2.0 mg naltrexone/mg of butorphanol IV or IM) (Bush 2003; Bush et al. 2002; S. Citino, pers. obs. and unpubl. data, 2011). A few sudden deaths have occurred after IV administration of alpha-2 adrenergic and opioid antagonists in giraffes, so these drugs are preferentially given intramuscularly (S. Citino, pers. obs. and unpubl. data, 2011).

Sedation and Tranquilization

Standing sedation for hands-on procedures is rarely attempted in older giraffes outside of a restraint device due to the potential danger these animals pose to handlers. Alpha-2 adrenergic agonists at the suggested doses above can be used for safer manipulations in enclosures and chutes, for getting reluctant dams to allow calves to nurse, and to calm animals in stressful or dangerous situations (Bush 2003; Bush et al. 2002; S. Citino, pers. obs. and unpubl. data, 2011; Fischer et al. 1997). It should always be remembered that giraffes under alpha-2 adrenergic agonist sedation can still kick, strike, and rapidly arouse from sedation and become very dangerous. Azaperone has also been used at 0.20–0.50 mg/kg IM as a short-acting, calming, and stress-reducing agent in giraffes (S. Citino, pers. obs. and unpubl. data, 2011). Intermediate and long-acting neuroleptics that have been used in adult giraffes include haloperidol (male 20–30 mg IM, female 15–20 mg IM), zuclopenthixol acetate (100–300 mg IM), and perphenazine enanthate (100–250 mg IM) (S. Citino, pers. obs. and unpubl. data, 2011; Ebedes & Raath 1995). Haloperidol has its onset in about 15 minutes and its effects last for 15–24 hours, zuclopenthixol acetate has its onset in 1–6 hours and its effects last about 3 days, and perphenazine enanthate has its onset in about 2–3 days and its effects last for 7–10 days (Ebedes & Raath 1995). Giraffes appear sensitive to these neuroleptic agents, with untoward effects such as anorexia and extrapyramidal effects common (S. Citino, pers. obs. and unpubl. data, 2011). Due to a significant potential for disorientation, unsteadiness on their feet, and collapse in their transport container, the use of sedatives and/or neuroleptic agents in giraffes during transport is considered risky and should only be done with great care.

Standing restraint in adult okapi for minor procedures such as venipuncture, physical examination, obstetrics, radiography, ultrasound, catheter placement, etc. has been accomplished with xylazine given at 125–300 mg IM

(0.50–1.20 mg/kg IM) (Citino 1996; Citino et al. 2006; Raphael 1999; Teare 2000). Xylazine can be partially reversed with yohimbine (0.10–0.20 mg/kg IV or IM) or tolazoline (0.50 mg/kg IV or IM) (S. Citino, pers. obs. and unpubl. data, 2011; Citino 1996; Raphael 1999). More complete reversal of xylazine has been achieved with the experimental alpha-2 adrenergic antagonist RX821002 (5.0 mg total dose IV) or combinations of yohimbine or tolazoline and atipamizole (30–100 μg/kg IV or IM) (S. Citino, pers. obs. and unpubl. data,2011; Citino 1996; Raphael 1999; Teare 2000). For okapi that appear resistant to xylazine alone, the addition of azaperone (0.20–0.40 mg/kg IM) may improve the standing restraint (S. Citino, pers. obs. and unpubl. data, 2011). Good standing restraint for venipuncture, catheter placement, vaginal insemination, etc. has also been achieved with xylazine (0.40–0.80 mg/kg IM) or detomidine (40–100 μg/kg IM) with butorphanol (80–200 μg/kg IM) (S. Citino, pers. obs. and unpubl. data, 2011; Teare 2000). Recently, medetomidine (60–90 μg/kg IM) with butorphanol (45–55 μg/kg IM) has successfully been used for standing restraint of okapi at one institution (J. Raines, pers. comm., 2011). Butorphanol has been reversed with naltrexone (1.0 mg/mg butorphanol IV or IM) (S. Citino, pers. obs. and unpubl. data, 2011) and medetomidine has been reversed with atipamezole at five times the medetomidine dose (J. Raines, pers. comm., 2011). Azaperone (0.20–0.50 mg/kg IM) and haloperidol (80–100 μg/kg IM) have been used to tranquilize flighty animals when moved or manipulated in enclosures (S. Citino, pers. obs. and unpubl. data, 2011; Citino 1996; Raphael 1999). Haloperidol (0.90–1.50 mg/kg) has also produced mild calming effects when given orally to okapi (S. Citino, pers. obs. and unpubl. data, 2011). The intermediate-acting neuroleptic zuclopenthixol acetate (0.40–1.0 mg/kg IM) has been used to reduce stress and calm animals during transport (S. Citino, pers. obs. and unpubl. data, 2011; Raphael 1999). A combination of zuclopenthixol acetate (100 mg IM 15 hours before move) and haloperidol (10–20 mg IM to facilitate crating) was used to load and transport two okapi that were not crate trained (Redrobe 2003).

Endotracheal Intubation

A 40–60-cm laryngoscope blade is required to visualize the glottis in adult giraffes, while a 30–40-cm laryngoscope blade will suffice in okapi (S. Citino, pers. obs. and unpubl. data, 2011). Adult giraffes will generally take endotracheal tubes with internal diameters of 24–30 mm, while adult okapi generally take tubes of 20–26 mm (S. Citino, pers. obs. and unpubl. data, 2011). Giraffids are best intubated using the Bush technique: visualizing the glottis with a laryngoscope, passing a tracheal exchange catheter through the glottis, threading the exchange catheter through the Murphy's eye of the endotracheal tube, and passing the tube through the glottis using the exchange catheter as a guide (Bush 1996). In large giraffes, the glottis can be digitally palpated and an endotracheal tube manually placed. Giraffids can also be intubated by passing a fiberoptic endoscope through the endotracheal tube, visually passing the endoscope into the trachea, and then using the endoscope as a stylet to place the tube. The authors recommend using a cuffed endotracheal tube to intubate giraffes that will be anesthetized for longer than 15 minutes. Oxygen can then be supplied by insufflation or jet ventilation and respiratory support can be given with a one- or two-demand valve system or field ventilator (Citino et al. 2007). If giraffids are inadequately anesthetized (tongue movement and swallow reflex present), stimulation of the pharynx during endotracheal intubation can initiate active regurgitation (see Figs 51.2 to 51.4).



Figure 51.2 Endotracheal intubation of an anesthetized giraffe.



Figure 51.3 An intubated giraffe receiving supplemental oxygen and ventilatory support.



Figure 51.4 Staged induction of a captive giraffe in a chute system.

Anesthesia of Giraffes

Even with the development of newer and safer drugs and improved physiological monitoring equipment, giraffe anesthesia remains a major challenge due to their unique anatomy and physiology. Despite the frequent need to capture and relocate this species *in situ*, giraffes are still considered a high-risk species for chemical capture due to their large size and unique physiology and handling problems. Due to their awkward shape, weight estimation and dosage calculation are difficult, especially in the field. All of these special characteristics predispose giraffes to life-threatening, anesthesia-related complications including (1) vomiting/passive regurgitation leading to fatal inhalation pneumonia, (2) respiratory depression and hypoventilation with resulting hypoxemia and hypercarbia, (3) tachycardia, hypertension, bradycardia, hypotension, or other significant cardiac emergencies, (4) self-induced trauma during induction and/or following reversal, and (5) hyperthermia and/or capture myopathy secondary to prolonged and stormy induction and incomplete anesthesia reversal (Bush 1993, 2003; Bush et al. 2002; Citino et al. 1984). The historical high morbidity and mortality encountered during giraffe anesthesia, in both captive and free-ranging settings, leads to a hesitancy to anesthetize them.

Historical verbal and published reports describe the use of several drugs and drug combinations for giraffe anesthesia. Drugs used alone or in combination have included succinylcholine, gallamine, hyoscine, atropine, hyaluronidase, glycerol guaiacolate, acepromazine, azaperone, xylazine, detomidine, medetomidine, ketamine, telazol, barbiturates, butorphanol, fentanyl, etorphine, carfentanil, and thiafentanil (A3080) (Bush et al. 1976, 1993, 2003; Bush & de Vos 1987; Bush et al. 1997, 2001, 2002; S. Citino, pers. obs. and unpubl. data, 2011; Fischer et al. 1997; Geiser et al. 1992; Gardner et al. 1986; Hirst 1966; Lamberski et al. 2004; Langman 1973; Morkel 1992, 1993; Rapley et al. 1975; J.P. Raath, pers. comm., 2006; Vahala 1990; Vogelnest & Ralph 1997; Wiesner & von Hegel 1989; Williamson & Wallach 1968; York 1975; York et al. 1973).

Many of the problems associated with anesthesia can be minimized in captive giraffes with careful preplanning and forethought. Experienced staff to assist with the critical induction and recovery phases of anesthesia and for monitoring the patient is essential. Fasting of giraffids is probably overemphasized and detrimental and should occur for no longer than 12 hours, with concentrate being the primary foodstuff to withhold. Animals should be prevented from drinking large quantities of water just prior to anesthesia by withholding water for 2–6 hours depending on climatic conditions. The site and method of induction are also critical for success. The use of a well-designed chute for giraffe induction can greatly reduce risk and allow a staged and controlled induction to occur (Bush 2003; Calle & Bormann 1988; S. Citino, pers. obs. and unpubl. data, 2011). The chute must be designed so forward pressing or falling will not compromise respiration, with no potential foot, leg, or neck traps, and with a complete side that swings open to allow

giraffe. If a suitable chute is not available a confined space with smooth, solid walls, lack of trip and fall hazards, and a catwalk for access to the animal's head during the procedure can be used. If a catwalk is absent around the induction area and a halter can be placed before or during induction, a ceiling pulley and rope apparatus can be used to suspend the giraffe's head and neck during induction to reduce falling injuries and prevent head slamming. If the giraffe must be induced in a larger area without head control, all tripping and falling hazards should be removed or minimized, and methods for keeping the giraffe away from dangerous pressing points and head and neck traps should be determined. No matter where giraffe anesthesia is accomplished, good footing is mandatory to prevent slipping and splaying. Also, adequate staff and/or equipment should be present to move an animal quickly, if necessary. Since complications can occur rapidly in anesthetized giraffes, close physiologic monitoring is essential for patient safety and should include both the usual visual and tactile monitoring as well as electronic monitoring (i.e., temperature, pulse oximetry, capnography, invasive and noninvasive blood pressure, electrocardiography, and arterial blood gas and pH measurements). Perhaps the hardest thing to do is to back off from a procedure. Many procedures involving giraffes require extensive coordination to make sure that people, facilities, and equipment are ready. Unless conducting an emergency procedure, if something is not going right or if there is a factor that can be changed to enhance the success of the procedure, it should be stopped and rescheduled. Even with the most careful planning and preparation, procedural complications can still occur in captive situations but are amplified in free-ranging giraffes since there is minimal control of the situation.

There are standardized procedures for handling an anesthetized giraffe in lateral recumbency, which include supporting the neck with a board or ladder so the head is maintained above the rumen with the nose pointed down to facilitate drainage of fluids. The neck should be kept straight without kinks or angulations. The angle of the neck is altered every 10–15 minutes and the neck can be massaged to minimize muscle spasms that in the post-recovery period can be life-threatening. Padding should be placed under the giraffe, particularly under the shoulder and radius to prevent pressure trauma to the radial nerve. Oxygen should be supplied by either nasal insufflation or endotracheal tube.

Recovery is a critical time in a giraffe anesthetic procedure. Good footing is essential during recovery, as is adequate space for the giraffe to rock forward and get momentum to stand. If the giraffe does not regain its feet within 45 minutes of administration of the antagonist, the prognosis is poor for the animal's recovery. The route of administration of the antagonist can greatly influence recovery. Intramuscular administration of the antagonists will generally provide a slow, controlled recovery, which is generally preferred (Bush 2003; Bush et al. 2002; S. Citino, pers. obs. and unpubl. data, 2011; Lamberski et al. 2004). Often with IV administration of antagonists, the giraffe will become excited, head slam and try to stand before ready, and will fall, potentially injuring itself.

The most widely used anesthetic regimens for giraffes have involved use of opioids alone or in combination with sedatives (e.g., xylazine), tranquilizers (e.g., azaparone), and/or absorption accelerants (e.g., hyaluronidase) and, most recently, the potent specific alpha-2 adrenergic agonist medetomidine with ketamine (Bush 1976; Bush 1993, 2003; Bush & de Vos 1987; Bush et al. 1997, 2001, 2002; Geiser et al. 1992; Hirst 1966; Lamberski et al. 2004; Langman 1973; Morkel 1992, 1993; Rapley et al. 1975; Vahala 1990; Vogelnest & Ralph 1997; Weisner & von Hegel 1989; Williamson & Wallach 1968; York 1975; York et al. 1973).

A staged protocol using etorphine and xylazine has been used commonly in the past for anesthesia of captive giraffes (Bush 1976, 1993, 2003; Bush et al. 2002). This approach tends to cause less respiratory depression since etorphine doses can be titrated to the needs of the individual animal and situation. This protocol is ideally carried out in a chute or confined area where head control can be maintained. Initially, giraffes are given xylazine (70–100 mg/adult or 30–40 mg/yearling IM). Atropine (7.0–8.0 mg/adult or 2.0–3.0 mg/yearling IM) can be given simultaneously to prevent xylazine-induced bradycardia. Five to 10 minutes after xylazine administration, signs of sedation occur (i.e., stargazing, ataxia, and tongue protrusion with slight salivation). About 15–20 minutes after the xylazine, a narcotizing dose of etorphine (1.5–2.5 mg/adult or 0.5–1.25 mg/yearling IM) is administered. This dose may induce recumbency within 15–20 minutes. Ideally a head halter, placed when the animal is narcotized, is used to help control the head and assist the animal to the ground, without tumbling over backwards. If the giraffe does not become recumbent after etorphine administration, it can be supplemented with etorphine (0.5–1.0 mg IM or IV), 5% guaifenesin solution IV to effect, or ketamine (100–400 mg IV) or can be physically cast. For reversal of etorphine, naltrexone (50–100 mg/mg etorphine, half IV, half IM or all IM) is given and for xylazine, yohimbine (0.10–0.20 mg/kg IV or IM) or atipamezole (50–100 mg total half IV, half IM or all IM) is given. It is possible to substitute carfentanil (1.2–2.1 mg/adult or 0.30–0.90 mg/yearling IM) for etorphine in this protocol (S. Citino, pers. obs. and unpubl. data, 2011) (Figs 51.4 to 51.7).

Current methods for capture of free-ranging giraffes utilize high doses of opioids alone for rapid induction and no lingering drug effects during transport. Etorphine (8.0–15.0 mg/



Figure 51.5 Staged induction of a captive giraffe. Note that the whole side of the chute opens, allowing the giraffe to be positioned in lateral recumbency.



Figure 51.6 Chute system for a captive giraffe. Note padding, attached deck for handlers to access the head, and one side swings open for access to the animal during induction.

adult), thiafentanil (8.0–16.0 mg/adult), or a combination of etorphine (4.0 mg/adult) and thiafentanil (8.0–16.0 mg/adult) with or without hyaluronidase are most commonly used (S. Citino, pers. obs. and unpubl. data, 2011; Morkel 1992, 1993). Giraffes become narcotized rapidly, but many must be cast with ropes. Once down, muscle relaxation is poor, animals require significant restraint, and most must be fully or partially reversed with diprenorphine or naltrexone to prevent severe hypoxemia while hoods, ear plugs, and ropes are applied. This anesthetic technique greatly limits what can safely be done to a giraffe while it is recumbent. Once reversed, giraffes are very active and can be a danger to themselves and the ground crew during loading for transport. This method is for capture only and requires a well-trained and experienced capture team to safely cast, restrain, and load the giraffe for transport (see Figs 51.8 and 51.9). Most recently, a combination of thiafentanil and



Figure 51.7 Chute system for handling a captive giraffe. Note that the animals walk through the chute daily to access the outside yard.

butorphanol has been used for capture of free-ranging giraffes, with less respiratory depression, probably due to the partial μ opioid receptor antagonist effect of butorphanol (J.P. Raath & L. Venter, pers. comm., 2006).

A non-narcotic alternative for giraffe chemical restraint is a combination of medetomidine and ketamine. This combination has been used successfully in captive and free-living giraffes with dosages correlated to the giraffe's shoulder height. In "calm" animals 150 μg of medetomidine and 3.0 mg of ketamine per centimeter of shoulder height provided a rapid and relatively uneventful induction (Bush 2003; Bush et al. 1997, 2001). Larger giraffes experienced a less desirable immobilization, which may indicate the dosage correlation to shoulder height may not be appropriate in larger animals. Another retrospective study in 30 captive giraffes recommends doses of medetomidine (subadult 18–20 mg, adult female 40–50 mg, adult male 50–70 mg) and ketamine (subadult 300–500 mg, adult female 800–900 mg, adult male 1000–1200 mg) (Lamberski et al. 2004). A nice characteristic of this combination is smooth inductions, with animals usually sitting down in sternal recumbency before rolling over laterally. With medetomidine-ketamine, an inverse relationship is observed between the level of excitement and the quality of the immobilization: the more excited the giraffe prior to and after darting, the more physical restraint is required to bring the animal to a sternal position. This combination



Figure 51.8 Free-ranging giraffe in Kruger National Park, South Africa shortly after reversal of thiafentanil anesthesia. Notice blindfold, halter, lead rope, body ropes, and capture crew in place for loading the giraffe into the field chariot for transport out of the veldt. Notice the potential for hindlimb splaying despite good footing in the field and the requirement for the giraffe to rock forward to stand.



Figure 51.9 Free-ranging giraffe starting to stand after reversal of thiafentanil-medetomidine-ketamine anesthesia. Notice blindfold, earplugs, halter, and ropes in place for loading the giraffe into the chariot in the background. Notice the potential for hindlimb splaying despite good footing in the field.

also produces a characteristic tachypnea (50–60 breaths per minute) and inadequate analgesia for painful procedures. Administration of atipamezole (350 μg/cm of shoulder height or five times the medetomidine dose IM) results in a rapid and usually complete reversal. Re-sedation has been seen in some giraffes given medetomidine 3–28 hours after reversal, therefore giraffes should be monitored closely during this time, and additional atipamazole should be administered if signs of re-sedation occur (S. Citino, pers. obs. and unpubl. data, 2011; Lamberski et al. 2004). Re-sedation appears to occur most commonly in the Rothschild's (*G. c. rothschildi*) and Southern giraffe (*G. c. giraffe*) subspecies and less commonly in the reticulated (*G. c. reticulata*) subspecies (S. Citino, pers. obs. and unpubl. data, 2011). Signs of medetomidine re-sedation include decreased awareness to surroundings, dull eyes, inappetance, lowered neck, widened stance, salivation, tongue protrusion, excessive licking, ataxia, leaning against objects, and recumbency (S. Citino, pers. obs. and unpubl. data, 2011; Lamberski et al. 2004).

A newer drug combination, thiafentanil-medetomidine-ketamine, has safely and successfully been used for chemical restraint of captive and free-ranging giraffes (Citino et al. 2006). Dosing requirements are markedly different between captive (thiafentanil 5.8 ± 1.5 μg/kg + medetomidine 12.9 ± 5.1 μg/kg + ketamine 0.65 ± 0.18 mg/kg IM), free-ranging, ground-darted (thiafentanil 6.6 ± 1.5 μg/kg + medetomidine 15.9 ± 3.7 μg/kg + ketamine 0.50 ± 0.19 mg/kg IM), and free-ranging, helicopter-darted (thiafentanil 10.0 ± 4.0 μg/kg + medetomidine 14.0 ± 9.4 μg/kg + ketamine 0.39 ± 0.20 mg/kg IM) giraffes. The degree of excitement associated with helicopter darting appears to negate the effects of medetomidine and makes this combination less suitable for helicopter darting. In calm animals, onset of action is ultra-rapid, with most animals down in 2–5 minutes. Giraffes exhibit excellent muscle relaxation and are very safe to work around with this combination. Analgesia appears very good and there is a long duration of action, so it appears useful for surgical and prolonged major procedures (Borkowski et al. 2009; Quesada et al. 2011). A marked apneustic breathing pattern is often seen and moderate to severe hypoxemia can occur, so oxygen supplementation and/or respiratory support are recommended. Anesthesia is reversed with naltrexone (30 mg/mg thiafentanil IV or IM) and atipamezole (three to five times the medetomidine dose IV or IM). Recoveries are best when antagonists are administered intramuscularly. As with medetomidine-ketamine, evidence of medetomidine-associated re-sedation is seen in some giraffes post reversal, requiring additional supplements of atipamezole (S. Citino, pers. obs. and unpubl. data, 2011). Re-sedation can be a potentially life-threatening problem in giraffes, especially during transport and when giraffes are not observed closely for signs of re-sedation post recovery.

The reader is referred to the references for published methods of giraffe anesthesia and for more detailed descriptions of these procedures.

Okapi Anesthesia

In comparison to giraffes, there are far fewer inherent problems that can occur during okapi anesthesia due to their more conventional size and shape. However,

complications associated with anesthesia are still one of the most significant causes of adult morbidity and mortality in the international captive population (S. Citino, pers. obs. and unpubl. data, 2011; Raphael 1999). The most common anesthesia-associated problems reported in okapi are regurgitation and aspiration of rumen contents and postanesthesia gastrointestinal stasis or ileus (S. Citino, pers. obs. and unpubl. data, 2011).

Chemical immobilization of okapi is most commonly accomplished with an opioid (carfentanil or etorphine) in combination with an alpha-2 adrenergic agonist (xylazine) or tranquilizer (acetylpromazine) (S. Citino, pers. obs. and unpubl. data, 2011; Citino 1996; Mortelmans 1978; Raphael 1999; Teare 2000). Okapi should not be fasted for longer than 12 hours prior to anesthesia as hypoglycemia and electrolyte imbalances can be induced (S. Citino, pers. obs. and unpubl. data, 2011). Water can be withheld for 2–6 hours, depending on climatic conditions. Inductions with opioid combinations can sometimes be stormy, with okapi stumbling, crashing, exhibiting opisthotonus, falling backwards, and flailing and head-slamming once down. It is important to induce okapi in relatively small enclosures with good footing, smooth walls, and lack of trip and fall hazards. Once an okapi is well-narcotized, two to three well-trained handlers should use controlled restraint to smooth the induction and prevent injury. A padded stall with a hinged crush wall also works nicely for preventing injuries during induction. Once down, the animal is placed sternal with its head above its rumen and nose down, blindfolded, and given oxygen by nasal insufflation. If the okapi must be placed in lateral recumbency, adequate padding should be placed under pressure points. As with most ruminants, okapi should not be rolled onto their back unless intubated, as this can stimulate regurgitation of rumen contents. Okapi should be kept warm during anesthesia as they have a tendency to become hypothermic (S. Citino, pers. obs. and unpubl. data, 2011) (Figs 51.10 to 51.12).

Over 170 successful okapi procedures without mortality have been completed using carfentanil and xylazine in a staged technique (S. Citino, pers. obs. and unpubl. data, 2011; Citino 1996). Xylazine (0.12 ± 0.02 mg/kg IM, adult total dose 30–45 mg IM) is given first and is followed in 15–20 minutes with carfentanil (4.7 ± 0.8 µg/kg IM, adult total dose 0.9–1.5 mg IM). This staged technique requires less opioid and produces a much smoother induction, with better muscle relaxation, than combining the opioid and xylazine together. The better the initial sedation from xylazine, the smoother the induction will generally be. Azaperone (50.0 mg average total adult dose) can be added to the xylazine to increase sedation and improve inductions in problem animals. For okapi receiving significant stimuli during anesthesia (e.g., electroejaculation), ketamine (1.0–1.5 mg/kg) can be added to the carfentanil dart to potentiate the xylazine and carfentanil. If supplements are needed to prevent struggling, improve muscle relaxation, or deepen anesthesia, xylazine (2.0–5.0 mg boluses IV), ketamine (50–200 mg boluses IV), and 5% guaifenesin solution IV drips have been used. Naltrexone (100 mg/mg carfentanil half IV, half SQ or IM) is used to reverse the carfentanil, and yohimbine (0.10–0.20 mg/kg IV or IM), tolazoline (100 mg IV or IM total adult dose), RX821002 (5.0 mg IV total adult dose), or atipamezole (0.125 mg/kg IV or IM) is used to reverse the xylazine. Reversals tend to be smoother when all antagonists are given intramuscularly (S. Citino, pers. obs. and unpubl. data, 2011). After reversal, two experienced handlers should stay with the okapi to prevent injury until it is standing. Re-narcotization is occasionally



Figure 51.10 Standing sedation in a captive okapi with xylazine and butorphanol for an echocardiography examination.



Figure 51.11 Anesthesia of an okapi in a field situation. Note there is adequate padding of the okapi in lateral recumbency. Side stream capnography is being used by placing a sampling adapter in the nostril, to estimate end tidal carbon dioxide readings on exhalation.



Figure 51.12 Anesthesia of an okapi in a field situation. Note the pulse oximeter is placed on the tongue and a side stream capnograph sampling adapter is placed in the nostril.

seen in okapi anesthetized with carfentanil, so animals should be observed closely for 24 hours and supplemented with naltrexone if necessary (S. Citino, pers. obs. and unpubl. data, 2011).

Etorphine can also be used in a staged anesthetic technique with xylazine (Citino 1996; Raphael 1999; Teare 2000). As above, xylazine (40–50 mg IM total adult dose) is given first, followed in 15–30 minutes by etorphine (4.0–5.0 mg IM total adult dose). There appears to be a greater risk of regurgitation with etorphine versus carfentanil in okapi (Citino 1996; Raphael 1999; Teare 2000). Etorphine is reversed with naltrexone (30–50 mg/mg etorphine IV) or diprenorphine (2.0 mg/mg etorphine IV).

The non-narcotic combination of medetomidine (60–155 μg/kg IM) and ketamine (1.0–3.9 mg/kg IM) can be used to induce a deep sedation in okapi that is adequate for most minor procedures (Citino 1996; L. Klein, pers. comm., 2011; Raphael 1999; Teare 2000). Deep IM injection (50–60-mm needle) is required with this drug combination and the higher end of the dosage range for medetomidine (100–155 μg/kg) generally produces a better anesthesia without the need for supplementation (L. Klein, pers. comm., 2011). First signs generally occur in 1–7 minutes, and animals are recumbent in 3–34 minutes, with an average of 15–20 minutes. Induction is generally much smoother than with opioid combinations. Adding midazolam (0.1 mg/kg) to this combination seems to speed induction and makes it smoother (L. Klein, pers. comm., 2011). In contrast to opioid combinations, okapi are aware and will still kick or flee during induction with this drug combination, so should not be approached until down and relaxed. Okapi should not be reversed for 15–20 minutes post-induction to reduce unsteadiness from residual ketamine. Some regurgitation can occur if animals are in lateral recumbency with their head and neck flat out, so the head should be kept elevated with nose point down. Medetomidine is reversed by atipamezole (5.0 mg/mg medetomidine IV or IM). There have been reports of post-anesthesia ileus, with some fatalities, in okapi receiving medetomidine and ketamine (S. Citino, pers. obs. and unpubl. data, 2011).

Recently, a combination of medetomidine (60–70 μg/kg IM), butorphanol (50–100 μg/kg IM), and ketamine (2–3 mg/kg IM) has been used for anesthesia of okapi at one institution for minor surgical procedures and hoof trimming (J. Raines, pers. comm., 2011). For longer or more invasive procedures, okapi were intubated and placed on isoflurane inhalation anesthesia.

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52

Deer

Nigel Caulkett and Jon M. Arnemo

Body Weight

Average body weights can be found in Table 52.1.

Physical Restraint

In captive situations deer may be effectively handled in drop-floor or hydraulic squeeze chutes.

It is always best to minimize physical restraint times to decrease the risk of trauma or stress-related complications. Long-acting neuroleptic drugs can be used to decrease the stress of repeat handling (Read et al. 2000). Free-ranging deer may be captured with the use of net guns, drive nets, or clover traps. As above, restraint times should be minimized, and supplemental sedation should be considered during handling (Cattet et al. 2004).

Drug Delivery Method

Vascular Access

Venous access is not difficult in deer. The cephalic vein, lateral saphenous vein and jugular vein can all be easily accessed (Fig. 52.2). The auricular artery can be easily cannulated in most species for direct blood pressure monitoring or to facilitate sampling for arterial blood gas analysis. Arterial blood samples may also be obtained from the femoral artery when auricular arterial catheterization proves to be difficult.

Endotracheal Intubation

Intubation can be difficult in cervids. The best technique is to maintain the animal in sternal recumbency with the head and neck extended upwards. Use a laryngoscope with a long flat blade and stiffen the endotracheal tube with a stylet. The epiglottis is long and mobile in cervids. The flat blade of the laryngoscope should be carefully placed on the dorsum of the epiglottis, depressing it ventrally. The opening to the glottis can then be visualized and intubation can proceed (Fig. 52.3). Animals induced with xylazine and ketamine may swallow or close the glottic opening during intubation. The depth of anesthesia may be increased, to facilitate intubation, with an additional dose of ketamine (1–2 mg/kg) or propofol (2–4 mg/kg) (Woodbury et al. 2005).

Drug Delivery Method

Captive deer can often be restrained in chute systems and drugs may be hand-injected into the muscles of the hindquarters. In well-restrained animals, drugs may be administered intravenously into the jugular vein. Intranasal drug administration has the advantage of a rapid onset time, reliability, and ease of administration. It is a useful technique to produce sedation in wild deer that are captured by physical means (Fig. 52.4). Xylazine administered intranasally at a dose of 1.5–2 mg/kg will produce reliable sedation and stress reduction in American elk (Cattet et al. 2004). Onset is rapid (often less than 1 minute) and the effects can be antagonized with yohimbine. Caribou cows can be effectively sedated for minor procedures and helicopter transport with intranasal medetomidine at a dose of 0.1 mg/kg. This dose is used routinely in British Columbia, Canada for sedation of caribou cows transported to maternal pens, and it is readily reversible with 0.5 mg/kg of atipamezole. Intranasal medetomidine has also been used to induce deep sedation in Svalbard reindeer at a dose of 8 mg (diluted to a volume of 2 mL) (Lian et al. 2019).

Remote drug delivery is typically used in free-ranging deer and the hindquarters are usually the best target. It is important to pay attention to dart needle length as this can

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Table 52.1 Recommended drug combinations for immobilization of deer.

Species	Drug combination	Reversal	Comment	Reference
White-tailed deer (*Odocoileus virginianus*) Body weight 60–150 kg	Butorphanol 0.6 mg/kg Azaperone 0.4 mg/kg Medetomidine 0.2 mg/kg	Naltrexone 1.2 mg/kg Atipamezole 1 mg/kg		Siegal-Willot et al. (2009)
	Medetomidine 0.15 mg/kg Azaperone 0.2 mg/kg Alfaxalone 0.5 mg/kg	Atipamezole at 5 times medetomidine dose	Captive deer	Pon et al. (2016)
	Xylazine 2.2 mg/kg Tiletamine-zolazepam 4.4 mg/kg	Yohimbine 0.1–0.2 mg/kg		Murray et al. (2000)
	Thiafentanil 0.1 mg/kg Xylazine 1 mg/kg	Naltrexone 2 mg/kg Tolazoline 2 mg/kg		Kreeger et al. (2023)
	Medetomidine 0.1 mg/kg Ketamine 2.5 mg/kg	Atipamezole at 5 times medetomidine dose		Caulkett et al. (2000)
Mule deer (*Odocoileus hemonius*) Body weight 75–135 kg	Butorphanol 0.6 mg/kg Azaperone 0.4 mg/kg Medetomidine 0.2 mg/kg	Naltrexone 1.2 mg/kg Atipamezole 1 mg/kg		Adapted from WTD dose and manufacturer information
	Medetomidine 0.15 mg/kg Azaperone 0.2 mg/kg Alfaxalone 0.5 mg/kg	Atipamezole at 5 times medetomidine dose	Wild mule deer, high volume requirement in large deer	Mathieu et al. (2017)
	Xylazine 2.2 mg/kg Tiletamine-zolazepam 4.4 mg/kg	Yohimbine 0.1–0.2 mg/kg		Adapted from Murray et al. (2000)
	Thiafentanil 0.15 mg/kg Xylazine 1 mg/kg	Naltrexone 2 mg/kg Tolazoline 2 mg/kg		Kreeger et al. (2023)
	Medetomidine 0.1 mg/kg Ketamine 3 mg/kg	Atipamezole at 5 times medetomidine dose		Kreeger et al. (2023)
American elk (*Cervus canadensis*) Body weight 230–318 kg	Medetomidine 18 mg Azaperone 30 mg Butorphanol 46 mg	Atipamezole 25 mg Tolazoline 600 mg	Total adult dose	Wolfe et al. (2014a)
	Xylazine 1 mg/kg Tiletamine-zolazepam 2 mg/kg	Tolazoline 2–3 mg/kg		Read et al. (2001)
Red deer (*Cervus elaphus*) Body weight 60–180 kg	Medetomidine 0.11 mg/kg Ketamine 2.2 mg/kg	Atipamezole 0.5 mg/kg		Arnemo et al. (1994)
	Xylazine 2.5 mg/kg Tiletamine-zolazepam 2.5 mg/kg	Tolazoline 2 mg/kg	Prolonged recoveries	Janovsky et al. (2000)
Moose (*Alces alces alces*)	Thiafentanil 7.5–10 mg per adult	Naltrexone at 10 mg per 1 mg of thiafentanil	Total adult dose	Barros et al. (2018); Kreeger et al. (2005)
	Etorphine 7.5 mg per adult	Naltrexone at 10 mg per 1 mg of etorphine	Total adult dose	Arnemo et al. (2003)
	Medetomidine 0.1 mg/kg Ketamine 1.5 mg/kg	Atipamezole 0.3 mg/kg		Kreeger et al. (2023)
Caribou and reindeer (*Rangifer taransdus*) Body weight 80–300 kg	Medetomidine 0.1–0.2 mg/kg Ketamine 0.75–2.5 mg/kg	Atipamezole at 5 times the medetomidine dose		Lian et al. (2019)

Table 52.1 (Continued)

Species	Drug combination	Reversal	Comment	Reference
Fallow deer (*Dama dama*) Body weight 40–100 kg	Medetomidine 0.1 mg/kg Tiletamine-zolazepam 1 mg/kg	Atipamezole at 5 times the medetomidine dose		Fernandez-Moran et al. (2000)
	Etorphine 0.02 mg/kg Xylazine 0.3 mg/kg	Naltrexon 0.2 mg/kg Yohimbine 0.125 mg/kg		Kreeger et al. (2023)
Axis deer (*Axis axis*) Body weight 40–110 kg	Xylazine 2 mg/kg Ketamine 3 mg/kg	Yohimbine 0.15 mg/kg IM and 0.15 mg/kg IV	Pretreatment with oral haloperidol 1 mg/kg reduced capture stress	Johns et al. (2020)
Brown Brocket deer (*Mazama gouazoubira*) Body weight 8–25 kg	Midazolam 0.5 mg/kg Xylazine 0.3 mg/kg Ketamine 7 mg/kg			Pinho et al. (2010)
Marsh deer (*Blastocerus dichotomus*) Body weight 80–150 kg	Midazolam 0.5 mg/kg Xylazine 0.5 mg/kg Ketamine 5 mg/kg			Pinho et al. (2010)
Pampas deer (*Ozotoserus bezoarticus*) Body weight 22–34 kg	Xylazine 1 mg/kg Tiletamine-zolazapam 2.5 mg/kg	Yohimbine 0.2 mg/kg		Munerato et al. (2015)

IM, intramuscular; IV, intravenous.
Body weights are referenced from Kreeger et al. (2023).



Figure 52.1 Wapiti restrained in a hydraulic squeeze chute.

have a major influence on induction time. The influence of needle length on induction time was compared in free-ranging fallow deer immobilized with etorphine-acepramazine-xylazine. A comparison of 2.0 × 30 versus 2.0 × 40–mm barbed needles with side ports demonstrated that time to retrieval of the animal was approximately 20 minutes longer when animals were darted with the shorter needles (Bergvall et al. 2015). The time between induction and hands on the animal is a time when major complications often occur, therefore optimal needle length should be considered to reduce the risk of complications, particularly with free-ranging deer.



Figure 52.2 Intravenous drug administration via the cephalic vein in a white-tailed deer.

Sedation/Tranquilization/Anesthesia Techniques

Sedation

Captive white-tailed deer and mule deer typically require 2–3 mg/kg body weight of xylazine intramuscular (IM) to produce recumbent sedation. American elk require



Figure 52.3 Intubation of a white-tailed deer.



Figure 52.4 Intranasal drug administration to a white-tailed deer.

approximately 1 mg/kg IM to produce recumbent sedation (Caulkett 1997). Once the xylazine has been administered, the animal should be left alone until it assumes a position of lateral or sternal recumbency with its head down. The deer can be cautiously approached and a towel should be placed over its eyes to decrease stimulation; noise should be kept to a minimum. Animals may appear to be very sedate under xylazine sedation, but they can rouse suddenly. To decrease the chance of sudden arousal, administer 1 mg/kg of ketamine into the jugular vein. Anesthesia can be maintained with 1–2 mg/kg of ketamine intravenous (IV), as required (generally at 10–15-minute intervals).

Yohimbine is effective in most cervids at a dose of 0.1–0.2 mg/kg body weight. Administer 0.1 mg/kg IV and 0.1 mg/kg IM. Tolazoline is also effective, and can be used at a dose of 2–4 mg/kg. Atipamezole can be used at 1 mg IM per 10 mg of xylazine. The intranasal use of medetomidine has been described above. This drug can also be used for IM sedation in most deer species at a dose of 0.05–0.1 mg/kg. Medetomidine should be antagonized with atipamezole at five times the medetomidine dose.

Neuroleptic Agents

Neuroleptics can be extremely useful in the management of wild and semidomesticated deer. These drugs will facilitate transport of deer and decrease stress in acutely captured deer. They have the potential to decrease the risk of trauma and capture myopathy. Azaperone (0.2 mg/kg) can be used immediately post reversal to facilitate short translocations (6 hours or less). Zuclopenthixol acetate (1 mg/kg) will provide up to 4 days of tranquilization (Read et al. 2000). Animals treated with this drug demonstrate decreased flight distance, decreased indices of stress, and improved water and food consumption compared to untreated animals (Read et al. 2000). Neuroleptic drugs can also be used to reduce the stress of handling and immobilization in captive deer. Captive spotted deer, premedicated with oral haloperidol prior to xylazine-ketamine anesthesia, demonstrated a significant reduction in serum cortisol, body temperature, and lactate when compared to control animals. The haloperidol was delivered at a dose of 1 mg/kg, in a banana, 6 hours prior to darting (Johns et al. 2020). This is a simple approach to stress reduction, prior to immobilization, in captive deer.

Combinations for Immobilization of Deer

Butorphanol-Azaperone-Medetomidine

A combination of butorphanol, azaperone, and medetomidine has proven to be useful for immobilization of a number of captive and wild deer species (Mich et al. 2008; Siegal-Willot et al. 2009). In the United States the combination is available as BAM kits, a commercial preparation that allows for easy dosing. The combination can be delivered at a relatively low volume and is rapidly and reliably antagonized with atipamazole and naltrexone (Mich et al. 2008; Siegal-Willot et al. 2009) The major side effect of BAM is hypoxemia, which is readily treated with supplemental inspired oxygen (Mich et al. 2008; Siegal-Willot et al. 2009).

Nalmefene-Azaperone-Medetomidine

This combination is very similar to the BAM combination and has been described in American elk (Wolfe et al. 2014b).

Alfaxalone-Azaperone-Medetomidine

Alfaxalone can be combined at a subanesthetic dose (0.5 mg/kg) with azaperone and medetomidine to induce immobilization in captive and free-ranging deer. The combination has been described in white-tailed deer and mule deer (Pon et al. 2016; Mathieu et al. 2017). The major side effect of this combination is hypoxemia. Currently the major limitation to this mixture is the volume required with commercial alfaxalone (10 mg/mL). A more concentrated form of alfaxalone (40 mg/mL) is currently under investigation (Patterson et al. 2018). If this formulation becomes available, it will greatly increase the utility of this combination in wildlife.

Xylazine-Tiletamine-Zolazepam

Xylazine-tiletamine-zolazepam is a useful mixture for the capture of wild deer (Millspaugh et al. 1995; Murray et al. 2000), and for chemical immobilization and light anesthesia in game-farmed or zoo animals. This combination will provide approximately 45 minutes to 1 hour of anesthesia. Anesthesia may be prolonged with IV ketamine at a dose of 1–2 mg/kg, every 15 min. Once the procedure has been completed, antagonism of xylazine is recommended with tolazoline or yohimbine. The major complication associated with this technique is hypoxemia, which can be effectively treated with supplemental inspired oxygen (Read et al. 2001).

Medetomidine-Ketamine

Medetomidine-ketamine has effectively replaced xylazine-ketamine in locations where concentrated medetomidine is available. The major advantage of medetomidine-ketamine is that ketamine requirements are lower than with xylazine. This factor allows for an earlier antagonism of the combination, i.e. the alpha-2 agonist can be antagonized with less risk of unmasking convulsive activity or rigidity from residual ketamine. Hypoxemia and hypertension are the major complications that may be encountered with medetomidine-ketamine in deer (Caulkett et al. 2000). The use of concentrated (200 mg/mL) ketamine significantly reduces volume requirements.

Potent Opioids

Potent opioids, such as etorphine, carfentanil (no longer available), and fentanyl, have been widely used for immobilization of several different deer species (Moresco et al. 2001; Caulkett et al. 2000; Haigh 1991, 1990). In most cases they have been combined with xylazine, acepromazine, or other sedatives to achieve optimum immobilization. The choice of opioid for use in deer may be governed as much by availability as by any other factor.

Thiafentanil is another potent opioid anesthetic that has proven to be extremely useful for the capture of deer. Doses in North American elk as high as 100 μg/kg provided very rapid immobilization (<1 minute in some cases) and numerous elk have been immobilized at doses near 50 μg/kg (Smith et al. 1993). A complete overview of thiafentanil can be found in Lance and Kenney (2011).

A variety of opioid antagonists have been used in deer, including nalorphine, diprenorphine, naloxone, nalmefene, and naltrexone. Of these products, naloxone has the shortest half-life. Narcotic recycling, or resedation, especially of animals immobilized with carfentanil or etorphine, has been reported when naloxone is used (Haigh 1991). Naltrexone is a pure antagonist and has a much longer duration of action than any of the other antagonists listed (Kreeger et al. 2023). When adequate doses of naltrexone are used, i.e. 10–20 mg per 1 mg of etorphine or thiafentanil, recycling is generally not a problem (Kreeger et al. 2023).

Inhalational Anesthesia

Inhalational anesthesia is recommended for prolonged or very invasive procedures. A small animal circle system can be used on animals weighing up to 150 kg (Fig. 52.3). Cervids premedicated with xylazine can usually be maintained on approximately 1.3% isoflurane. Adult deer can be immobilized with any of the injectable techniques described and IV ketamine, propofol or alfaxalone can be administered to deepen the plane of anesthesia for intubation. Fawns are usually easy to handle and can be induced with IV diazepam 0.2 mg/kg, followed by 0.05 mg/kg butorphanol IV, followed by 2–3 mg/kg ketamine.

Airway protective reflexes are absent under inhalational anesthesia, and regurgitation and aspiration can occur, therefore intubation is recommended. Hypoventilation may be encountered, necessitating intermittent positive pressure ventilation. Usually, cervids maintain a relatively high blood pressure; hypotension may be encountered if rumenal tympany is present. The respiratory and hemodynamic compromise produced by rumenal tympany can be severe. The incidence of rumenal tympany can be decreased if food is withheld for 24–36 hours prior to anesthesia. Water should be withheld for 12 hours prior to anesthesia. Rumenal tympany may be resolved by passage of a rumen tube. If not, the anesthesia may be terminated or emergency rumenal trocharization performed. Passive regurgitation can occur. Inflate the cuff on the

endotracheal tube to ensure an adequate seal of the airway. The animal should be extubated when the swallowing reflex occurs, and the endotracheal tube should be removed with the cuff partially inflated. Animals that have been premedicated with alpha-2 agonists should receive an antagonist to speed recovery.

Complications and Other Considerations

Preanesthetic Concerns

Several factors can influence the method of anesthesia and the means of drug administration. It is important to plan the capture carefully, as prolonged chase times can result in capture myopathy, trauma, or hyperthermia.

Elective procedures in captive animals should be planned for the cool hours of the day. Rumenal tympany can be a complication during anesthesia. If the procedure is elective, captive deer should be fasted for 24 hours. Deer are prone to hypoxemia during anesthesia (Read et al. 2001; Murray et al. 2000; Moresco et al. 2001; Paterson et al. 2009). Hypoxemia is exacerbated by positioning in dorsal or lateral recumbency. Alpha-2 agonist drugs such as xylazine or medetomidine will also exacerbate hypoxemia (Read et al. 2001). Chronically debilitated animals and animals with severe fluid deficits or blood loss are generally not good candidates for anesthesia and are at increased risk for complications.

Pulmonary Function

Whenever possible, deer should be positioned in sternal recumbency. The head and neck should be extended to maintain a patent airway. The animal should be monitored for hypoxemia, ideally with a pulse oximeter. A multisite sensor applied to the tongue generally provides a good signal. Normal hemoglobin saturation should be 95–98%; below 85% is considered hypoxemic. Severely hypoxemic animals are often tachycardic. Heart rates above 150 beats per minute in mature deer may result from a stress response due to hypoxemia, hypercarbia, pain, or hypotension. Supplemental inspired oxygen should be considered in hypoxemic animals. Oxygen can be easily delivered via nasal insufflation (Read et al. 2001). A nasal catheter should be placed and threaded as far as the medial canthus of the eye. A flow rate of 1–2 L/min is generally sufficient for smaller species, such as white-tailed deer (Fahlman et al. 2014). Higher flow rates may be required in larger deer species, such as red deer and moose (Paterson et al. 2009).

To conserve oxygen and prolong tank life, the flow should be adjusted downwards to find the minimum flow that will allow maintenance of $SpO_2 \geq 95\%$. An alternative strategy is to use a portable oxygen concentrator. These devices have proven effective in treating hypoxemia during anesthesia of reindeer (Fahlman et al. 2012).

Monitoring the Cardiovascular System

Heart rate should be monitored, at minimum, every 5 minutes. The auricular artery is easily palpated in deer. If the auricular artery cannot be palpated, a femoral pulse can be used. Blood pressure can be easily measured with an oscillometric cuff placed proximal to the carpus.

Thermoregulation

Rectal temperature should be monitored every 5–10 minutes. Deer are prone to hyperthermia (Read et al. 2001; Moresco et al. 2001). Rectal temperatures greater than 40°C are cause for concern, and attempts should be made to cool the animal. Rectal temperature in excess of 41°C is an emergency and should be treated aggressively. It is difficult to actively cool large animals and often the best option is to antagonize the immobilizing agents and allow the animal to recover. Hyperthermia, in the face of hypoxemia, is a particularly serious complication, as hyperthermia increases metabolic oxygen demand. Hyperthermic animals should receive supplemental inspired oxygen to offset hypoxemia.

Species-specific Considerations

White-tailed Deer (*Odocoileus virginianus*) and Mule Deer (*Odocoileus hemonius*)

White-tailed deer and mule deer are not difficult to anesthetize as long as they are kept calm during immobilization. Excited deer tend to override the sedative effects of alpha-2 agonists and often require higher doses for induction.

White-tailed deer and mule deer can be effectively anesthetized with xylazine-tiletamine-zolazepam (Murray et al. 2000), BAM (Mich et al. 2008; Siegal-Willot et al. 2009), medetomidine-azaperone-alfaxalone (Pon et al. 2016), medetomidine-ketamine (Caulkett et al. 2000) or thiafentanil-xylazine (Kreeger et al. 2023).

North American Elk (*Cervus canadensis*) and Red Deer (*Cervus elaphus*)

Chemical immobilization of elk can be induced with BAM (Wolfe et al. 2014a), xylazine-tiletamine-zolazepam (Read et al. 2001), or NalMed-A (Wolfe et al. 2014a). Net gunned elk can be readily sedated with intranasal xylazine (Cattet et al. 2004). The major side effect of chemical immobilization in elk is hypoxemia, which is readily treated with supplemental inspired oxygen (Paterson et al. 2009)

Red deer are distributed throughout Europe and are smaller than elk but considerations are similar. The drug of choice for red deer capture is medetomidine-ketamine (Arnemo et al. 1994). A good alternative is xylazine-tiletamine-zolazepam (Janovsky et al. 2000). However, due to the long elimination time of tiletamine-zolazepam recoveries are often prolonged.

American Moose (*Alces americanus*) and European Moose (*Alces alces alces*)

Anesthesia of moose is very similar to anesthesia of other deer. All the same precautions apply, and particular attention must be paid to the prevention of bloat, capture myopathy, and hyperthermia. One of the major complicating factors with moose is their large size. There are several drug choices for anesthesia of moose. In the past carfentanil-xylazine was advocated in North America (Seal et al. 1985). The addition of xylazine to carfentanil will decrease the incidence of muscle rigidity; unfortunately, the addition of xylazine will also increase the risk of regurgitation and aspiration pneumonia (Kreeger 2000). As carfentanil is no longer available, thiafentanil at a dose of 7.5–10 mg per adult is a good alternative (Barros et al. 2018; Kreeger et al. 2005). Reversal can be achieved with naltrexone at 10 mg per 1 mg of thiafentanil.

Currently, the drug of choice for free-ranging moose is etorphine alone at a dose of 7.5 mg of etorphine per adult and half this dose in calves (Arnemo et al. 2003).

European moose have been effectively immobilized with medetomidine-ketamine (Kreeger et al. 2023). Immobilization can also be achieved with xylazine-tiletamine-zolazepam. A dose of 1.5 mg/kg of xylazine combined with 3 mg/kg of tiletamine-zolazepam has proven effective (N. Caulkett, unpubl. data) but recoveries may be prolonged following xylazine reversal. Immobilization can be partially antagonized with yohimbine, tolazoline, or atipamezole. This combination has been used in ground darted animals. Potent opioids are the preferred choice for helicopter darting of moose.

Caribou and Reindeer (*Rangifer tarandus*)

Caribou often have high drug requirements when compared to other deer species. The drug combination of choice for rangifer is medetomidine-ketamine (Lian et al. 2019), Dose rates in *Rangifer* are very variable depending on the capture technique, the degree of human conditioning (domestic vs. wild), and the subspecies being captured.

Fallow Deer (*Dama dama*)

A variety of techniques have been used to anesthetize fallow deer, often with unreliable effects. One potentially reliable drug combination for fallow deer is 0.1 mg/kg of medetomidine + 1 mg/kg of tiletamine-zolazepam (Fernandez-Moran et al. 2000). In free-ranging fallow deer etorphine-xylazine should also be considered (Kreeger et al. 2023).

Axis Deer (*Axis axis*) and Hog Deer (*Axis porcinus*)

Axis deer can be effectively anesthetized with xylazine-ketamine. Pretreatment of captive animals with 1 mg/kg of haloperidol PO significantly reduced capture stress (Johns et al. 2020).

Hog deer require 0.5 mg/kg medetomidine + 1.5 mg/kg ketamine (Kreeger et al. 2023). If needed, ketamine at 1–2 mg/kg IM can be used to deepen or prolong anesthesia. The effects of medetomidine can be effectively reversed by atipamezole IM at 5 mg/mg medetomidine (Kreeger et al. 2023).

Neotropical Deer Species

Midazolam at a dose of 0.5 mg/kg has been combined with ketamine (7 mg/kg) and xylazine (0.3 mg/kg) in brown brocket deer (*Mazama gouazoubira*). Midazolam (0.5 mg/kg) has also been combined with ketamine (5 mg/kg) and xylazine (0.5 mg/kg) for the chemical immobilization of marsh deer (*Blastocerus dichotomus*). Free-ranging marsh deer have also been successfully anesthetized with 0.8 mg/kg of xylazine and 2 mg/kg IV of tiletamine-zolazepam, with rapid, smooth recovery following antagonism of the xylazine with yohimbine (Pinho et al. 2010). Pampas deer (*Ozotoserus bezoarticus*) can also be successfully immobilized with either xylazine-midazolam-ketamine or xylazine-tiletamine-zolazepam at a dose of 1 mg/kg of xylazine combined with 2.5 mg/kg of tiletamine-zolazepam (Munerato et al. 2015). A complete review of the capture and restraint of neotropical cervids can be found in Pinho et al. (2010).

Analgesia and Analgesic Techniques

Postoperative analgesia can be achieved with 0.025–0.05 mg/kg of butorphanol. Meloxicam can also be used at a dose of 0.5 mg/kg.

Local Analgesia for Velvet Antler Removal

The simplest way to block velvet antler is to perform a ring block at the base of the antler pedicle. Lidocaine HCl (without epinephrine) is administered at a dose rate of 1 mL/cm of pedicle circumference (Wilson et al. 2000). The block will produce surgical analgesia in 1–2 minutes and will last approximately 90 minutes.

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Gazelles

Kristen A. Phair and Matthew Kinney

Introduction

The subfamily Antilopinae comprises a wide range of small to medium-sized ruminants within the family Bovidae. The taxonomy of this subfamily is regarded by many as confusing and it remains highly controversial, potentially the least understood of all the Bovidae subfamilies. Based on recent literature, the division of Antilopinae into two tribes is generally accepted: Antilopini (gazelles) and Neotragini (dwarf antelopes) (Grubb 2001; Hernandez-Fernandez & Vrba 2005; Vrba & Schaller 2000).

Tribe Antilopini consists of the medium-sized gazelles of the genera *Eudorcas* (e.g., Thomson's gazelle), *Gazella* (e.g., Speke's gazelle), and *Nanger* (e.g., Dama gazelle), but also encompasses additional species including the springbok (*Antidorcas marsupialis*), blackbuck (*Antilope cervicapra*), and gerenuk (*Litocranius walleri*). In general, these nervous animals are of moderate body build with slender fragile limbs and are capable of running at high speeds, up to 80 km/h in the blackbuck and springbok (Nowak 1999). The majority of species are native to Africa, but a few are endemic to Asia (e.g., blackbuck). There is minimal size difference between sexes and both typically have horns. Some species are highly gregarious, forming large herds (e.g., springbok). Species differ in their preferences for grazing versus browsing. Of the browsers, the gerenuk is notable for its elongated neck, long limbs, and agile ability to stand on its hind legs to reach up high for leaves. For the purposes of this chapter, the term "antelope" will be used to describe species within the tribe Antilopini.

Within the tribe Neotragini are some of the smallest and most delicately hooved animals, including the royal antelope (2–3 kg) and dik-dik species (3–7 kg) (Nowak 1999). All are native to Africa and typically browse selectively for food items. Only males possess horns, which are short, vertical, and spike-like (Huffman 2020; Nowak 1999). In most species, both sexes have prominent preorbital scent glands. Males and females may form monogamous pairs. The dik-dik's name derives from the characteristic call it makes resembling "zik-zik" or "dik-dik" as it erratically leaps away when disturbed (Nowak 1999). The klipspringer (*Oreotragus oreotragus*) is unique in its ability to climb and navigate rocky terrain using specialized hooves that provide traction.

Both Antilopinae tribes face declining population numbers due to habitat alterations, encroaching agricultural development, and excessive hunting (Nowak 1999). For the purposes of this chapter, the authors will concentrate on the most commonly housed species within institutions accredited by the Association of Zoos and Aquariums (AZA) based on a recent survey (*AZA Antelope and Giraffe Tag Annual Report*; Association of Zoos and Aquariums 2019). Tribes, species, and adult weight ranges are listed in Table 53.1.

Preanesthetic Considerations

Prior to immobilization, various factors should be considered to appropriately tailor the restraint approach to the situation and intended goals. Considerations include the species, temperament, medical history of the individual, enclosure design, personnel available, and environmental conditions.

As with most ruminants, fasting is generally recommended when possible to reduce the risks of regurgitation and potential aspiration during either manual or chemical restraint. There are various approaches to fasting, including a complete fast from food and water, or modified fasts where hay may be fed but concentrates withheld. Fasting duration can also vary, ranging from 0 to 24 hours depending on institutional preference and ambient conditions, but it is not recommended to exceed 24 hours due to association with metabolic acidemia (West 2007).

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Table 53.1 Commonly held Antilopinae species and adult weight ranges.

Scientific Name	Common Name	Adult weight range (kg)
Tribe Antilopini*		
Antidorcas marsupialis	Springbok	27–48
Antilope cervicapra	Blackbuck	25–43
Eudorcas rufrifrons	Red-fronted gazelle	20–30
Eudorcas thomsoni	Thomson's gazelle	13–27
Gazella spekei	Speke's gazelle	11–25
Gazella cuvieri	Cuvier's gazelle	15–35
Gazella leptoceros	Slender-horned gazelle	13–30
Litocranius walleri	Gerenuk	27–54
Nanger dama	Dama (addra) gazelle	40–75
Nanger granti	Grant's gazelle	35–50
Nanger soemmerringii	Soemmerring's gazelle	28–45
Tribe Neotragini		
Madoqua kirkii	Kirk's dik-dik	3–7
Oreotragus oreotragus	Klipspringer	8–18
Raphicerus campestris	Steenbok	7–16

* For the purposes of this chapter, the term "antelope" will be used to describe species within the tribe Antilopini.
Sources: Association of Zoos and Aquariums (2019), Nowak (1999), Huffman (2020), and AZA Ungulates (2020).

Isolation and confinement of the patient is ideal to facilitate immobilization. This may be challenging in herd situations. For animals in large mixed-species field exhibits, a boma can be useful to confine the target population. The desired individual can be further isolated from the group using shift stalls or runway/chute systems. Pre-immobilization enclosures should be quiet and have visual barriers to reduce the stress of the animal, have tall fences or walls to limit attempts to jump and escape, and be free of unnecessary barriers and objects that might lead to injury. Depending on the size and temperament of the animal, some patients may even be amenable to desensitization training in a boma, chute, squeeze, or crate (Anderson et al. 2016). If crate trained, the patient can be safely transported to an ideal procedure location for manual or chemical restraint.

Scheduled immobilizations are recommended to occur early in the day. This provides ample time during recovery to monitor the patient for complications associated with capture and/or anesthesia, including myopathy and renarcotization. Additionally, in hot climates, early morning procedures tend to be cooler, with reduced risk for hyperthermia. It is best to avoid any form of restraint in warm temperatures when possible.

Physical Restraint

Manual restraint is the preferred initial method of restraint for the smallest Antilopinae, but may also be a viable option for some of the medium-sized species. Manual restraint is appropriate for short duration, minimally invasive examinations or procedures such as neonate examinations, abbreviated preshipment examinations, blood collection, and topical or parenteral drug administration. It can also be used as the preliminary form of restraint to facilitate administration of intravenous (IV) or intramuscular (IM) anesthetic induction agents when darting or other restraint techniques are considered higher risk.

When working with small species like dik-dik, it is best if the animal is initially confined in a small, solid-walled enclosure. Lighting should be dimmed, but not so dark as to hinder the vision of the restrainer. If the stall is small enough, one restrainer enters the enclosure and swiftly grabs the dik-dik as it runs past. The animal is immediately lifted off the ground away from any walls it might kick. The restrainer concentrates on restraint of the head and neck with one arm while holding around the mid-body with the other arm. With the animal in hand, an additional restrainer enters the stall and positions themself to hold the neck and horns (or head only in females). A third restrainer may be utilized to restrain the caudal half of the body and hind legs if needed (typically with the legs stretched back and held in extension), or the primary restrainer can shift their hold to incorporate the hind legs into a tucked position (Fig. 53.1). The animal is held firmly against the restrainer's body to minimize struggling and limb movement. It is often beneficial to apply a light blindfold such as a bandana or small towel to the animal while in hand to reduce visual stimulus, making sure to leave the nares exposed to allow unobstructed breathing.

For the medium-sized species which are often held in larger stalls, a minimum of four or five restrainers are needed. Pre-planning to determine which section of the body each person will restrain is important. Restrainers enter the enclosure and in a coordinated fashion smoothly and quickly approach the animal to lift it off the ground. If the animal has horns, often the horns (at the base) are first restrained by one person while a second person restrains the body around the axilla, and a third person holds around the abdomen in front of the hind legs. Additional restrainers are positioned to help with immobilization of the front and hindlimbs in extension (Fig. 53.2).



Figure 53.1 Manual restraint of a Kirk's dik-dik (*Madoqua kirkii*). The hindlimbs are tucked tight against the restrainer's body. The eyes are covered with a blindfold. Restrainers protect themselves from sharp hooves and horns with long sleeves and work gloves.

A few calmer species, particularly gerenuk, may be amenable to physical restraint with the use of large pads. Multiple restrainers (four or five) enter the stall with large rectangular restraint pads and slowly approach and surround the animal to corner it against a wall using the pads as a barrier (Fig. 53.3a). A pad is also directed from above the animal to prevent jumping and encourage the animal to the ground. This method capitalizes on this species' tendency to tuck into a sternal position and can be encouraged (but not forced) by applying light downward pressure to the animal through the pads. Once seated, the pads are partially folded back to restrain the horns and access different parts of the body for examination or drug administration (Fig. 53.3b). If the animal resists light pressure intended to direct the animal into a sternal position, additional force should not be applied as back injuries have been known to occur.

To safely release the animal from manual restraint, a coordinated approach is needed. For animals elevated off the ground, restrainers must synchronize their release to occur as soon as the animal's feet are allowed to touch the ground, usually letting go of the horns last, and then quickly backing away. The release should happen in an open part of the stall away from barriers, with an open path for the animal to move away from people. For animals restrained in sternal recumbency with pads, restrainers first ensure that the head and horns are covered with the pads, and then synchronize lifting the pads and backing away.

Additional variations of physical restraint include netting and chute restraint. Netting poses more significant risk to the animal, especially limb entanglement, and is only recommended for smaller species when other restraint options are not possible (West 2007). Chute restraint may be appropriate for some of the larger Antilopinae and a drop floor chute has been used successfully in blackbuck to facilitate noninvasive, brief procedures (Haigh 1999). It is ideal if the animal can be familiarized with the pen and chute design before employing this technique. Chute restraint requires significant experience to perform safely.

Risk of injury to the animal can be high if proper precautions are not taken. Animals may run into walls or try to jump barriers in an attempt to flee people. Trauma in all forms, but particularly limb fractures and horn



Figure 53.2 Manual restraint of a Thomson's gazelle (*Eudorcas thomsoni*). The eyes are covered with a blindfold. Restrainers protect themselves with long pants, gloves, and eye protection.



Figure 53.3 Pad restraint of a gerenuk (*Litocranius walleri*). (a) The restrainers approach the cornered animal using rectangular pads. (b) The animal tucks into a sternal position and pads are used to lightly hold the animal down. The horns are restrained and covered with irrigation tubing for protection. The pads are shifted to allow access to the interscapular area for subcutaneous fluid administration.

avulsions or breaks are concerns. Even in hand, especially with the small delicate species, limb fractures are still a risk if the animal is able to kick or gets a leg caught in clothing. Injuries to the horns can be reduced by applying sheaths or bumpers to the horns to pad and reinforce them once the animal is restrained. Rubber irrigation hosing often works well for this purpose and has the added benefit of helping protect restrainers from the sharp horn tips (Fig. 53.3b). Horn restraint should be avoided in younger animals where horn avulsions are more likely to occur. Additional risks include hyperthermia and myopathy (see the section on complications and other considerations), which can be minimized but not entirely eliminated by ensuring the catch-up is swift and the time in hand is brief.

Human safety is critical during manual restraint. Experience is paramount to success and safe capture. Restrainers should wear long sleeves and pants to protect their limbs; two layers can be useful for protection if small hooves or horns happen to tear through the outermost layer. Clothing should be form-fitting, with special attention paid to avoid pockets, exposed belt-loops, or loose folds that might catch on the animal. Work gloves are helpful to protect the hands and also improve grip on the horns and other body parts. Eye protection in the form of sunglasses or safety glasses is important to prevent inadvertent eye trauma from hooves, horns, or kicked up substrate. Although the Antilopinae are small to medium in size, the power of their horns and limbs should not be underestimated and proper teamwork is needed to ensure human safety when restraining these animals.

Induction

The purpose of the anesthetic event should be discussed with all personnel involved to determine which type of restraint or immobilization will allow the team to safely accomplish the goals of the procedure and ensure that all personnel involved are aware of their roles and responsibilities throughout the induction, maintenance, and recovery of the animal. Additionally, discussing the purpose or goals prior to the procedure will allow the team to prioritize the order of the procedures and determine which aspects of the procedures are necessary, which are ancillary, and which can be cancelled or rescheduled for a later date if unexpected complications arise that necessitate truncating the procedure. Once the purpose and priorities of the procedure have been established, it is essential that the proper equipment and personnel are put in place to safely anesthetize the patient and manage anticipated complications.

Mask Induction

Induction using inhalant anesthesia such as isoflurane, sevoflurane, and desflurane can be considered in neonate Antilopinae that are small enough to be easily restrained or those that have strong tucking responses to handling and manipulation. Adult Antilopinae are unlikely to relax during manual restraint for mask induction and inductions will likely be prolonged and potentially dangerous to staff and the animal, therefore intravenous or intramuscular inductions are better options in adult Antilopinae. Commonly, mask induction can be used in adult animals



Figure 53.4 An appropriately fitting facemask is used to provide flow-by oxygen prior to intubation in a slender-horned gazelle (*Gazella leptoceros*). Note the rubber diaphragm is creating a tight seal, but not collapsing the soft tissues around the nasal cavity. The eyes are covered to minimize visual stimulation.

as a supplementary anesthetic to deepen the plane of anesthesia to facilitate intubation following intramuscular or intravenous anesthetic administration. When selecting a mask for induction, make certain the rubber diaphragm fits loosely around the nose of the patient (Fig. 53.4). Most Antilopinae, even neonates, have redundant soft tissue surrounding the nares that can collapse when circumferential pressure is applied using a mask that is too snug, resulting in limited airflow through the nares. Intubation should be strongly considered to protect the airway and allow for positive pressure ventilation if the procedure is anticipated to be of significant duration.

Intravenous Induction

Intravenous anesthesia can be achieved by delivering anesthetics directly into a vein using a needle or a previously placed intravenous catheter. When injecting directly into a vein, the jugular vein is the easiest and safest route. Oftentimes capture for manual restraint takes place in a dimly lit stall, so consideration should be given to bringing a focal light source such as a headlamp or flashlight to facilitate visualization. The restrainer should maintain head control of the animal at all times and fully extend the neck. The anesthetist should use their nondominant hand to occlude the jugular vein at the distal cervical region, which will result in the jugular vein becoming visible and palpable. Using an appropriately sized luer-lock syringe and a 1-inch needle with the bevel facing up, the tip of the needle should be pointed towards the head. The jugular vein can be entered at a shallow angle, the plunger withdrawn slightly to confirm intravenous placement, and the anesthetics delivered slowly. The restrainers and the anesthetist should be aware of the position of the horns and hooves to prevent injury. If the patient moves, repeat aspiration to confirm continued intravenous placement of the needle is advisable prior to complete administration. The restrainer should maintain control of the animal and expect progressive, rapid relaxation until the patient is fully induced. When intravenous anesthesia induction is administered through an indwelling catheter, the anesthetist should be aware of all medications that are being administered to the patient and the most recent time of administration. Care should be taken to ensure the anesthetics being delivered are compatible with all medications and the rate of administration will not cause unwanted hemodynamic alterations or fluid overload. This is particularly important when the infusion port is a considerable distance from a small patient, which is often the case when intravenous support is being provided in hospital, and a relatively large volume bolus is needed to clear the intravenous catheter extension set to facilitate delivery of the anesthetics to the patient (Fig. 53.5). If an indwelling catheter is used for



Figure 53.5 A 1.3-kg neonate Soemmeriing's gazelle (*Nanger soemmerringi*) receives intravenous fluids and partial parenteral nutrition. The fluid volume within the intravenous catheter extension set and medications being administered to the patient must be considered if this route of induction is selected. For this patient, a fluid bolus to clear the extension set would result in volume overload. Administration of anesthetics at the port near the head or an alternative induction route is recommended.

Table 53.2 Intravenous induction agents commonly used in Antilopinae.

Drug	Dosage (mg/kg)	Comments
Propofol	4–6	Smaller species may require higher doses. Speke's gazelles have been given up to 10 mg/kg (Kleinschmidt et al. 2018)
Propofol Ketamine	2–4 1–2	Combining propofol and ketamine allows for lowering the dose of both agents and provides a longer period of time until supplemental anesthesia is needed
Ketamine Midazolam	2–4 0.1–0.2	Midazolam at this dose and route rarely requires antagonism with flumazenil
Tiletamine/zolazepam	2–4	Pas (2014)

induction, the port closest to the animal that can be safely accessed should be used. Propofol is a commonly used intravenous induction agent in Antilopinae, with small species often requiring higher doses than larger ones. Speke's gazelles have been given 10 mg/kg for induction (Kleinschmidt et al. 2018). In goats administered propofol at 4 mg/kg, the half-life was 15.5 minutes (Reid et al. 1993) and based on clinical experience of anesthesia duration using propofol in Antilopinae, a similar half-life is considered likely. Propofol should be administered intravenously at a slow rate and the anesthetist should be prepared for an apneic patient with equipment needed for intubation. Alfaxalone has been used in sheep at 2 mg/kg IV with minimal adverse effects and uneventful recovery (Andaluz et al. 2012), but further investigation into the utility of this agent in Antilopinae is needed. See Table 53.2 for intravenous anesthetic induction agents used in Antilopinae.

Intramuscular Induction

Intramuscular anesthetic administration is necessary for immobilization of many free-ranging antelopes and those maintained in zoological facilities. Intramuscular administration is the most common route of anesthetic delivery and can be facilitated by hand injection or a remote drug delivery system and will depend on the species, enclosure, equipment, personnel available for the procedure, and experience of the anesthetist.

When administering a hand injection for induction, a luer-lock syringe with a large-gauge needle (18 gauge for most species) should be used to prevent dislodgement of the needle from the syringe and facilitate rapid administration. When manual restraint is being used, care should be taken to visualize and palpate a large muscle of the hindlimb. Once the intramuscular injection is complete, and assuming the animal is contained in a small space free of hazards, it is often safest for the patient and personnel to release the patient from restraint, dim the enclosure lights if possible, and minimize the stimulus outside the induction area as the patient is being induced. If the patient is being restrained in a drop chute or hydraulic squeeze system for hand injection, the expected time of induction should be discussed to facilitate release of the patient to an ideal site as the animal progressively relaxes and becomes fully anesthetized. Pole syringes are not recommended for anesthetic induction in Antilopinae unless no other safe delivery options are available or the animal is anticipated to be severely compromised and unable to rise. Heavily padded squeeze systems have been developed for the smallest of patients that have a high potential for iatrogenic injury following darting, and investment in this equipment may be considered for collections that included dik-dik, steenbok, and other small Antilopinae.

Remote immobilization of antelopes can be accomplished using a variety of projectile systems such as blowpipes, CO_2-powered pistols, or CO_2-powered rifles. Powder-charged projectile systems are less commonly used for anesthesia induction in antelopes maintained in zoological collections, but are still used in some instances for immobilization of free-ranging animals. Prior to selecting which projectile system to use, the anesthetist should consider the exhibit size, anticipated distance between the anesthetist and the animal, size of the animal, behavior of the animal when approached, prior experience with immobilization of the individual animal or herd-mates, and equipment and personnel available for the procedure. Planning elective immobilizations during poor environmental conditions such as extreme warm or cold weather or wet field conditions should be avoided.

The relatively small size of most antelopes, their quick movements, and long flight distances, increase the risk of iatrogenic trauma compared to other nondomestic hoofstock. Mitigation of the risks of iatrogenic trauma to an antelope can be accomplished by reviewing the following principles:

1) Dart location: Ideal dart placement is perpendicular to a large muscle. In most antelopes, the caudal or lateral aspect of the rear limb is the best option. However, some anesthetists prefer the shoulder for larger, more robust species. Attempts should be made by the individual darting to be on the same vertical plane as the target muscle. For smaller animals, this may necessitate crouching or kneeling when darting.

2) Needle size: A needle that will penetrate the skin and subcutaneous space to allow for an intramuscular injection should be selected. Needles that are longer than necessary may result in intraosseous drug administration and increase the risk of penetrating the abdomen or thorax if suboptimal dart placement occurs. Determining whether to use a collared or uncollared needle is clinician dependent. Impact and placement of the dart are more predictive of whether the dart will remain embedded in the large muscle for a full intramuscular injection than the use of a collared or uncollared needle. Common needle sizes used in antelopes include either 30 or 40 mm (length) and 1.5 or 2 mm diameter.
3) Force of impact: Newton's second law of motion states that force equals mass times acceleration ($F = ma$), illustrating that both the mass of the dart and acceleration dictate the force of impact. To minimize the impact force to avoid iatrogenic injury, the dart size and volume should be minimized. Most anesthetics used for immobilization of antelopes are concentrated such that small volumes can be used, allowing for use of 1.5-mL darts that minimize the mass of the projectile. Acceleration of the dart can be manipulated by adjusting the CO_2 pressure of the pistol or the rifle being used and attempts should be made to maximize dart accuracy while minimizing the acceleration by using the lowest CO_2 pressure that allows for an accurate shot. Maximizing accuracy while minimizing CO_2 pressurization can be equipment specific and individuals should consider practicing with the equipment they will be using at various anticipated distances before darting a live animal. An excellent review of the physics of projectile darting systems can be found in Koch and Burroughs (2012) and Cattet et al. (2006).
4) Hazard limitations: Potential hazards during anesthetic induction include, but are not limited to, water drinkers, feed troughs, hay racks, rocks, stumps, logs, steep hills, rocky ledges, standing water, wet grass, nonpadded walls, vehicles, conspecifics, and other species in mixed-species exhibits. Minimizing exposure to these hazards should be attempted. In small enclosures, many potential hazards can be removed, turned off (drinkers), or covered (drinkers and feed troughs). Alternatively, a dedicated induction stall can be used for anesthetic induction and recovery. Ideally these stalls have padded walls, nonslip flooring, dimmable lights, and a movable wall to reduce the space the animal has available to navigate during induction (Fig. 53.6). When antelopes are immobilized in semifree-ranging or free-ranging conditions, potential hazards should be discussed with the immobilization team. Identified hazards are often unable to be removed entirely, so efforts should be focused on minimizing exposure. Examples include stationing personnel near water features to encourage movement away from standing water, pre-identifying aggressive herd-mates or species and distracting these individuals or groups with food or enrichment, and temporarily vacating a certain safe area of a large exhibit to encourage the darted animal to move towards areas with limited hazards. Antelopes frequently run towards bodies of water during anesthesia inductions in large field exhibits. As such, stationing a team of personnel near the shoreline as physical or visual barriers should be strongly considered. Additionally, identified personnel should empty their pockets of valuables in case water entry and patient recovery is needed.



Figure 53.6 Features of a dedicated induction stall that can be used for antelopes such as the Soemmerring's gazelle (*Nanger soemmerringii*). The features of this induction stall include nonslip flooring, padded walls, door handles flush with the walls that do not protrude into the animal space, multiple windows at eye level to facilitate darting, a dimmer lighting system, closed-circuit video capabilities, an overhead hoist system, and a movable wall that can be used to reduce the stall space during induction and recovery.

Prior to darting, the anesthetist should be aware of the potential for a missed shot and the consequences. In particular, the anesthetist should insist that no personnel are near the direction of fire. Consideration should also be given to the potential inadvertent darting of conspecifics or other species in mixed-species enclosures. Antagonists

should always be drawn up prior to darting an animal in the event of accidental human or animal exposure that requires immediate reversal. Inadvertent darting most often occurs when a dart misses over the dorsum of the animal. The individual being targeted for darting should be as isolated as possible from the herd (Fig. 53.7) with particular attention to animals that might be in the direction of fire over the dorsum of the animal. Figure 53.8 illustrates the potential challenges with determining if an individual is truly isolated.

An additional challenge that should be anticipated when darting in a large herd is the potential for animals to be accidentally darted once the anesthetist has raised the gun and sighted the animal using a scope. While rifle scopes are essential for accurate dart placement from long distances, they greatly reduce peripheral vision and there is increased potential that the anesthetist will not visualize an animal that walks into the line of fire. If this is a concern, the anesthetist should consider having a trusted spotter that can communicate the location of other animals to the



Figure 53.7 An ideally positioned antelope for field immobilization. This red-fronted gazelle (*Eudorcas rufifrons*) is on the same vertical plane as the darter, isolated from the herd, the large muscles of the left rear limb are perpendicular to the darter, and the distance allows for a high-percentage shot to be taken at a relatively low velocity.



Figure 53.8 (a) A gun-mounted camera illustrates a dart in flight that is directed towards a large rear limb muscle of a Grant's gazelle (*Nanger granti*) seemingly isolated from the herd. (b) This image was taken approximately 15 milliseconds after (a) and demonstrates the presence of another Grant's gazelle immediately adjacent to the target animal. Fortunately, the target animal was darted, but the presence of a second animal immediately adjacent to the target gazelle was unknown to the anesthetist, who was stationed in a blind.

anesthetist once the gun is raised and the targeted animal is being tracked using the rifle scope.

Due to the highly unpredictable and variable direction of travel for Antilopinae, avoid darting moving Antilopinae unless required for an emergency immobilization. Similarly, darting a standing animal is preferred over an animal laying down. Darting antelopes immediately after rising from sternal to standing is a good option, as many antelopes will stand motionless for a few moments if they are encouraged to stand in a calm and quiet manner. In some instances, darting from a blind, a tree, outside of the field exhibit, during routine feeding or servicing times, or from a vehicle the antelopes are accustomed to is necessary to allow for a shot that has a high likelihood of the dart being administered into an ideal location.

Commonly used intramuscular immobilization combinations are listed in Table 53.3. These doses should be considered as a starting point and alterations should be made based on the purpose of the immobilization, expected duration of the procedure, demeanor of the animal, and previous experience at the veterinarian's institution. Note, when an ultra-potent agonist and alpha-2 agonist-based protocol is used, ketamine (0.5–1 mg/kg) or azaperone (0.25–0.5 mg/kg) can be added to the dart to allow for a more balanced anesthesia. Snyder et al. (1992) demonstrated that the addition of xylazine and ketamine to an etorphine dart resulted in lowering of the ultra-potent opioid dose by 30%, highlighting the advantage of using a multidrug combination for additive effects and balanced anesthesia. The most commonly used alpha-2 agonists for immobilization of Antilopinae are xylazine and medetomidine. Medetomidine and xylazine can be used with thiafentanil or etorphine depending on drug availability and preference of the anesthetist (see Table 53.3).

Table 53.3 Commonly used intramuscular induction agents in Antilopinae.

Drug	Dosage (mg/kg)	Comments
Thiafentanil Medetomidine	0.06–0.08 0.05–0.08	Consider adding ketamine 0.5–1 mg/kg and/or azaperone 0.25–0.5 mg/kg
Ketamine Medetomidine Butorphanol	2–4 0.05–0.1 0.2–0.4	Induction times are often longer than an ultra-potent opioid-based protocol Azaperone can replace ketamine or be added at 0.25–0.5 mg/kg Thomson's gazelles were anesthetized using ketamine 4.9 mg/kg, medetomidine 0.04 mg/kg, and butorphanol 0.4 mg/kg (Chittick et al. 2001)
Etorphine Xylazine	0.06–0.08 0.08–0.2	Etorphine and thiafenanil are often dosed interchangeably in antelopes and drug selection is based on availability and experience

For most antelopes a combination of an ultra-potent opioid and an alpha-2 agonist is used as a starting point for determining a suitable induction combination. A dissociative (ketamine) or a butyrophenone (azaperone) is often added to act synergistically to further induce loss of consciousness and promote muscle relaxation while allowing for a decreased dose of an ultra-potent opioid or alpha-2 agonist. An induction combination of an ultra-potent opioid, alpha-2 agonist, and either ketamine alone or in combination with azaperone is used to minimize induction times and mitigate induction-related morbidity associated with habitat features, conspecifics, and co-maintained species. In the smaller Antilopinae that are housed in a more controlled environment, ketamine, medetomidine, and butorphanol are commonly used. In some instances, patients may require supplemental anesthetics to reach a plane of anesthesia that is safe and the anesthetist should be prepared to provide supplemental anesthesia, most commonly in the form of ketamine 0.5–1 mg/kg IV or IM or propofol 1–2 mg/kg IV.

Historically, a commonly used ultra-potent opioid for antelope anesthesia was carfentanil (0.018–0.022 mg/kg). Carfentanil had been in use since the early 1980s, but this anesthetic agent is no longer available and has been largely replaced by thiafentanil (Lance 2012). Readers should refer to previous editions of this text for carfentanil dose recommendations. When using carfentanil, antagonism with naltrexone 100 mg for every 1 mg of carfentanil should be used (Mutlow et al. 2004). Ketamine and xylazine combinations have been used in antelopes historically and these combinations might be considered if drug availability is limited. Springbok (*Antidorcas marsupialis*) were administered ketamine 8–9 mg/kg and xylazine 0.5 mg/kg IM (Jacobson 1983). Goitered gazelles (*Gazella subgutturosa*) were administered ketamine 5.4–5.9 mg/kg and xylazine 6.8–7.4 mg/kg IM, and Arabian mountain gazelles (*Gazella gazelle*) were administered ketamine 9.3–12.2 mg/kg and xylazine 11.7–15.2 mg/kg IM (Foster 1999). Blackbuck (*Antilope cervicapra*) were administered ketamine 2 mg/kg and xylazine 0.25 mg/kg with reliable anesthesia in 5–7 minutes (Sontakke et al. 2009). Zoo-housed juvenile Thomson's gazelles (*Eudorcas thomsonii*) were administered ketamine 4.9 mg/kg, medetomidine 0.04 mg/kg, and butorphanol 0.40 mg/kg by hand injection following brief restraint (Chittick et al. 2001). Animals became recumbent by 8 minutes post injection. Physiological monitoring revealed hypoxia, bradycardia, and hypoventilation.

The animals were standing 12 minutes following administration of atipamezole 0.2 mg/kg and naltrexone 0.02 mg/kg. Alternatively, if ultra-potent opioids are unavailable, tiletamine-zolazepam 4 mg/kg and medetomidine 0.4 mg/kg intramuscular has been recommended (Pas 2014). Table 53.3 can be used as a starting point for selection of a suitable anesthetic induction protocol, but drug availability, institutional experience, personal preferences, conference proceedings, and published protocols should also be used to augment the decision-making process for induction drug selection.

Additional Induction Considerations

Underdosing an antelope, especially if free-ranging or in a large field exhibit, can have catastrophic consequences such as prolonged induction resulting in hyperthermia and subsequent morbidity or mortality due to exertional myopathy. Underdosing can be due to inaccurate weight estimates, ineffective drug or dose selection, or partial drug administration due to poor dart placement, lack of muscle penetration, or darting at too high a velocity, resulting in a "bounce and spray," whereby the dart might penetrate tissue, but the recoil from the skin, muscle, or bone is so powerful that the dart bounces out before complete injection. If a partial anesthetic injection is suspected, the anesthetist should immediately start considering repeat darting, supplementation options, and initiate discussion with supporting personnel on opportunities to position the anesthetist to administer a second dart. In some cases, a patient may receive a partial injection, but the anesthetist is unable to get close enough to administer a second dart. In these instances, visual of the animal should be maintained in case more complete induction occurs over time, conspecific or enclosure-mates aggression occurs, or the animal is nearing a hazard (water or rocky cliff). If a partial injection is suspected and a patient is not progressing towards recumbency by 8 minutes post darting with an ultra-potent opioid based protocol, it is unlikely that complete induction will occur. In these instances, a second dart is usually necessary. Most cases of partial injections are due to poor dart placement or darting at too high a velocity, resulting in a "bounce and spray" and it is nearly impossible to estimate the percentage of induction agent that was administered in these instances. As such, it is recommended that the second dart contain at least 50% of the initial immobilization dosage and in many cases using 100% of the initial immobilization dosage is recommended (Morris 2001). Repeated underdosing or partial injections often results in a prolonged procedure and potential catastrophic consequences due to excessive running, hyperthermia, and myopathy. Strong consideration should be given to placing an intravenous catheter and hospitalizing patients that experience prolonged inductions due to partial injections or "bounce and sprays."

When using an anesthetic induction combination of an ultra-potent opioid and alpha-2 agonist, antelopes may become recumbent with decreased consciousness, but still have the ability to kick, control their head, and attempt to rise early in the course of induction. Oftentimes it is necessary to secure the head of the animal to position it appropriately with the nose pointed down to mitigate the risk of regurgitation and subsequent aspiration or to prevent the patient from injuring themselves on habitat features. When this pattern of induction is observed, it is suspected to be because the anesthetic effects of the ultra-potent opioid are beginning to take effect before the alpha-2 agonists exert their effect (Allen et al. 1991). If the personnel and patient are in a safe position, often waiting a few minutes allows for the alpha-2 agonist effects to increase will result in a safely anesthetized animal without the need for supplemental intravenous anesthesia. With experience, an anesthetist will get a better feel for instances where time alone is needed to allow for the alpha-2 agonists to exert effects or supplementation in the form of ketamine or propofol is required.

Respiratory improvement following administration of butorphanol to an ultra-potent opioid based protocol has not been well described in antelopes, but has been noted to improve respiration and reduce apnea by some authors (Pas 2014). It is suspected that the improvement in respirations is mediated through antagonism of the μ opioid receptor, but this has not been investigated as completely in antelopes as in other species (Bush et al. 2012). Similar to other veterinary patients, when using ketamine as part of the anesthetic induction protocol during antelope immobilizations, disorientation and inability to stand can occur if antagonists are administered to the animal before ketamine has been metabolized. The severity of disorientation at recovery is dependent on the procedure time and dose of ketamine administered. When ketamine doses >1 mg/kg are used, anesthetic reversal of the other drugs in the protocol should be avoided until 20–30 minutes after darting if possible.

Xylazine has been associated with significantly reduced uterine artery flow and increased uterine vascular resistance in late-gestation cows (Hodgson et al. 2002). In pregnant sheep, xylazine resulted in doubling of myometrial activity and decreased fetal diaphragmatic electromyographic activity (Jansen et al. 1984). The impacts of xylazine on the fetal–maternal unit in Antilopinae have not been studied, but consideration should be given to the impacts of xylazine on pregnant patients.

Maintenance and Monitoring

Intubation

Intubation should be considered for anesthesia of Antilopinae to mitigate the risk for aspiration and allow for positive pressure ventilation. While preparing for intubation, patients should be provided supplemental 100% oxygen via nasal cannulation with a red-rubber catheter or a face mask. For field immobilizations, portable compressed oxygen (E tanks) works well. Intubation of Antilopinae can be challenging due to their narrow dental arcade, limited ability to open the mouth compared to other species, oral debris and secretions from cud chewing, distally placed pharynx, and horns that can limit full neck extension in some species. Consideration should be given to the following that will help facilitate intubation of Antilopinae:

1) Proper anesthesia depth: Consider supplementation if the animal is moving its head, the mouth cannot be fully opened, gentle traction is insufficient to allow for the rostral aspect of the tongue to be pulled out of the oral cavity, or the animal is chewing or swallowing. Supplementation is often easiest in the form of inhalant anesthesia using a face mask or an intravenous bolus of an anesthetic such as propofol.
2) Move the animal to a flat location that is at an appropriate height for the individual intubating. Consider placing on a gurney or truck lift gate to get the patient off the ground.
3) Have all intubation equipment available and within reach. This should include the following (Fig. 53.9):
   a) The anticipated endotracheal tube and a size smaller and larger (Table 53.4).

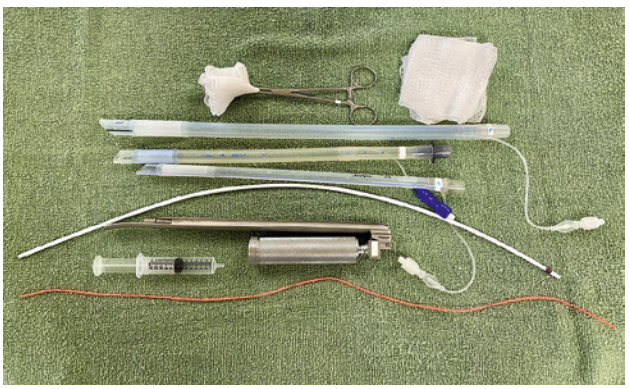


Figure 53.9 The equipment that should be available for intubation: the anticipated endotracheal tube and a size above and below, a polypropylene stylet, dry 4 × 4 gauze, a long-handled hemostat with 4 × 4 gauze attached, a laryngoscope, a cuff syringe, and material to tie in the endotracheal tube once placed.

Table 53.4 Endotracheal tube sizes for commonly anesthetized adult Antilopinae.

Common Name	Scientific Name	Endotracheal Tube Size (mm)
Springbok	*Antidorcas marsupialis*	7–9
Blackbuck	*Antilope cervicapra*	7–9
Thomson's gazelle	*Eudorcas thomsoni*	7–9
Red-fronted gazelle	*Eudorcas rufrifrons*	7–9
Speke's gazelle	*Gazella spekei*	7
Slender-horned gazelle	*Gazella leptoceros*	6–8
Gerenuk	*Litocranius walleri*	6.5–8.5
Dama gazelle	*Nanger dama*	8–9
Grant's gazelle	*Nanger granti*	8–11
Soemmerring's gazelle	*Nanger soemmerringii*	9–10
Kirk's dik-dik	*Madoqua kirkii*	4.5–6
Klipspsringer	*Oreotragus oreotragus*	5
Steenbok	*Raphicerus campestris*	4

   b) A laryngoscope with a confirmed working light. In many cases an adequate laryngoscope blade is longer and narrower than anticipated compared to other species of similar weight.
   c) A polypropylene guide stylet or a similar stylet that is of a small diameter and rigid enough to be inserted between closed arytenoids. The stylet should be twice as long as the endotracheal tube.
   d) Dry 4 × 4 gauze to digitally grasp the tongue to allow for gentle rostral traction.
   e) A long-handled hemostat with 4 × 4 gauze to swab the oral cavity of accumulated debris or saliva that might preclude visualization of the distal oropharynx.
   f) String or kling to tie in the endotracheal tube once placed.
   g) A syringe to inflate the cuff of the endotracheal tube following intubation.
4) Place the entire animal in ventral recumbency, including the hips.
5) Have an assistant fully extend the head and neck. This will align the oral cavity, pharynx, and trachea in the dorsal ventral plane, and improve visualization and passage of the endotracheal tube through the arytenoids (Fig. 53.10).

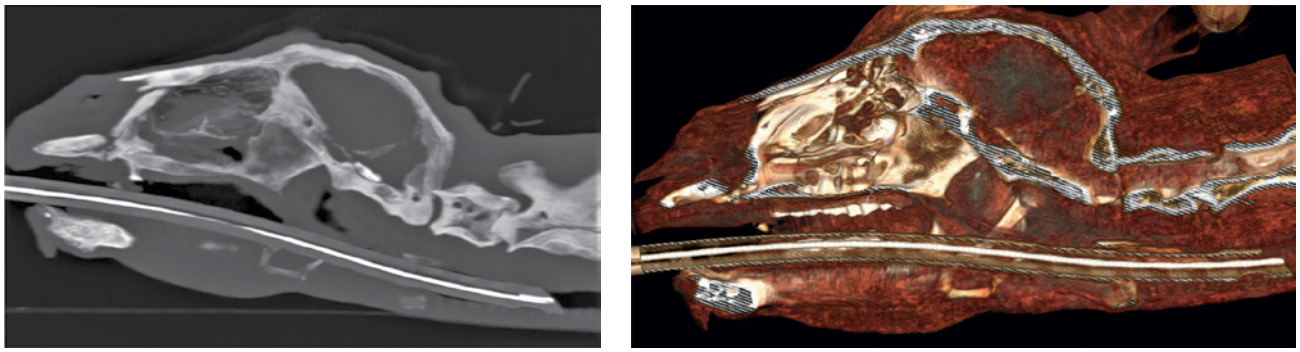


Figure 53.10 A skull and rostral cervical computed tomography reconstruction of an intubated Grant's gazelle (*Nanger granti*) with the head and neck extended. This figure demonstrates the proper position for intubation. In this position, the oral cavity, pharynx, and trachea are in the same dorsal ventral plane, which facilitates visualization and passage of the endotracheal tube.

6) Gently advance the laryngoscope between the dental arcades in a caudal direction. The authors intentionally keep the distal tip of the laryngoscope blade in the dorsal aspect of the oral cavity along the soft palate during advancement and slowly rotate the tip of the blade in a ventral direction once at the level of the epiglottis. This helps prevent moving debris in the oral cavity into the distal pharynx and assists in displacing the epiglottis from the soft palpate if it is dorsally displaced (Fig. 53.11).

Adhering to these considerations and having the proper equipment available and in working order results in successful intubation, even in animals with pharyngeal pathology. Blind intubation is rarely successful. Endoscopic assistance can be considered if the anesthetist is inexperienced, but this approach is rarely needed for Antilopinae. Direct visualization of the endotracheal tube placed between the arytenoids is difficult, but intubation can be confirmed by providing a breath and ausculting the lung fields for air flow, attaching a capnograph to document expired carbon dioxide, observing fogging or condensation in the endotracheal tube, or temporarily placing a small instrument on the end of the endotracheal tube that produces an auditory sound when expired air is passed through

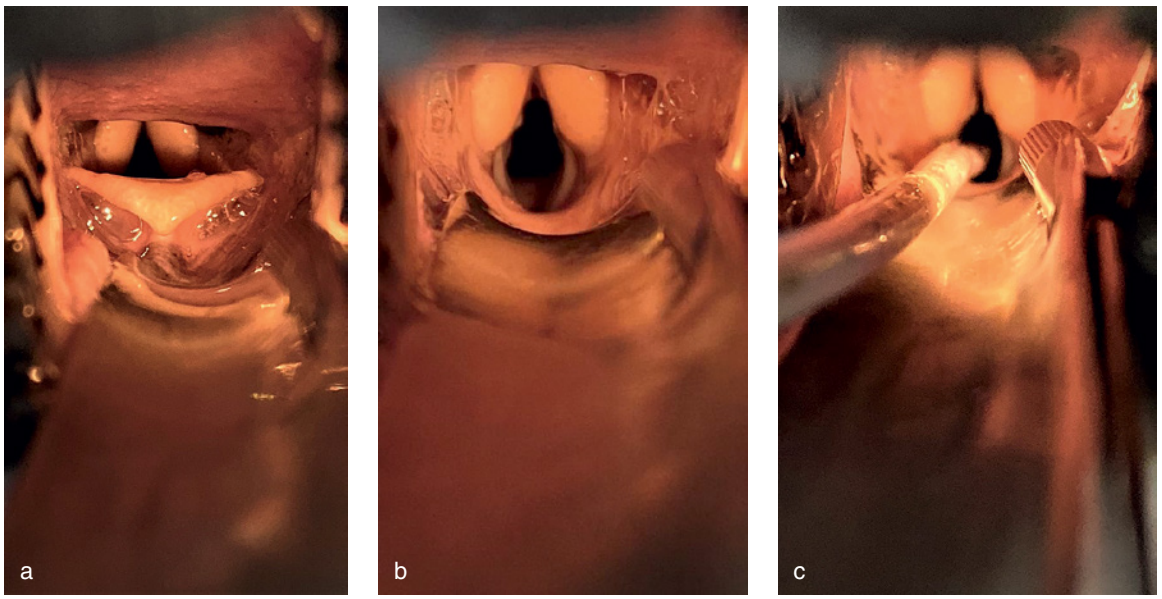


Figure 53.11 Intubation of a properly positioned slender-horned gazelle (*Gazella leptoceros*). (a) The most frequent appearance of the distal pharynx when a laryngoscope is initially placed in the oral cavity. Note the position of the epiglottis obscures clear visualization of the arytenoids. (b) Improved visualization following placement of gentle pressure on the distal tip of the laryngoscope resulting in ventral deflection of the epiglottis and clear visualization of the epiglottis and proximal trachea. (c) Passage of a polypropylene stylet into the proximal trachea. The endotracheal tube is then passed over the stylet to facilitate intubation. Note the stylet needs to be approximately twice as long as the endotracheal tube to use this technique. If the stylet is shorter, the Murphy's eye of the endotracheal tube should be passed over the stylet.

the instrument. Esophageal intubation should be quickly identified and resolved to prevent gas distension of the esophagus and rumen, and limit the duration of time a patient has an unprotected airway.

Anesthesia Maintenance

Most anesthetic induction protocols used in Antilopinae do not require supplemental anesthetic agents to maintain loss of consciousness for short, nonpainful, and minimally stimulating procedures. However, for prolonged or painful procedures, supplemental inhalant or injectable anesthesia should be available. Isoflurane and sevoflurane are the most commonly used inhalant anesthetics. Minimal alveolar concentrations (MACs) have not been published for Antilopinae species, however MACs published for isoflurane and sevoflurane in sheep (1.42% and 1.92%) and goats (1.29% and 2.33%), respectively, can be used as starting points (Okutomi et al. 2009; Hikasa et al. 1998). Based on clinical experience, following induction using an injectable protocol, isoflurane can be administered to Antilopinae at 1–2% to maintain loss of consciousness for prolonged procedures. In most instances an anesthetist should be prepared to provide positive pressure ventilation to anesthetized patients. Ventilation can be provided using compressed oxygen and a demand value, manually ventilating by closing the pop-off value and manually insufflating with an anesthetic reservoir bag, or placing an animal on a mechanical ventilator. Compared to dogs and cats, early intervention with positive pressure ventilation is preferred due to the higher potential for gastrointestinal pressure against the diaphragm and subsequent early and more severe atelectasis. A propofol constant rate infusion administered at 0.4 mg/kg/min was delivered to adult Speke's gazelles (*Gazella spekei*), with depth and physiological variables compared to those administered isoflurane at 1–3% (Kleinschmidt et al. 2018). Animals maintained using a propofol constant rate infusions (CRI) had lower respiratory rates than isoflurane-maintained gazelles. However, gazelles anesthetized using a propofol CRI maintained blood pressure values closer to physiologically normal ranges when compared to those maintained with isoflurane. Kleinschmidt et al. concluded that propofol 0.4 mg/kg/min is an effective maintenance anesthetic when the animals are intubated and provided with intermittent positive pressure ventilation, and the use of a propofol CRI can be considered if inhalants are unavailable.

Patient Positioning

The anesthesia team should be aware of the head position of anesthetized Antilopinae at all times. Every attempt should be made to maintain the head above the rumen with the nose pointed down to discourage regurgitation and subsequent aspiration. A nose-down position allows for drainage of rumen contents out of the oral cavity if regurgitation does occur while the airway is unprotected. A lightweight towel and tape can be used to cover the patient's eyes to minimize visual stimulation and provide protection from dust and debris that may accumulate during transport or the procedure. The eyes should be lubricated similar to other veterinary patients. Long cotton-tipped applicators, 4 × 4 gauze attached to long-handled hemostats, and suction units should be available to clear the oral cavity of debris if regurgitation occurs. The animal should be placed on padding for the procedure and the anesthetist should be prepared to provide supplemental heat for procedures that are anticipated to last longer than 20 minutes. Antilopinae can be maintained in right lateral, left lateral, ventral, or sternal recumbency during procedures, but the anesthetist should monitor for rumen distension in all types of recumbency and consider altering the position to the sternal or contralateral position if distension is noted. If repositioning does not improve rumen distension, consideration should be made to passing an orogastric tube to relieve the distention and the patient should be intubated immediately to protect the airway from aspiration and allow for positive pressure ventilation. Trocharization through the left lateral body wall can be performed to relieve bloat in an emergency. Patients placed in dorsal recumbency often require positive pressure ventilation to prevent atelectasis and ventilating the patient early in the procedure should be considered. If positioning in dorsal recumbency is required, the position of the head should be maintained such that the nose is pointed down so oronasal secretions and passive regurgitated material is allowed to drain and accumulation in the caudal pharynx is prevented.

Monitoring

Cardiopulmonary monitoring in Antilopinae is similar to that in other veterinary species. Auscultation using a stethoscope can be used to monitor heart rate, rhythm, and character, along with bronchovesicular sounds. Nonintubated patients will frequently have referred upper airway noise noted during chest auscultation. Pulse oximetry probes can be placed on the tongue, cheek, or vulva. Capnography can be used to confirm intubation and monitor end-tidal CO_2. Indirect blood pressure can be obtained using a cuff placed on the forelimb or rearlimb. The tail for small Antilopinae species is too small for cuff placement. Arterial access for direct blood pressure monitoring is most easily accomplished using the medial metatarsal artery. This artery is superficial and relatively fixed at the dorsal



Figure 53.12 Arterial blood gas sampling from the medial metatarsal artery of a gazelle. The artery in this location is superficial, easily palpable, relatively immobile, and a preferred site for arterial blood gas sampling and catheterization for direct blood pressure monitoring.



Figure 53.13 (a) Location and appearance of the right jugular vein in an anesthetized Grant's gazelle (*Nanger granti*). Note that digital occlusion results in a prominent superficial vein. (b) Location and appearance of the lateral saphenous vein as it passes on the lateral surface of the tibia from cranial and distal to caudal and proximal.

aspect of the medial metatarsus (Fig. 53.12). Auricular arteries can be palpated, especially in larger patients, but catheterization is often limited by artery diameter and length. The mandibular artery can be used to palpate pulses and obtain samples for arterial blood collection, however the short length and mobility makes catheterization challenging. Digital pulse can be palpated between the heels of the hooves and fetlock on all four limbs. Monitoring anesthetic depth can be challenging in small patients because ventromedial globe rotation is unreliable and species with peri-ocular scent glands will continue to have palpebral responses at an anesthetic plane. Frequent evaluation of jaw tone and careful monitoring for changes in heart rate, blood pressure, and respiratory rate are valuable indicators of anesthetic depth in Antilopinae.

Vascular Access

The jugular, lateral saphenous, and cephalic veins are accessible in euhydrated adult Antilopinae (Fig. 53.13). In severely dehydrated animals and hypothermic neonates, jugular vein and lateral saphenous vein palpation can be challenging. If venous access cannot be readily established, consider actively warming the patient and providing subcutaneous fluids. These interventions often improve vascular accessibility. Indwelling catheters are most easily placed and maintained in the jugular vein and an 18-gauge catheter can readily be placed in patients >15 kg. The lateral saphenous or cephalic vein can be catheterized, most commonly with a 18–22-gauge catheter for procedures, but maintaining a catheter in this location in an awake patient is very difficult and not recommended. Briefly, for jugular vein catheterization the animal should be positioned in lateral recumbency with the neck supported, the lateral cervical area should be clipped and prepared in a sterile manner, and sharp dissection should be used to create a 1–1.5-cm skin defect over the jugular vein, while taking care to not lacerate the vessel. The jugular vein should be readily identifiable and catheterized. Care should be taken to secure the catheter and associated extension sets to allow for appropriate head and neck movement without tension placed on the fluidline when the patient extends its head or flexes to feed. Readers should refer to Lamberski and Fuller (2012) for detailed equipment and step-by-step instructions for indwelling catheter placement in nondomestic ruminants. Fluid correction (body weight in kg × percentage dehydration = liters of

fluids needed for correction) and maintenance fluid rate (60 mL/kg/day) are similar to small domestic ruminants. Smaller species, neonates, and those with ongoing losses, most commonly from diarrhea, will require increased maintenance fluid rates. Colloids and partial parenteral nutrition can be administered to Antilopinae.

Recovery

Antilopinae should be recovered in a dry, flat, quiet, dimly lit environment with close attention paid to removal of potential obstacles that might cause injury. Ideally the environment will have a nonskid flooring, padded walls, and the ability to monitor using a closed-circuit camera system. Animals should be placed in sternal recumbency with the head supported above the rumen and the nose pointed down. Prior to recovery, the anesthetist should confirm that the antagonists are drawn up, an ambu bag or compressed oxygen with a demand value is available to provide positive pressure ventilation, and a cuff syringe to deflate the endotracheal tube cuff is readily available. Extubating with a partially inflated endotracheal tube is recommended to mechanically remove accumulated material from the caudal oropharynx and prevent aspiration at anesthetic recovery. Consideration should also be given to having a long-handled hemostat with 4 × 4 gauze to swab the oral cavity if needed, ophthalmic rinse to maintain corneal hydration, and a laryngoscope in case complications are noted and re-intubation is necessary. When trailer or field recovery is necessary, the anesthetist should make certain the patient is directed away for potential hazards (physical objects or aggressive animals) and the trailer is on a relatively flat surface, well ventilated, and the temperature is appropriate. Small Antilopinae species may be recovered in crates. Species, drug induction and maintenance protocol, recovery location, and antagonist timing influence recovery behavior. In some instances, Antilopinae will quickly rise explosively with minimal warning while others will slowly regain head control and stand in a gradual, controlled manner. As such, the anesthetist should take care to avoid potential injury by maintaining control or avoiding the head, horns, and hooves. Patients induced with azaperone will often remain in sternal recumbency with head control during recovery. Commonly used dosages for anesthetic antagonists are provided in Table 53.5. Unless emergency anesthetic recovery is necessary, antagonists are administered intramuscularly (Mutlow et al. 2004).

Table 53.5 Anesthetic antagonists commonly used in Antilopinae.

Drug	Dosage	Comments
Naltrexone	50 mg of naltrexone for every 1 mg of thiafentanil or etorphine 2–5 mg of naltrexone for every 1 mg of butorphanol	Intramuscular administration recommended unless emergency recovery needed, intravenous can be used Suggested when using a butorphanol, ketamine, alpha-2-based protocol
Diphenorphine	2–3 mg for every 1 mg of etorphine	Koch & Burroughs (2012)
Atipamezole	5 mg of atipamezole for every 1 mg of medetomidine	
Yohimbine	0.125–0.25 mg/kg IM	Koch & Burroughs (2012)
Tolazoline	1–2 mg/kg	Given intramuscularly to reverse alpha-2 agonist in blackbuck (Sontakke et al. 2009)
Flumazenil	0.01 mg/kg IM	Rarely required in Antilopinae

IM, intramuscular.

Neuroleptics and Sedatives

Antelopes are herd animals and it can be assumed that they are least stressed when housed in groups. However, transport or veterinary intervention may necessitate housing individuals or groups of antelopes in an unfamiliar location. In these instances, husbandry considerations should strive to minimize the amount of stress, which may include limiting the following: visual, auditory, or olfactory exposure to predators, environmental and anthropogenic stimulation, and the time the animal is isolated from the herd. Practical considerations to accomplish these goals may include hospitalizing the patient in a quiet area of the hospital with minimal foot traffic, hanging browse or fire hose visual barriers that create hiding areas, providing calf hutches or a lean-to shelter for small species, using solid fencing or slats in chain-linked to minimize visual stimulation, and temporarily hospitalizing a con-specific if the animal under treatment is hospitalized for a noninfectious etiology. In some instances, even the most intentional husbandry modification may fail to adequately reduce the stress in an individual and pharmaceutical agents need to be considered. Refer to Chapter 1 on clinical pharmacology for detailed drug classification, mechanism and duration of action, indications, and potential adverse effects. In general, sedative, neuroleptic, and tranquilization options are dependent on geographic location, drug availability, and route of administration. Most dosing recommendations are empirical, with a paucity of

Table 53.6 Neuroleptic and sedative drugs used in Antilopinae.

Drug Class	Drug Name	Dosage (mg/kg)	Notes	Reference
Benzodiazepine	Midazolam	0.1–0.5	Can be used to calm neonate antelopes to facilitate initial nursing during hand-rearing	
	Diazepam	0.5–1	Ideally given IM 15 minutes before handling	Pas (2014)
Butyrophenone	Azaperone	0.5–2.5	Volume limiting if included in initial dart	Blumer (1991)
	Haloperidol lactate	0.1–0.3	Oral dose 0.5–1.0 mg/kg	Blumer (1991)
			Bongo given 1 mg/kg per os	Mikota (1999)
	Haloperidol decanoate	1.0–4.5	Most commonly used at 10×x the dose calculated for haloperidol lactate	Blumer (1991)
Phenothiazine	Acepromazine	0.05–0.25		Koch & Burroughs (2012); Blumer (1991)
	Perphenazine enanthate	0.1–0.5		Blumer (1991)
		3.5 IM	Mohor gazelle	Gonzalez et al. (2008)
Thioxanthene	Zuclopenthixol acetate	0.5–1	Multiple species dosed at 1 mg/kg	Ebedes & Raath (1995)
	Zuclopenthixol decanoate	2	Most commonly used at 4× the dose of zuclopenthixol acetate	
Serotonin modulator	Trazodone	10	Oral administration in domestic goats	Prud'homme (2019)
			Limited studies to date in nondomestic hoofstock	

published recommendations. However, the neuroanatomy and neurotransmitters of mammalian species are highly conserved and therefore human and domestic animal models can serve as a dosing foundation for Antilopinae. Table 53.6 highlights available drug options.

Adverse reactions following appropriate dosing in Antilopinae species are less common than in larger hoofstock, but the reader should be aware of potential adverse effects so recognition can be rapid and intervention can be pursued if necessary, especially in the case of accidental overdosing. The most commonly observed adverse effects in antelopes following treatment with midazolam, azaperone, and zuclopenthixol acetate are excessive sedation, reluctance to stand, and subsequent anorexia. In most instances, cessation of treatment is sufficient, but in some cases intravenous fluid support may be needed in animals that are overly sedate for multiple days following administration of high doses of zuclopenthixol and are not eating or drinking. The extrapyramidal symptoms of haloperidol have been well described in hoofstock with a variety of case examples (Zuba & Oosterhuis 2007). Briefly, the most common adverse effects following haloperidol administration include repetitive muscle movements of the face, mouth, and limbs, restlessness, inability to stand still, tremors, and muscle rigidity. These adverse effects should be addressed quickly as they rarely resolve without intervention and can intensify. The three mainstays of treatment include discontinuation or lowering the haloperidol dose, sedative administration if excitatory signs are predominant, and administration of an anticholinergic, most commonly parenteral diphenhydramine. Repeat treatment is often necessary and close monitoring should occur until there is improvement or resolution of clinical signs.

Complications and Other Considerations

Exertional Myopathy

Exertional myopathy can occur as sequelae to both physical and chemical restraint. The etiology of exertional myopathy is thought to be multifactorial and not always predictable (Paterson 2014). Certain species and specific high-stress individuals may be at greater risk. With both capture methods, the risk of myopathy increases with prolonged chase and time in-hand, severe exertion, chemical

immobilization, use of ultra-potent opioids, prolonged recovery, renarcotization, hyperthermia, confinement, and long transport times (Wallace et al. 1987; Anderson et al. 2016; Paterson 2014). Time to onset is variable (0–72 hours) and clinical signs can include pain, stiffness, muscle tremors, hyperthermia, depression, and myoglobinuria (Wallace et al. 1987). Clinical pathology may show acidemia, hyperkalemia, azotemia, and elevations in muscle enzyme values, including creatinine kinase and aspartate aminotransferase (Wallace et al. 1987; Paterson 2014). Lactate may be useful as a screening tool for myopathy and hypoxemia, and was found to be elevated in Speke's gazelles that were manually captured and restrained for anesthetic induction (Kleinschmidt et al. 2018). In a retrospective review of mortality in a Saudi Arabian captive population of Arabian gazelles housed in field enclosures from 1988 to 2011, myopathy was noted as a significant cause of death (2.8%) (Soares et al. 2015). Another publication noted a mortality rate as high as 40% two days post-capture in gazelles anesthetized with etorphine, prompting a switch to a ketamine-xylazine protocol that appeared to have fewer complications (Foster 1999). In a more recent mortality review from 27 US zoological institutions from 1996 to 2014, myopathy was considered an infrequent cause of death in gazelles (1.9%), with improvement attributed to better awareness of the condition and more effective prevention strategies (Anderson et al. 2016). Treatment is well described elsewhere, but typically consists of aggressive supportive care including fluid therapy (to prevent and/or treat myoglobinuric renal failure), analgesics, muscle relaxants, and antioxidants such as vitamin E and selenium (Wallace et al. 1987; Paterson 2014). Prognosis is usually poor.

Hyperthermia and Respiratory Changes

Hyperthermia and respiratory changes are other complications of restraint and can be precursory conditions to exertional myopathy. Antilopinae species can quickly become hyperthermic with restraint, even under ideal conditions. Dik-dik can readily become hyperthermic under brief manual restraint and will start panting heavily to compensate (Maskrey et al. 1978). Active cooling measures can be attempted, but it is often best to end the restraint as soon as possible. Hypoxemia is a particular concern with chemical restraint. Oxygen supplementation is always recommended, either intranasally or via intubation and ventilation. Animals may already be hypoxic from the initial exertion during capture and restraint, and this is often compounded by the respiratory depressant effects of the chemical immobilization agents, particularly the ultra-potent opioids. Dama gazelles immobilized with carfentanil were noted to have decreased arterial oxygen saturation (SaO_2) and relative arterial oxygen saturation (SpO_2) values, prompting oxygen supplementation (Schumacher et al. 1997). Thomson's gazelles anesthetized with medetomidine, ketamine, and butorphanol were supplemented with intranasal oxygen at 0.5–1.0 L/min due to frequent oxygenation saturations less than 90% (Chittick et al. 2001). While not a replacement for measuring arterial oxygen saturation, pulse oximetry may be useful to suggest trends in hemoglobin oxygen saturation (Schumacher et al. 1997). Pulse oximetry probe type (reflectance versus transmission) and chosen location (with consideration of tissue pigment and tissue perfusion) may affect the accuracy of this monitoring tool (Schumacher et al. 1997). Hypercapnia and respiratory acidosis are other potential complications of chemical anesthesia (Martin-Jurado et al. 2011; Chittick et al. 2001) and can be addressed with ventilation if needed.

Renarcotization

Renarcotization is possible when ultra-potent opioids are used for chemical induction. Carfentanil is the most common culprit (West 2007; Allen 1989) but the other ultra-potent opioids can also carry this risk. Thiafentanil is the least likely to cause renarcotization due to more effective reversal with antagonists. The individual patient, the patient species, ultra-potent drug choice, drug dose, route of injection, and antagonist protocol (antagonist choice, dose, and route) all may influence whether a patient renarcotizes. Nonetheless, renarcotization events remain unpredictable without clear indications of cause. In general, Antilopinae species do not commonly experience renarcotization. Addra gazelles and slender-horned gazelles have been reported to renarcotize (Allen 1996). Addra gazelles induced with carfentanil were less likely to renarcotize if reversed with naltrexone rather than nalmefene (Allen 1996). Vigilant monitoring during the recovery period (up to 72 hours) allows for early detection and treatment. Clinical signs are similar to those reported in other species, including lethargy, pacing, disorientation, and recumbency. Renarcotization can lead to additional complications, including hyperthermia, myopathy, metabolic derangements, increased vulnerability to attack, and death (Allen 1989). Treatment with intramuscular administration of additional opioid antagonist (e.g., naloxone or naltrexone) is usually effective (Schumacher 2008) but may need to be repeated depending on the severity and duration of clinical signs. Naltrexone is the recommended opioid antagonist due to its potency and extended duration of action (Mutlow et al. 2004). Recommended naltrexone doses for treatment of renarcotization are anywhere from

10 to 100 mg of naltrexone for every 1 mg of ultra-potent opioid used in the initial anesthetic protocol. Intramuscular administration via hand injection or darting is the most practical and effective route for treating most renarcotized patients.

Regurgitation and Aspiration

Antilopinae, like all ruminants, are at risk for regurgitation during restraint. Compromised patients requiring immobilization may already have rumen abnormalities or some degree of ileus, which increases the risk for regurgitation (Anderson et al. 2016). Additionally, manual restraint and recumbency can place increased pressure on the rumen. Chemical immobilization agents may contribute by decreasing lower esophageal sphincter tone and allowing gastrointestinal contents to reflux into the esophagus. The alpha-2 agonists and opioids can decrease gastrointestinal motility and lead to tympany and post-anesthetic ileus (West 2007). Induction protocols including alpha-2 agonists such as medetomidine or xylazine have been reported to produce moderate to profuse salivation (Chittick et al. 2001; Foster 1999). If the airway is not protected, aspiration and subsequent development of pneumonia is possible, especially under anesthesia (Duncan et al. 1997; Foster 1999). Bronchopneumonia was noted as the second most common cause of mortality in all gazelle species according to one study, with 45% of the pneumonia cases being directly related to a recent anesthetic procedure (ranging from 2 days to 3 weeks prior) (Anderson et al. 2016). To reduce regurgitation and risk for aspiration, it is recommended to avoid placing pressure on the rumen, position the animal in a sternal to semi-right lateral position, and elevate the head and neck above the rumen with the nose tilted down to direct regurgitated material away from the larynx. Additional prevention measures include appropriate fasting of the animal, minimizing induction and recovery times, intubating as soon as possible if needed, frequent suctioning of the oropharynx, and administering appropriate anesthetic antagonist drugs to decrease the potential for renarcotization (Anderson et al. 2016). Of particular note are sick gerenuk, which seem to be exceptionally prone to regurgitation and aspiration. In this species it is therefore recommended to consider performing a swift intravenous anesthetic induction under manual restraint immediately followed by intubation before a compromised gerenuk is moved.

Trauma

Trauma is an unfortunately common reason for restraint and anesthesia, as well as a potential complication of handling these animals. In one study, trauma was the most significant cause of death in multiple gazelle species (Anderson et al. 2016). Animals in open enclosures may collide with fence lines and other barriers or fall victim to aggression from exhibit-mates (Soares et al. 2015). Induction and recovery are very vulnerable times for the patient. Even under more confined and controlled conditions, limb fractures can occur during restraint and are often devastating injuries necessitating euthanasia (Foster 1999). Appropriate pre-planning for restraint accounting for the species and the enclosure is key to preventing and minimizing traumatic injuries.

Sudden Death

Sudden death under restraint and anesthesia is a risk and can occur for a couple of reasons. Acute stress in compromised animals under restraint may trigger a sudden catecholamine release, resulting in cardiac arrhythmia and death. Another scenario is sudden death after alpha-2 antagonist administration due to rapid vasodilatory effects. This is less likely to occur when the antagonist is administered intramuscularly rather than intravenously (West 2007).

Pre-existing Conditions

There are various common medical conditions in the Antilopinae species that may impact the success of a restraint procedure and require additional consideration. As indicated above, respiratory disease is a frequent finding (Anderson et al. 2016) and can affect patient stability under anesthesia. Patients may be weak and hemodynamically unstable if suffering from parasite-induced anemia and hypoproteinemia. Gastrointestinal diseases including rumenitis, abomasitis, and enteritis are common findings in most gazelle species and contribute to mortality (Anderson et al. 2016). Renal disease may be a reason for patient presentation and a challenge to manage under anesthesia. Amyloidosis has been documented in various gazelle species, including Soemmerring's, Grant's, and Speke's gazelles (Anderson et al. 2016). A hematuria syndrome has been reported in Grant's gazelles, but a cause has not been identified (Anderson et al. 2016; Georoff et al. 2009). Bladder rupture has also been documented (Wallace et al. 1987). Pregnant animals deserve extra consideration and caution before restraint and anesthesia due to risks to both dam and fetus. Xylazine can have an oxytocin-like effect on the pregnant uterus. For this reason, detomidine or medetomidine may be preferable in pregnant animals (West 2007). The nutritional status of an animal can also have an effect on their response to physical or chemical restraint. Anorexic animals or maternally

neglected calves may be hypoglycemic and dehydrated. Animals deficient in vitamin E or selenium may be more prone to exertional myopathy. These conditions should be assessed and treated accordingly.

Analgesia and Analgesic Techniques

Analgesic management using opioids is challenging in nondomestic hoofstock, including antelopes. Often an ultra-potent opioid is necessary for immobilization of antelopes (see Table 53.3) and an opioid antagonist is administered to facilitate recovery. Opioid antagonists have a high affinity for opioid receptors and exert effects by displacing the opioid agonists from these receptors, resulting in return to consciousness, but also reversal of opioid-induced analgesia. This often presents a clinical dilemma, as opioid antagonism is necessary to recover an animal from anesthesia, but occupation of this receptor can prevent agonist binding to receptors that provide analgesia. In cases where significant pain is considered likely, such as a fracture, a clinician can consider using a nonopioid-based protocol such as a dissociative and a benzodiazepine along with supplemental isoflurane or propofol to complete induction, thus circumventing the need for administration of an opioid antagonist postoperatively to facilitate recovery. This then allows for use of an opioid agonist or partial agonist to control intraoperative and postoperative pain. In many instances safe field removal of the animal without the use of an ultra-potent opioid is unrealistic and advanced determination of the level of pain due to a specific pathology is unknown prior to immobilization, so an induction protocol based on an ultra-potent opioid cannot be avoided. Buprenorphine (0.01–0.05 mg/kg) has been administered empirically to gazelles undergoing soft tissue and orthopedic surgery with no adverse effects, however pharmacokinetic and pharmacodynamics data are lacking. An excellent review of CRI used in zoological medicine is available in Fontenot et al. (2012), and drugs and doses provided can serve as a starting point for CRI use in Antilopinae. Lidocaine, medetomidine, or ketamine have been used separately or in combination in Antilopinae and other hoofstock for pain unresponsive to NSAIDs or buprenorphine.

Nonsteroidal Anti-inflammatories

Nonsteroidal anti-inflammatories (NSAIDs) are commonly administered to Antilopinae. Minimal pharmacokinetic or pharmacodynamic studies are available, so domestic hoofstock models are often used as a starting point. Flunixin meglumine is commonly administered at 1.1 mg/kg IV or IM, meloxicam at 0.2 mg/kg IV or IM or 0.5–1.0 mg/kg orally, carprofen at 2.2 mg/kg IM, and phenylbutazone at 4–5 mg/kg orally. NSAIDs should be used with caution in Antilopinae with evidence of gastrointestinal bleeding, bleeding disorders, dehydration and subsequent suspected poor renal perfusion, and animals with hepatic disease.

Regional and Local Anesthesia

Regional and local anesthesia should be considered when orthopedic or soft tissue surgery is performed in Antilopinae. Many techniques can be translated from domestic ruminants, for which there are excellent reviews (Edmondson 2016). Lidocaine 2% is commonly used because it is efficacious, readily available, and inexpensive. The maximum safe dose of lidocaine in small ruminants is 4 mg/kg, which is significantly lower than that reported in cattle (10 mg/kg). Maximum doses have not been evaluated in Antilopinae, so it is recommended to err on the side of caution and not administer more than 4 mg/kg.

Due to the diversity of skull and horn anatomy in Antilopinae species and uncertainty of innervation of the horn by the corneal nerve, a ring block around the base of the horn can be used when local anesthesia is desired for horn removal or wound care secondary to injury. Alternatively, descriptions of anatomy landmarks for zygomaticotemporal nerve blockade in domestic ruminants can be consulted, but adjustments will likely need to be made to account for anatomic variability. A well-illustrated description of the clinically important landmarks for mandibular and maxillary regional anesthesia has been reported in blackbuck (*Antilope cervicapra*) (Choudhary & Singh 2015).

Infiltration of the spermatic cord or testicles should be considered during castration. In gazelles the spermatic cord is palpable at the base of the scrotum. After shaving and cleaning, a needle can be used to deliver 1 mg/kg of lidocaine directly into the spermatic cord bilaterally. Alternatively, an intra-testicular injection can be administered to deliver local anesthetic directly into the testicular tissue, which will desensitize the spermatic cord. A Thomson's gazelle (*Eudorcas thomsonii*) received lidocaine split between the scrotal skin and spermatic cord prior to castration with no reported concerns (Chittick et al. 2001).

Laparotomy is another indication for local anesthesia that should be considered in Antilopinae. The most common indication is a Cesarean section using a para-lumbar approach. Similar to domestic ruminants, a proximal paravertebral, distal paravertebral, inverted L, or a line block can be considered. The authors most commonly use either a distal paravertebral block or an inverted L block as these do not require a high volume of local anesthetic and pose little risk

of complicating surgical incision healing secondary to local tissue infiltration. Briefly, a distal paravertebral nerve block is used to desensitize both the dorsal and ventral rami of spinal nerves T13, L1, and L2. This is accomplished by palpating the transverse processes of L1, L2, and L4, infusing lidocaine in a fan-shaped pattern dorsal to the transverse processes, pulling back the needle, repositioning ventral to the transverse process, and infusing lidocaine in a fan-shaped pattern. This provides desensitization of both the dorsal and ventral rami of T13, L1, and L2. An inverted L block is performed similar to domestic ruminants, with landmarks including the caudal aspect of the last rib and the ventral aspect of the lumbar transverse processes. For both procedures, consideration should be given to calculating a maximum lidocaine dose of 4 mg/kg prior to infiltration. Dilution can be performed if an increased volume is desired. Alternatively, a bupivacaine liposome suspension (NOCITA®) has been administered during incisional closure in small gazelles during Cesarean section at the recommended dose for dogs (5.3 mg/kg) with no adverse effects. Care should be taken when administering bupivacaine in gazelles to avoid intravenous injection. Presently the cost and limited shelf life once a vial of bupivacaine liposome suspension is punctured limits its use in most zoological institutions.

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54

Antelopes

Elizabeth E. Hammond and Holly J. Haefele

Introduction/Taxonomy

Although not a taxonomic designation, the term "antelope" describes a grouping of cetartiodactyla in the family Bovidae that vary greatly in size. This group also includes pronghorn (*Antilocapra americana*), but they are in their own family, Antilocapridae. Of the 91 antelope species almost one third are threatened with extinction (IUCN 2023). Anesthesia for gazelles, wild sheep and goats, and nondomestic cattle, including bison, is addressed elsewhere in this textbook. Manual and device-assisted restraint can help reduce anesthetic procedures, but the behavior, size, and strength of some species require anesthesia for safe management. Safety of personnel and the animal is paramount.

It is important to practice good welfare by reducing fear and stress, thus decreasing the incidence of capture myopathy and injuries. By maintaining detailed anesthesia and capture records and reviewing protocols, immobilization techniques can continuously be improved (Chinnadurai et al. 2016; Zeiler & Meyer 2017b).

Handling and Restraint

Manual capture and restraint are generally reserved for small, young, nonhorned, or very sick animals. A baffle board can be placed between the handler and the animal during catch-up to reduce the risk of injury to personnel. In small pens, antelopes may run into or jump the walls, which may result in traumatic injury. This must be taken into account when planning manual restraint. Mechanical restraint, such as a box, hydraulic squeeze, or drop-floor chute (Fig. 54.1), can be useful for quick, nonpainful procedures such as phlebotomy, hoof trimming, and TB testing, among other things (Cisneros et al. 2011; Palmer et al. 2017; Wirtu et al. 2005; Wolfe 2015). A drop-floor chute is used at one author's (E.H.) institution to deworm a herd of 150 blackbuck (*Antilope cervicapra*) in 1–2 days. Chutes require trained personnel to operate, and animal injuries may occur. Pre-procedure oral tranquilizers may limit injuries. Manual or chute restraint followed by intravenous (IV) induction can be helpful as it typically lowers the total amount of induction drugs needed. Intranasal xylazine has been used to help calm elk (*Cervus elaphus manitobensis*) restrained in net guns and may be useful in antelope species (Cattet et al. 2004). Training animals for hand-injection may facilitate anesthetic induction.

While this chapter focuses on immobilization of captive semi-free-ranging antelopes, information on wild animal capture techniques, including overviews of helicopter use, mass capture bomas, and net guns, is available elsewhere (Caulkett & Arnemo 2015; Kreeger & Arnemo 2018; Kock & Morkel 2021; La Grange 2021; McTaggart et al. 2021).

Field Immobilization

Prior to any immobilization, the capture team should discuss the procedure and perform a risk assessment. Factors to take into consideration include, but are not limited to, the following: water, geographic hazards, fences and other structures, ambient temperature, and behavior of other animals in the vicinity. Vehicles can be used to discourage animals from approaching bodies of water or other hazards, taking care not to chase the animals with the vehicles. Some species and even conspecifics will attack or simply approach an animal that is in the beginning stages of anesthesia. This may stimulate the animal and hinder induction. Other animals may simply be curious and approach the immobilization team. In this instance, it can be helpful to park vehicles strategically around the immobilized

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Figure 54.1 Drop-floor chute for manual restraint of an antelope. (a) Note the animal's eyes are covered with a blindfold and its legs are dangling. (b) There are hoses on the horns to protect the handlers, who are also wearing eye protection.

animal and capture team to create a corral barrier so that other animals are unable to approach.

A preoperative health assessment may include body condition scoring, evaluation of temperament and demeanor (is the animal habituated to people?), pregnancy and other health status, fecal evaluation, and weight estimate. Ideally, an exact weight and preanesthetic bloodwork would be available, but this is rarely the case in a field setting. It is better to overestimate the animal's weight because underdosing of ultra-potent opioids (UPOs) causes excitation and prolonged induction (Caulkett & Arnemo 2015). Additionally, because darting is stressful, higher drug doses are usually needed in this situation than with hand-injection (Ryeng et al. 2001). Subclinical illness may present unforeseen complications during or after anesthesia. Immobilization of antelopes is a dynamic process; a routine examination can quickly become an emergency. If there is availability to transition into a controlled clinical environment after induction, this is recommended. It is important to have as much ready as possible prior to the procedure to limit anesthesia time. A checklist of drugs and supplies needed for the procedure is beneficial.

Potential complications of a field immobilization include, but are not limited to, capture myopathy, hyperthermia, aspiration pneumonia, drowning, traumatic injury, and attack by other animals, including conspecifics. Aspiration pneumonia is a serious and often deadly consequence of regurgitation during anesthesia of ruminants. It is difficult to treat, so prevention is key. Following domestic ruminant recommendations, withholding grain for minimally 12–24 hours and water for 8–18 hours is ideal to minimize regurgitation and aspiration (Riebold 2015). However, fasting is often not possible in the wild or in captivity if there is an emergency or the animal is on pasture. Fasting neonates is not recommended due to potential hypoglycemia (Riebold 2015). In addition, the risk of regurgitation is lower when the young antelope is immobilized before it transitions to full ruminant status. Generally, in the authors' experience, concentrate is withheld for 24–48 hours but hay, pasture, and water are offered for most species without complication. Some larger species are more prone to regurgitation; this may be related to subclinical rumenitis (Ball & Hofmeyr 2014). In these species, such as greater kudu (*Tragelaphus strepsiceros*), roan (*Hippotragus equinus*), and common eland (*Tragelaphus oryx*), it is prudent to withhold grain for the maximum time possible and withhold water for 12 hours when possible. One author (E.H.) utilizes metoclopramide in the initial dart to reduce the chance of regurgitation during induction. Whatever remaining metoclopramide dose that did not fit in the dart is given on first approach of the anesthetized animal. Metoclopramide has a potential secondary benefit of improving blood oxygenation (discussed later) (Meyer et al. 2010).

Drug delivery is either remote, via dart gun, blow pipe, or pole syringe, or delivered by hand syringe if the antelope is already manually restrained or trained for hand-injection. Comprehensive reviews of darting systems can be found in other resources (Kock et al. 2021a,b; Kreeger & Arnemo 2018).

The first approach of an anesthetized animal is a critical time. Approach too soon, and the animal may not be fully anesthetized and try to stand. Darting or the use of a pole syringe may be a safer way to administer supplemental anesthesia. Wait too long to approach, and the animal could be compromised by regurgitation and aspiration, obstruction of airway, etc. Although technique for first approach is dictated by the capture team's experience, in general it is best to wait until the animal is recumbent with its head down, does not respond to loud noise and will be unlikely to rise. If possible, it is good to handle the animal prior to its rolling into lateral recumbency. Times to approach will vary by individual preference, immobilization drugs used, and species, among other things. It is important to reduce external stimuli by placing ear plugs and covering the eyes. Additional safety measures include strategically placing ropes to prevent the animal from kicking its legs if it arouses from anesthesia.

Proper positioning of the immobilized antelope is critical for preventing anesthetic complications. The animal should be placed in sternal recumbency with the head up, the nose down to allow for secretions/regurgitant to drain downward, and the neck stretched out, straight and unkinked, to open the airway. The head can be held by a member of the capture team or placed on a towel, low stool, or other similar object to reduce the strain on personnel. It is better for the antelope to be placed in right sternal recumbency because this puts less pressure on the rumen, thus reducing the chance of regurgitation (Ball & Hofmeyr 2014). Sternal recumbency also lessens the weight of abdominal contents on the diaphragm, thus improving ventilation and blood flow (Meyer et al. 2015). During prolonged anesthesia, bloating and tympany may occur. Supplies for passing an orogastric tube or trocharization should be readily available. Often the animal will belch when rolled from one side to the other. In most cases this will relieve the bloat, although regurgitation may occur. Ruminants should be maintained in sternal recumbency if they are not intubated due to the risk of regurgitation and aspiration if they are rolled onto their back.

In most cases it is prudent to intubate the antelope and place an orogastric tube if it is going to be placed in lateral or dorsal recumbency. In addition, thick padding should be placed under pressure points (i.e., the shoulder) to prevent muscle and nerve compression and reperfusion injury, especially in larger species.



Figure 54.2 Bull sable under anesthesia transported on a glide.

Moving the anesthetized animal can be performed using a stretcher or large animal Glide (Fig. 54.2). It is important to protect the handler from horns by placing horn protection, such as garden hoses, pool noodles, large syringe cases taped to the horn, tennis balls, etc.

Anesthesia Monitoring and Vascular Access

Anesthesia monitoring is critical because most of the anesthetic drugs used to immobilize antelopes can cause significant changes in physiology, including respiratory depression with hypoxemia and hypo- or hypertension. Although machines to monitor physiologic parameters are convenient and easy to use, they can be erroneous. It is best to rely on auscultation for heart rate, palpation of an artery to monitor pulse quality, rate and volume of thoracic excursions, mucous membrane color, and refill time. It is important to monitor trends. Even the color of drawn blood can help assess perfusion. Commonly used measures of anesthetic depth include presence/absence of swallow reflex, muscle relaxation and purposeful movements of head and limbs, palpebral response, and jaw tone (Riebold 2015). Pulse oximetry is commonly used for estimating oxygen saturation (SpO_2), and there are several

brands of portable, battery-powered pulse oximeters available. Pulse oximeters measure the amount of oxygenated hemoglobin based on infrared light absorption. They rely on blood pressure to differentiate between arterial and venous blood, therefore they are a monitor of peripheral pulse quality as well. Unlike arterial blood gas, pulse oximeters provide continuous monitoring. Placement of the probe is important, but ideal site placement may vary among species. Preferred sites have minimal hair and nonpigmented tissue (Haskins 2015). The tongue, pinna, perineum, vulva, tail fold, scrotum, anus, and prepuce are all possible sites for probe placement. Rectal probes are also available. In one study in impala (*Aepyceros melampus*) anesthetized with a UPO, placing the probe on the tail provided the most accurate and precise readings when the saturation values were greater than 90%; however, there was high variability in the readings (Mtetwa et al. 2020). Because pulse oximeters are calibrated for human or domestic dog parameters, they may not provide an accurate reading if the heart rate is too high or too low. Other factors that may interfere with the SpO_2 reading include excessive movement, dry or cold tissue, hypotension, and aberrant types of hemoglobin (e.g., methemoglobinemia). Dark/pigmented skin may hinder the pulse oximeter reading; using a scalpel to scrape away the most superficial layer of tissue may alleviate this. In most animals, hypoxemia is defined as SpO_2 less than 90% (Haskins 2015). Supplemental oxygen should be given during the immobilization, via either nasal cannula or endotracheal tube. Portable oxygen concentrators may be a good option for remote field conditions (Fahlman et al. 2012).

Arterial blood gas is the gold standard for oxygenation level and can be obtained most easily from the auricular or facial artery. Portable analyzers are commercially available, although in the authors' experience they may fail in the field due to high or low ambient temperature. An in-depth explanation of blood gas parameters is beyond the scope of this chapter, but monitoring trends is helpful during the immobilization event (Boyd et al. 2000; Fahlman et al. 2012; Haskins 2015; Zeiler & Meyer 2017a). Generally, the most significant risks during antelope anesthesia involve the respiratory system, so monitoring respiration, ventilation, and oxygenation is important. A basic understanding of the pharmacological effects on cardiopulmonary physiology is equally important. Hypoxemia can lead to hypoxic tissues, especially the central nervous system and myocardium, with severe consequences. Anesthetized ruminants are prone to V/Q mismatch resulting from altered blood flow, hypoventilation, and atelectasis from body position and the weight of abdominal contents on the diaphragm, which is worse in dorsal and lateral than sternal recumbency. Other causes of V/Q mismatch include low cardiac output, pulmonary edema, and hypotension. When V/Q mismatch is severe, oxygen supplementation does not help because blood is shunting past the alveoli (McDonell & Kerr 2015). Lactate is an indirect measure of microvascular perfusion and indicates anaerobic metabolism. It is often measured on portable blood gas analyzers. Lactate levels <2.5 mmol/L are considered normal in dogs and humans (Kohen & Hopper 2018). Lactic acidosis occurs when inadequate oxygen is delivered to cells, such as during severe hypoxemia, overexertion, regional hypoperfusion, and shock. Hypoxemia, overexertion, and hypoperfusion of large muscle bodies are all possible complications of antelope anesthesia. Ideally, an elevated lactate will begin to normalize with treatment including fluid therapy, oxygen supplementation, and/or repositioning.

Capnography is a way to measure carbon dioxide (CO_2) that is released on expiration, thus measuring ventilation, perfusion, and metabolism. There are several portable, battery-operated in-stream capnographs that are commercially available and are useful in a field setting. The animal must be intubated to obtain an accurate reading. If values rise above 50 mmHg, ventilation is inadequate and intermittent positive pressure ventilation (IPPV) manually or with a ventilator should be performed. A portable demand valve (Fig. 54.3) attached to an oxygen tank can be used to administer IPPV in the field, and for the largest antelope

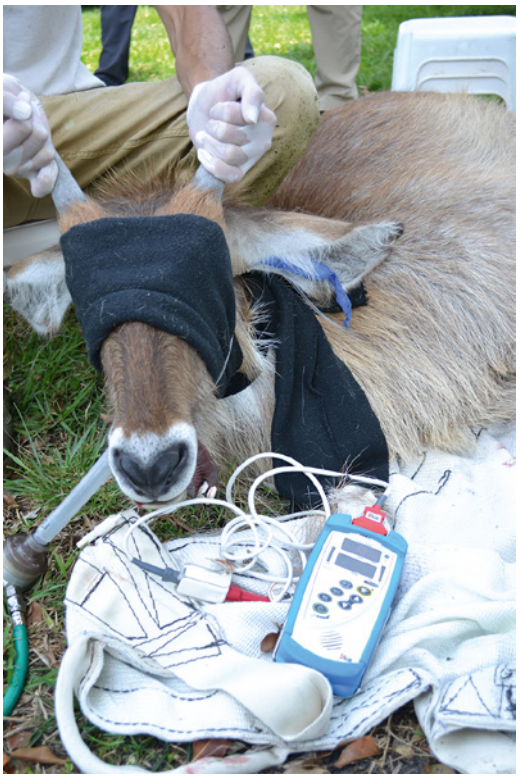


Figure 54.3 Juvenile waterbuck under anesthesia. The animal is intubated and is given intermittent positive pressure ventilation with the use of a demand valve.

(>350 kg) the Mega-vertebrate Demand Ventilator (aka Zubinator; www.incaseofanesthesia.com) can be used to provide assisted ventilation. As with all parameters, rechecking the equipment is important for ruling out a spurious result due to machine or operator error. The endotracheal tube (ETT) should be evaluated for a good fit; ETTs with cuffs that are leaking or that are too small may cause spurious CO_2 readings. Bloat and nonrespiratory gases from the rumen may also affect the CO_2 value. The Breathe Safe respiratory monitor is an audible tool for monitoring the respiration of intubated animals, beeping when the animal exhales. It also has an apnea alert, which is a continuous beeping sound that alerts personnel to cessation of breathing by the patient (Mama 2019).

Monitoring blood pressure during anesthesia is important for evaluating blood perfusion status. Direct blood pressure measurement using an aneroid manometer is an accurate way to obtain mean arterial blood pressures and can be done in the field (Haskins 2015; Mama 2019). This equipment is portable, inexpensive, fairly easy once practiced, and most antelopes have readily catheterized caudal auricular arteries (Fig. 54.4). Although less accurate, oscillometric indirect blood pressure is easy to obtain in the field and is useful for monitoring trends. However, poor agreement was found when comparing direct auricular and indirect oscillometric blood pressure in thiafentanil/xylazine anesthetized addax (*Addax nasomaculatus*) (Zalesak et al. 2022). Sites for cuff placement include distal limbs and tail. A general rule for selecting cuff length is one that is greater than or equal to 80% of the circumference of the appendage. The width of the cuff should be about 30–40% of the circumference (Haskins 2015). In general, excessive hypotension is defined as a mean blood pressure below 60 mmHg or systolic blood pressure below 80 mmHg. It can be corrected by IV crystalloid and/or colloid fluid shock bolus therapy, inotropic drug administration, and adjusting or antagonizing the immobilization drugs when possible (Kaiser-Klingler 2012). In contrast, hypertension is defined as mean blood pressure greater than 140 mmHg or systolic exceeding 180 mmHg (Haskins 2015). Hypertension is not uncommon, especially with protocols using medetomidine and/or thiafentanil. In one author's (H.J.H.) experience, sable antelopes (*Hippotragus niger*) immobilized with thiafentanil-medetomidine-azaperone and those immobilized with thiafentanil-xylazine had direct mean auricular blood pressures of 120–130 mmHg and 140–150 mmHg, respectively.

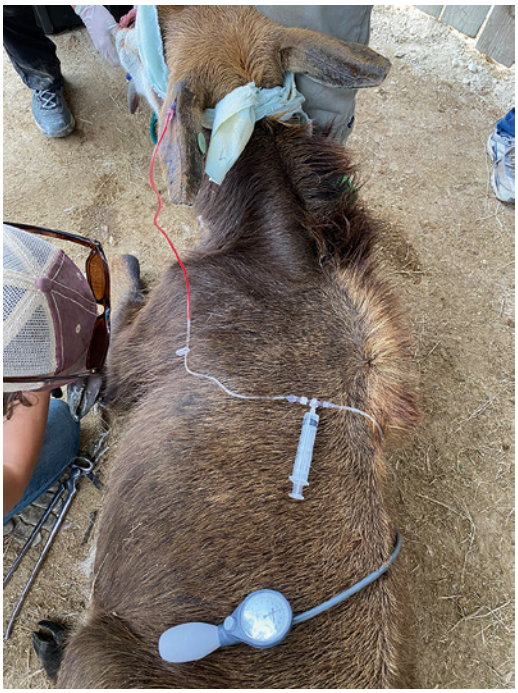


Figure 54.4 Photo of a field set-up of direct blood pressure on the auricular artery of an anesthetized sable.

Maintaining the animal's normal body temperature during the procedure is important. Although normal body temperature is not published for most antelope species, a study in blesbok (*Damaliscus pygargus phillipsi*) implanted with temperature-sensitive data loggers recorded a mean resting body temperature of 38.8°C (101.8°F) (Sawicka et al. 2015). Hypothermia can prolong recovery, and hyperthermia can be a medical emergency. Ambient temperature, stress level, quality of induction, and drugs used (especially alpha-2 agonists) have significant effects on body temperature (Meyer et al. 2008). Core body temperature can be obtained by an esophageal probe, but more commonly rectal temperature is used. However, when severe hyperthermia requires a cold-water enema for cooling, the rectal temperature is no longer accurate. In these cases it is important to take an axillary temperature prior to cooling and then monitor the axillary temperature for trends. Hyperthermia can be corrected by administering a cold-water enema, applying cold water topically, focusing on areas with high vascular flow, placing ice packs on the animal, or IV chilled fluid therapy (Sawicka et al. 2015).

Doppler and electrocardiography (ECG) are additional methods of monitoring anesthesia but are less likely to be used in a field setting. ECG is important if the animal has a cardiac arrythmia or if there is reason to believe the animal has an electrolyte imbalance.

Vascular access during the immobilization is important to provide intravenous fluid therapy to maintain blood pressure and perfusion. It is also important for emergency access for supplemental anesthetic and other drugs. Vascular access in antelopes is similar to domestic bovids, and the jugular, cephalic, and saphenous veins are good sites to use. However, the skin may be thick in some animals, and a surgical cutdown may be needed for catheterization. Long, large-gauge (14-gauge, 5.5-inch,

14-cm) catheters are appropriate for jugular vein placement in most antelopes. Short, small-gauge (18- to 20-gauge, 1–2-inch, 2.5–5-cm) catheters are better for peripheral veins or small, young antelopes. Injection of potentially tissue-irritating substances in the auricular vein should be avoided because extravasation can cause sloughing of the pinna. It is important to secure the catheter because it can easily dislodge when moving the animal during the procedure. Suturing or tissue adhesive around the catheter may be useful for the jugular vein, while tape is usually sufficient for peripheral veins. Auricular and facial vessels are ideal for obtaining small amounts of blood. Caution should be used if accessing a vessel in the back leg because the animal may reflexively kick if the anesthetic plane becomes light.

During anesthesia it is important to have emergency resuscitative drugs available, such as epinephrine, atropine, and doxapram. The latter may be used to stimulate respiration and can be injected sublingually in addition to intramuscularly if IV access is not possible. However, doxapram is mentioned less frequently in recent cardiopulmonary resuscitation protocols, and there is evidence that it decreases cerebral oxygen flow in laboratory animals and human infants (Pang 2015). In addition to reducing the risk of regurgitation, metoclopramide and other serotonin agonists have been reported to improve respiratory function and blood oxygenation in impala (*A. melampus*) anesthetized with UPOs (Meyer et al. 2010). Nitroprusside may also help with oxygenation by decreasing systemic and pulmonary vascular resistance and increasing cardiac output (Chapman et al. 2017; Lakhdhir et al. 2019). Another effective way to stimulate respiration is using the acupuncture philtrum point VG 26 (Jen Chung). A short, 25-gauge needle is placed in the middle of the nasal philtrum and gently turned (Janssens et al. 1979) (Fig. 54.5). In extreme emergencies, it is acceptable to reverse the anesthetic drugs, wake up the animal, and abort the procedure.



Figure 54.5 Acupuncture philtrum point VG 26 (Jen Chung) to stimulate breathing in an anesthetized eland.

Intubation

Intubation is recommended for longer anesthetic procedures, if the animal needs respiratory support, if the animal cannot be maintained in sternal recumbency, or if it is a species prone to regurgitation. Proper anesthesia level and restraint for ideal positioning are essential for intubation. The animal must be at a deep enough plane of anesthesia prior to intubation or swabbing the oropharynx; if the animal's anesthesia plane is too light, manipulation of the oral cavity may prompt active regurgitation (Riebold 2015). The head and neck should be extended into a straight line in alignment with the spine; in some species, the horns can be used as a lever to facilitate this. The mouth should be held open as wide as possible; common techniques include using gauze or rope to manually open the oral cavity or a mouth gag (Fig. 54.6). The oral cavity should be cleaned out using gauze attached to long forceps. Food may be hidden in the buccal pockets, so it is important to check this area too. A bite block placed between the dental arcades on one side will also protect the anesthetist from reflexive biting by the animal. However, this may also reduce the working space in the mouth, especially in animals with narrow muzzles.

Ideally, a laryngoscope will enable the operator to visualize the epiglottis and observe the ETT entering the trachea. A blade that is 250–350 mm will be adequate for smaller antelopes, but for larger antelopes, a blade up to 550 mm may be needed. If intubating in field conditions, a towel or blanket placed over the head of the clinician and animal's head will help block the ambient light to maximize the efficacy of the laryngoscope light. A semi-rigid stylet that has a narrow diameter can help guide the ETT into the trachea. As a general rule, the stylet should be three times the length of the ETT (Riebold 2015). It can be challenging to find long commercially available stylets. A simple stylet made of two cattle artificial insemination (AI) pipettes joined by tape or nonabsorbable suture is inexpensive and can be replaced often. Using tape to connect the pipettes has its drawbacks; not only is it difficult to disinfect, but it can also separate from the pipette, causing the stylets to



Figure 54.6 (a) Equine mouth gag placed on a gemsbok to facilitate opening of the mouth. (b) Example of field intubation of a sable. Note the brown gauze used to open the mouth, the long laryngoscope, and the stylet inside the endotracheal tube.

come apart. Commercially available 305-cm long, 8–10-mm diameter polyoxymethylene (plastic) rods are also useful for intubating large antelopes. Alternatively, 183-cm long, 4-mm diameter, fiberglass electrician wire fishing rods are inexpensive and readily available at hardware stores. For small or young antelopes with narrow oral cavities, such as wildebeest (*Connonchaetes taurinus*), the tip of the AI pipette stylet can be angled with heat for easier placement. The stylet is fed through the ETT and then placed directly into the trachea after visualization of the arytenoid cartilages (Fig. 54.7). If the epiglottis cannot be visualized, the tip of the laryngoscope or stylet can be used to elevate the soft palate, which in relaxed animals can obstruct the epiglottis. The tube can then be gently advanced into place. If there is difficulty advancing the tube past the larynx, try timing with inspiration, slapping the chest of the animal to stimulate a breath (using caution because it may cause eructation), rotating the tube, repositioning the neck, manipulating the epiglottis through the skin or applying a topical anesthetic to decrease the laryngeal reflex. For larger animals such as bull kudu (*T. strepsiceros*), manual orotracheal placement of the ETT may be faster. However, there is some risk to the operator, and a bite block placed between the teeth is recommended to protect the hand from reflexive biting.



Figure 54.7 View of the oral cavity of an antelope during intubation. The laryngoscope blade is covering the tongue and epiglottis. The soft palate is elevated by the stylet, revealing the arytenoid cartilage. Beyond the cartilage the tracheal rings can be observed.

Extubation can occur at the end of the procedure after reversal of the anesthetic drugs, once the animal has its head and is able to swallow. Prior to extubation, ensure that the animal is not bloated. Shifting the animal's weight to the opposite side can release ruminal gases. In some cases, it may be necessary to pass an orogastric tube to relieve bloat. It is recommended to clear the oral cavity of any regurgitated ingesta or saliva because secretions can be a problem once extubated (Riebold 2015). It may also be helpful to keep the ETT lightly inflated during extubation to pull out any ingesta that may have gone around the tube. Portable suction may also be useful in clearing out secretions.

Immobilization Drugs

Chemical immobilization is key for wildlife management, research, and conservation for both captive and free-ranging antelopes. Ideally, it is best to have drugs that are convenient to give, safe for personnel, minimize

cardiopulmonary effects, cause smooth, rapid induction and recovery, and provide reliable levels of immobilization (Williams et al. 2018).

Intramuscular (IM) placement of the immobilization drugs is important to ensure good absorption. Large muscle masses such as the biceps femoris, vastus lateralis, or triceps are good options for dart placement. Subcutaneous injection may cause a prolonged induction. Hyaluronidase helps to speed induction, which can be important in field conditions (Dittberner et al. 2015; Meyer et al. 2021). Not only will rapid induction reduce the risk of capture myopathy, but it can also prevent the animal from getting lost in its environment. An accurate weight for calculating anesthetic doses is preferred, but often an estimated weight is the only thing available. Anesthetic protocols may vary depending on the setting, species, individual, and drugs available, among other things. Safety of personnel and the animal is paramount, and the level of anesthetic depth may vary slightly for different procedures. For instance, a quick immobilization to move an animal to a different area may not require as deep of a plane of anesthesia compared to intubation and surgery. Institutional preference may also be a factor in dosing; some immobilization teams might prefer an animal in a deeper plane of anesthesia than others. Supplemental drugs, such as ketamine, propofol, alfaxalone, etc., may be required to ensure the animal is safe to handle.

Excellent reviews of chemical restraint in antelopes exist, and this chapter focuses on the basics and recent literature, including the use of non-UPO combinations, IV anesthesia, and several author-preferred protocols (Ball & Hofmeyr 2014; Burroughs et al. 2021; Hahn 2019; Kreeger & Arnemo 2018; Wolfe 2015).

Ultra-potent Opioids

UPOs are commonly used to immobilize antelopes because they provide fast-acting analgesia and sedation, are potent, can be delivered in a small projectile dart, and are reversible. When used alone, they can cause significant muscle rigidity, so they are often combined with other drugs to mitigate these effects. In addition, combining drugs from different classes may have a synergistic effect and reduce the amount of individual drugs needed. UPOs have significant side effects, such as respiratory depression. In some species, such as waterbuck (*Kobus ellipsiprymnus*), these drugs induce an excitatory phase during induction. It is more dangerous to underdose UPOs than overdose, as underdosing can result in prolonged induction and risk of overheating and capture myopathy, among other complications. It is recommended to use a full immobilization dose of UPOs when recumbency is not achieved in the expected time from the first dart, usually 10–15 minutes.

UPOs are dangerous to humans; human narcotic safety protocols should be available (Zuba & Greenburg 2019). These drugs are federally regulated in the United States and are Schedule II substances. Accurate record keeping, ordering, and storage of these drugs are mandatory and regulated by the Drug Enforcement Agency (DEA). Examples of UPOs include carfentanil, etorphine (M99), and thiafentanil (A3080). Although previously widely used in zoological and wildlife medicine, carfentanil is no longer available. Etorphine is a μ, κ and δ opioid agonist, is estimated to be 6000 times more potent than morphine, and is available in both 1 and 10 mg/mL formulations (Zuba & Greenburg 2019; Pfitzer et al. 2021). Thiafentanil is a newer UPO formulated at 10 mg/mL and has recently replaced carfentanil in North America. It is a pure μ agonist and has some advantages over related drugs. It has a shorter half-life than carfentanil and etorphine (Lance & Kenny 2012); if the animal is lost after darting, it may recover without reversal. Some animals have quicker induction times with thiafentanil, although some are dose dependent (Cooper et al. 2005; Pearson et al. 2020). Additionally, one study in impala (*A. melampus*) did not see a statistically significant difference in time to recumbency when comparing thiafentanil and etorphine immobilization. Thiafentanil also requires less antagonist for reversal, which may decrease the overall cost of the immobilization. In the authors' experience, etorphine and thiafentanil mg/kg doses are similar and they are used in a ratio of 1.7–2:1 when compared to carfentanil.

Non-ultra-potent Opioid Combinations

Non-UPO combinations may be preferable in species that are particularly sensitive to the deleterious side effects of UPOs. For example, impala (*A. melampus*) experience respiratory depression due to etorphine, and waterbuck (*K. ellipsiprymnus*) tend to run during induction (Gerlach et al. 2017). Although induction may be slower than with UPO combinations, some non-UPO protocols may provide longer anesthesia. This might be preferable with prolonged procedures, such as surgery. In addition, a non-UPO protocol may reduce the risk to the capture team. However, although not controlled in the United States, alpha-2 adrenergic (A2) receptor agonists are dangerous, especially concentrated medetomidine; human safety protocols should be available (Zuba & Greenburg 2019).

Depending on the situation, non-UPO anesthesia may not be as useful for immobilization of wild, free-ranging animals (i.e., helicopter immobilization) due to longer induction times, although hyaluronidase may improve this

(Semjonov et al. 2018). Also, rousability after recumbency may be observed depending on the combination (Harms et al. 2018).

Butorphanol is a non-UPO that when combined with A2 agonists, UPOs, dissociative anesthetics, and/or tranquilizers can enhance anesthesia, provide some analgesia, and minimize adverse effects. In addition to the small animal formulation, there is a commercially available, more potent formulation, which is attractive for use in remote darts. Butorphanol is a mixed agonist-antagonist and can be used to decrease the respiratory depression associated with the UPOs, especially in impala (*A. melampus*) (Buck et al. 2017). However, in one study (Gerlach et al. 2017), the butorphanol anesthetic combination had longer recumbency and reversal times in impala (*A. melampus*) than compared to one without it. Another study in captive Nile lechwe (*Kobus megaceros*) showed that a combination of butorphanol, detomidine, and midazolam produced safe and adequate anesthesia in this species with minimal cardiorespiratory changes (Laricchiuta et al. 2012). One author (E.H.) has used medetomidine, ketamine, butorphanol, and midazolam in *Kobus* sp. to good effect in a semi-free-ranging setting (see Table 54.1). Induction times are adequate, with minimal running around and excellent muscle relaxation. However, extreme relaxation of the soft palate may cause obstruction of the airway, necessitating intubation. Butorphanol is reversible, although in some cases it may be desirable to keep the analgesic effects of this drug post anesthesia.

Nalbuphine is a synthetic opiate receptor κ agonist/partial μ antagonist with analgesic and sedative effects. It is related to compounds such as butorphanol, but in the United States it is not regulated by the DEA. Although most published reports of its use are limited to non-antelope species, it may be a good option to combine with other drugs for anesthetizing antelopes (Wolfe et al. 2017). It may be cost prohibitive to use this drug in large animals.

Alpha-2 Adrenergic Agonists

A2 agonists have CNS depressant properties; this class of drugs is also a sedative, muscle relaxant, and analgesic. One advantage of A2 agonists is their reversibility (see Table 54.2). When used alone, they cause unreliable anesthesia in wild animals, so they are usually combined with other anesthetic drugs. Provided the animal is in a safe position, the handler should wait 10–15 minutes after darting and 2–5 minutes after recumbency before approaching because animals are more arousable initially than with UPOs (Jalanka & Roeken 1990). High noradrenaline levels can override the negative feedback mechanism of A2 agonists (Gerlach et al. 2017). A2 agonists impair an animal's thermoregulatory ability, which may result in hyper- or hypothermia (Caulkett & Arnemo 2015). While A2 agonists' cardiovascular effects (bradycardia, alterations in blood pressure) are of greatest concern to the anesthetized patient, respiratory depression from A2 agonists will increase when administered in combination with other commonly used anesthetic drugs, therefore oxygen supplementation is recommended (Rankin 2015). In sheep A2 agonists produce significant hypoxemia, associated with intra-alveolar inflammation and edema, and it is unclear if this response occurs in other ruminants (McDonnel & Kerr 2015). In addition, A2 agonists may cause premature labor or fetal hypoxia in pregnant animals (Depenbrock 2017; Rankin 2015).

Historically, the A2 agonist xylazine has been combined with an UPO to anesthetize antelopes (Ball & Hofmeyr 2014). It causes good muscle relaxation and some analgesia but can cause respiratory depression. It may take 15–20 minutes for full effect when given intramuscularly. This drug reduces gastrointestinal motility, including rumen contractions, and reversal should be considered even when sedative effects are not clinically significant after UPOs are reversed. Xylazine is commercially available as 100 mg/mL, but it is also sold in a more potent formulation (300 mg/mL). Due to recent illicit drug activity, xylazine may be controlled in certain areas.

Medetomidine is similar to xylazine but has more specific agonist activity (Citino 2007). It often induces bradycardia, and there is an initial increase and then decrease in blood pressure. There may be a peripheral vasoconstriction, which may make mucous membranes pale, making it more difficult for the pulse oximeter to gather a signal (Rankin 2017). Although anticholinergics such as atropine can counteract the bradycardia, they may also induce hypertension and tachycardia in dogs, and presumably in other species (Alibhai et al. 1996). Their use for A2 agonist-induced bradycardia is not recommended (Rankin 2015). Also, the anticholinergics are not as effective for reducing salivary secretions in ruminants; they may make secretions more viscous and harder to clear (Riebold 2015; Seddighi & Doherty 2016).

Dexmedetomidine is a racemic enantiomer of medetomidine that is marketed for small animal medicine and is used relatively interchangeably with medetomidine. It is more potent than medetomidine, but it is currently only available in a relatively dilute formulation, limiting its use to smaller antelope species (see Table 54.1).

Detomidine is another A2 agonist that can be used in combination with other drugs for antelope immobilization. There are reports of using it with etorphine for addax (*A. nasomaculatus*) anesthesia (Portas et al. 2003), with butorphanol and midazolam for Nile lechwe

Table 54.1 Drug doses for anesthesia induction protocols in selected antelope species (all doses are mg/kg, given intramuscularly, unless otherwise noted).

Common Name	Species	Weight (kg)[a]	Thiafentanil	Etorphine	Xylazine	Medetomidine	Dexmedetomidine	Detomidine	Azaperone
Addax	*Addax nasomaculatus*	F 114 M 120	0.035						0.34
			0.025		0.14				
			0.015			0.018			0.1
Arabian oryx	*Oryx leucoryx*	F 89, M 93	0.031		0.215				
			0.016			0.0175			0.109
			0.025						0.573
Blackbuck	*Antilope cervicapra*	F 30 M 39	0.05		0.28				
					0.51–0.66		0.012-0.016		
					0.25				
Blesbok	*Damaliscus pygargus phillipsi*	F 58		0.09					
		F 58	0.09						
		M 49+/−10, F 46.6 +/−7		0.05–0.09					0.68–1.0
		M 52.5–69.3, F 52.0–71.0				0.14			0.14
		F 55.5–60.0		0.09					±0.35

Acepromazine	Telazol®[b]	BAM™ (mL)[c]	Ketamine	Midazolam	Butorphanol	TTR min[d]	TTS min[e]	N	Reference	Notes
						2.7	7.6	57	Eddy et al. (2019)	Captive, electroejaculation study, isoflurane maintenance
						3.5	2.75	4	FRWC[f]	
						3.8	6.3	6	FRWC	
						3.1	3.1	22	FRWC	
						5	13.5	2	FRWC	
						4.5	4.2	17	FRWC	Same individual
						1.5	3.25	11	FRWC	
	2.5–3.3		2–2.6	0.06–0.8				Multiple	LCS[g]	Reconstitute 1 bottle of Telazol® with xylazine 100 mg (1 mL) and ketamine 400 mg (4 mL); do not reverse; prolonged recovery so recover in controlled environment (barn)
			2			5 to 7		22	Sontakke et al. (2009)	77 events; captive adults; tolazoline successfully reversed anesthesia within 0.5–1.5 min; yohimbine failed to antagonize the effects of xylazine
						2.48		8	Pfitzer et al. (2021)	Wild captured females in controlled environment; mild hypertension and hypoxemia noted
						2.16		8	Pfitzer et al. (2021)	Wild captured females in controlled environment; hypertension more signif but hypoxemia less than with etorphine
								14	Sawicka et al. (2015)	Male and female, captive, boma-housed, actual weight
					0.34	9.6 (5.1)	4.8	9	Semjonov et al. (2018)	Male and female, private game farm, mild hypoxemia, bradycardia and mild hypertension noted; significantly reduced indution time (in parentheses) with hyaluronidase 113–152 units/kg; actual weight
								12	Gaudio et al. (2020)	Female, boma-housed, hypertension, deeper anesthesia with azaperone but more ventilatory impairment; oxygen supplementation recommended, actual weight

(*Continued*)

Table 54.1 (Continued)

Common Name	Species	Weight (kg)[a]	Thiafentanil	Etorphine	Xylazine	Medetomidine	Dexmedetomidine	Detomidine	Azaperone
Bongo	*Tragelaphus eurycerus*	F 220, M 300	0.029		0.1				
		150–200						0.15–0.2	
Common eland	*Taurotragus oryx*	F 270–340, M 400–500	0.04		0.79				
Gemsbok	*Oryx gazella*	F 195, M 225	0.031		0.13				
			0.02			0.02			0.13
		F 250	0.04						0.2–0.32
		138–240	0.022–0.045			0.022–0.045			
		150–180	0.036		0.11–0.13				
Greater kudu	*Tragelaphus strepsiceros*	F 160, M 270		0.04		0.047			
			0.03			0.04			
Hartebeest	*Alcelaphus buselaphus*	F 200, M 220		0.021	1.2				
	Sigmoceros lichtensteinii	138–245	0.021			0.008			
Impala	*Aepyceros melampus*	F 34.3–42.9	0.052			0.057			
		F 36.2–44.6		0.05		0.054			

Acepromazine	Telazol®[b]	BAM™ (mL)[c]	Ketamine	Midazolam	Butorphanol	TTR min[d]	TTS min[e]	N	Reference	Notes
						3.5	3.1	15	FRWC	
					0.13–0.15	N/A	N/A	2	Bouts et al. (2017)	Standing sedation
			0.42	0.02				13	LCS	16 anesthetic events, quick induction, 1 animal renarcoticized, metoclopramide given to some animals
						3.1	2.1	19	FRWC	Tachypnea observed in half of procedures
						3.6	4.9	16	FRWC	
			0.48–0.6	0.02–0.06		3.5	3	2	LCS	Late-term pregnant females in a barn setting, anesthesia sufficient for phlebotomy but required supplemental anesthesia
			200 per animal			3.3	5.3	18	Grobler et al. (2001)	Free-ranging, thiafentanil and medetomidine had a wide dose range
						2.7	2.6	12	Kilgallon et al. (2010)*	Hypertension noted (indirect measurement), actual weight
			0.94					24	LCS	44 anesthestic events, run around during induction, add metoclopramide up to 0.2 mg/kg to dart to reduce risk of regurgitation
			0.9					3	LCS	One fatal event due to aspiration pneumonia - animal was not fasted and metoclopramide was not used; subjectively, induction was not shorter with thiafentanil
			1					3	LCS	Five events, one was hyperthermic - slow induction?
			1.1			3.5	1.8	13	Citino et al. (2002)	Boma-captured, moderate hyperthermia, hypoxemia, hypoventilation, and hypertension noted (all mild), actual weight
						12.2		10	Zeiler & Meyer (2017c)	Adult, wild-caught females in outdoor boma, more apnea compared to etorphine protocol, butorphanol improved breathing and relaxation, hypoxemia noted, actual weight
						14.5		10	Zeiler & Meyer (2017c)	Adult, wild-caught females in outdoor boma, butorph given to some impala due to apnea, hypoxemia noted, actual weight

Table 54.1 (Continued)

Common Name	Species	Weight (kg)[a]	Thiafentanil	Etorphine	Xylazine	Medetomidine	Dexmedetomidine	Detomidine	Azaperone
		F 22–39		0.015					
		F 22–39				0.109			
		F 33–41	0.09						
		F 33–41		0.09					
		F 50, M 60		0.022	0.43				
Nile lechwe	*Kobus megaceros*	28–70						0.2	
			0.028			0.026			
		60–140				0.07			
Nilgai	*Boselaphus tragocamelus*	180			1.43				
Nyala	*Tragelaphus angasii*	160		0.029		0.048			
		16.2–125				0.3			0.25
		16.2–125				0.17			0.22
		37–87	0.04–0.05			0.06–0.08			
Pronghorn	*Antilope americana*		0.1		±0.56				

Acepromazine	Telazol®[b]	BAM™ (mL)[c]	Ketamine	Midazolam	Butorphanol	TTR min[d]	TTS min[e]	N	Reference	Notes
0.15						7	3	9	Perrin et al. (2015)	Adult, zoo-housed females, good relaxation, actual weight
			4.4			17.5	6	9	Perrin et al. (2015)	Adult, zoo-housed females, unpredictable induction, hypertensive (direct blood pressure), actual weight
						2			Pfitzer et al. (2021)	Wild-caught, female boma-acclimated, faster induction but greater hypertension (direct) and decreased respiration than etorphine, hypoxemia, actual weight
						3.9			Pfitzer et al. (2021)	Wild-caught, female boma-acclimated, hypoxemia was less than with thiafentanil, actual weight
			1	0.15				6	LCS	11 anesthetic events, half of the animals received ketamine
				0.31	0.2	13.4	13.4	9	Laricchiuta et al. (2012)	Captive adults, two male, seven female, minimal cardiorespiratory changes, hyperthermia in three animals, actual weight
			1.84			<3		Multiple	S. Citino (pers. comm.)	Captive, semi-free ranging, prone to hyperthermia
			2.4	0.06	0.09	~5		24	LCS	36 anesthetic events, excessive relaxation may cause soft palate to obstruct epiglottis
	3.5			0.03				13	LCS	16 events, half of the individuals received midazolam
			0.95					4	LCS	12 events
					0.75	13.3	2.8	14	Black et al. (2020)	Hypoxemia, actual weight
						11.4	3.9	14	Black et al. (2020)	Alfaxalone 0.52 mg/kg substituted for butorphanol, longer induction than with thiafentanil, hypoxemia noted
			3.7			3.2–4.5	2.5	28	Cooper et al. (2005)	19 boma habituated (actual weight), nine free-ranging; ketamine 200 mg/animal, initial hypoxia
						<2.7	<0.7	31	Kreeger et al. (2001)	One male died in group without xylazine, muscle rigidity, rapid, shallow respiration

(*Continued*)

Table 54.1 (Continued)

Common Name	Species	Weight (kg)[a]	Thiafentanil	Etorphine	Xylazine	Medetomidine	Dexmedetomidine	Detomidine	Azaperone
						0.3			
		20.4–29.6				0.1			
								0.02–0.03	
		M 35.7–45.5						0.055–0.14	
Roan	*Hippotragus equinus*	F 250, M 275	0.025		0.1				
		90–275	0.01–0.03			0.005-0.006			
Sable	*Hippotragus niger*	F 182, M 227	0.03		0.12				
						0.11			0.1
			0.0162			0.0145			0.106
Scimitar horned oryx	*Oryx dammah*	F 140, M 150	0.035		0.17				
			0.02			0.019			0.15

Acepromazine	Telazol®[b]	BAM™ (mL)[c]	Ketamine	Midazolam	Butorphanol	TTR min[d]	TTS min[e]	N	Reference	Notes
			5						Kreeger & Arnemo (2018)	Captive
						1.25–1.3		10	Mama (2019)	Captive juveniles manually restrained, induced with either propofol or ketamine; hypoxemia, decreased arterial pressure (indirect), actual weight
	2.2–2.8		5.5–6.9					26	Miller (pers. comm.)	Adult males, modified boma technique, anesthetic drugs given IV; some animals were supplemented with propofol 0.36–1.1 mg/kg IV as needed; two mortalities (one human error, one due to regurgitation/aspiration)
			4.3–5.7		0.32–0.8			42	Miller (pers. comm.)	Adult males, modified boma technique, anesthetic drugs given IV; animals given azaperone IM were more tractable; two animals given higher dose of azaperone (20 mg) exhibited extrapyramidal signs that resolved with diphenhydramine administration; higher doses of butorphanol and detomidine needed when ketamine not used
						2.5	4.2	16	FRWC	
			0.3–0.6			2.5	8	20	Citino et al. (2001)	Boma-captured, wide margin of safety, actual weight
						2.1 ± 0.8	4.8 ± 3.3	34	Pearson et al. (2020)	Captive, semi-free-ranging
					0.28				Pearson et al. (2020)	Captive, semi-free-ranging
						2.6	12.6	10	FRWC	
						3.4	2.8	51	FRWC	Will often attempt to rise after initial recumbency
						3.2	16	5	FRWC	
		2.5 mL	0.67					21	LCS	59 events, excessive relaxation may cause soft palate to obstruct epiglottis; decrease medetomidine to improve breathing

(*Continued*)

Table 54.1 (Continued)

Common Name	Species	Weight (kg)[a]	Thiafentanil	Etorphine	Xylazine	Medetomidine	Dexmedetomidine	Detomidine	Azaperone
Waterbuck	*Kobus ellipsiprymnus*	F 182, M 240	0.028			0.03			0.13
						0.06			
Wildebeest	*Connonchaetes taurinus*	F 180, M 250	0.02		0.14				
			0.017			0.018			0.12
				0.01					0.1
				0.007					0.07

F, female; IM, intramuscular; IV, intravenous; M, male; N, number; N/A, not applicable.
[a] All weights are estimated unless otherwise stated.
[b] Telazol®: each vial contains 250 mg of tiletamine and 250 mg of zolazepam; label instructions recommend adding 5 mL of sterile water to reconstitute.
[c] BAM™: butorphanol 27.3 mg/mL, azaperone 9.1 mg/mL, medetomidine 10.9 mg/mL; mL amount per animal.
[d] TTR: time to recumbency from darting in minutes.
[e] TTS: time to standing from reversal in minutes.
[f] FRWC: Fossil Rim Wildlife Center; captive, semi-free-ranging setting.
[g] LCS: Lion Country Safari; captive, semi-free-ranging setting.
* Note doses are incorrectly written as ug/kg instead of mg/kg in the manuscript.

(*K. megaceros*) anesthesia (Laricchiuta et al. 2012), and for standing sedation in bongo (*Tragelaphus eurycerus erycerus*) (Bouts et al. 2017).

Romifidine is an A2 agonist that is approved for use in horses in the United States. There is one report of its use in sheep; it induced recumbency when used at a dose of 0.05 mg/kg (Coetzee 2021). It may prove useful in nondomestic ruminants and warrants further research.

Butorphanol-Azaperone-Medetomidine Combinations

BAM is a combination of butorphanol, azaperone, and medetomidine that is gaining in popularity. However, there is limited published information of its use in antelopes (Black et al. 2020; Semjonov et al. 2018). An extensive list of doses is available from Wildlife Pharmaceuticals and given in Kreeger and Arnemo (2018). One advantage of BAM is that it does not include UPOs. A fixed-dose combination (butorphanol 27.3 mg/mL, azaperone 9.1 mg/mL, medetomidine 10.9 mg/mL) can be purchased from Wildlife Pharmaceuticals with a veterinary prescription. It is reversed with atipamezole and naltrexone. Most premixed combinations are in a similar ratio, with some variations, and the volumes easily fit into a projectile dart (0.5–3 mL; Bush et al. 2012). If the veterinarian is preparing the combination, the ratios can be adjusted for the needs of specific species. The medetomidine doses are high in the commercially available formulation, but the azaperone may help mitigate the initial hypertension from medetomidine. Butorphanol is the only controlled drug in this combination, although potent medetomidine poses a risk to personnel (Zuba & Greenburg 2019).

Acepromazine	Telazol®[b]	BAM™ (mL)[c]	Ketamine	Midazolam	Butorphanol	TTR min[d]	TTS min[e]	N	Reference	Notes
						2.9	6.9	14	FRWC	
			1.8	0.048	0.06			40	LCS	68 anesthetic events, one died in recovery, excessive relaxation may cause soft palate to obstruct epiglottis, calm induction
						3	2.3	66	FRWC	
						3.7	6.1	8	FRWC	
		2.5–2.7 mL	0.95					13	LCS	16 events, calm induction
						5.38 (3.8, 3.5)		8	Dittberner et al. (2015)	Wild, boma habituated, significantly reduced indution time (in parentheses) with hyaluronidase 5000 or 7500 units
						4.46		8	Dittberner et al. (2015)	Wild, boma habituated, significantly reduced indution time with hyaluronidase 7500 units

Typically, inductions with BAM are controlled and smooth, with ~10 minutes to recumbency in blesbok (*D. pygargus phillipsi*) (Semjonov et al. 2018). If the animal is positioned safely, the capture team should wait several minutes after recumbency to handle the animal because it can be aroused with stimulation. Combining BAM with ketamine can lessen the chance of rousing. Muscle relaxation is usually quite good. Some animals are so relaxed that the soft palate obstructs the epiglottis, necessitating its elevation and/or intubation to improve oxygenation. Black et al. (2020) noted adequate anesthesia with BAM in lowland nyala (*Tragelaphus angasii*), but time to sternal recumbency was longer than with a thiafentanil-medetomidine-ketamine combination. This study documented hypoxemia despite SpO_2 levels >90%, thus oxygen supplementation is warranted. One author (E.H.) has used a combination of ketamine, butorphanol, azaperone, and medetomidine (KBAM) successfully in scimitar-horned oryx (*Oryx dammah*) and white-bearded wildebeest (*C. taurinus*) in a field setting (see Table 54.1). Anecdotally, the animals experience a calmer induction with less running as compared to UPO protocols.

Other Nonopioid Drugs

Ketamine is a controlled, cyclohexamine dissociative anesthetic agent that is used in combination with other drugs, such as A2 agonists and benzodiazepines. It is not reversible and is cardioprotective but may lower the seizure threshold. It causes minimal respiratory depression (Berry 2015). Ketamine is often helpful to supplement anesthesia or to facilitate intubation when the anesthetic plane is too light. Because it cannot be reversed, adequate time after administration of ketamine must be given prior

Table 54.2 Antagonist drugs and doses for use in antelope.

Antagonist	Drug that is Reversed	Dose	Administration	Comment	Reference
Atipamezole	Medetomidine	5× dose	IM	Resedation has occurred in giraffe immobilized with medetomidine	Delk et al. (2019)
	Detomidine	1.5× dose	IM		Bouts et al. (2017)
	Xylazine	0.1× dose	IM		Jalanka & Roeken (1990)
Butorphanol	Opioids		IV or IM	Mixed agonist-antagonist	
Diprenorphine	Etorphine	1.3× dose	IV or IM	Renarcotization has been seen, more rapid reversal with IV	Allen (1989); https://www.chemeurope.com/en/encyclopedia/Etorphine.html
Flumazenil	Benzodiazepines	0.02 mg/kg	IV	Can be given IM when IV access is unavailable; may be effective at lower doses (6 μg/kg)	Yavuz et al. (2021)
Naloxone	Opioids		IV or IM		
Naltrexone	Carfentanil	100× dose	Half IV, half IM	Can be given all IM	Lance & Kenny (2012); Wolfe (2015)
	Etorphine	50× dose	Half IV, half IM	Can be given all IM	Lance & Kenny (2012); Wolfe (2015)
	Thiafentanil	10–30 x dose	Quarter IV, three-quarters SC	Can be given all IM	Lance & Kenny (2012); Wolfe (2015)
	Butorphanol	5× dose	IM		
Tolazoline	Xylazine	2–3 mg/kg	IM	May cause adverse effects at high doses and IV, restores rumen activity sooner	Kreeger & Arnemo (2018); Mortenson & Robison (2011); Riebold (2015); Wolfe (2015)

IM, intramuscular; IV, intravenous; SC, subcutaneous.

to reversing the other anesthetic drugs, generally 30 minutes after IM injection and 20 minutes after IV injection. If other protocol drugs are reversed too soon after administration, ketamine can contribute to a rough recovery due to the antelope stumbling and falling when attempting to rise. Tiletamine is another dissociative anesthetic that is only available in combination with zolazepam (Telazol®, Zoletil™).

The benzodiazepines, such as midazolam, diazepam, and zolazepam, promote muscle relaxation and may prevent seizures, in addition to treating them. They are controlled and do not provide analgesia. Midazolam has rapid absorption when given intramuscularly and causes less pain on injection compared to diazepam (Rankin 2015). It is typically not used alone but is useful for supplemental anesthesia. Zolazepam is only available in combination with tiletamine under the brand names Telazol® and Zoletil™. Benzodiazepines can be reversed with flumazenil, although this is not usually necessary due to a short half-life. One author (E.H.) uses a Telazol®-ketamine-xylazine (TKX) combination for semi-free-ranging field immobilization of blackbuck (*A. cervicapra*). One bottle of 500 mg Telazol® (tiletamine 250 mg and zolazepam 250 mg) powder is reconstituted with ketamine 400 mg (4 mL) and xylazine 100 mg (1 mL) to make the TKX mixture. This combination is derived from one used for capturing wild cattle (Seddighi & Doherty 2016). Each milliliter of the combination contains 100 mg of Telazol®, 80 mg of ketamine, and 20 mg of xylazine. As per the manufacturer's label, Telazol® can be saved at room temperature for 7 days and refrigerated for up to 56 days, so presumably the TKX mixture can be stored the same way. The author stores this mixture in the freezer and thaws it as needed with no obvious changes to drug efficacy. To facilitate induction and recovery, dexmedetomidine and midazolam are also added to the dart (see Table 54.1). This protocol has the advantage of avoiding UPOs, thus reducing risks to the capture team. Recoveries can be prolonged, and animals are recovered in

a controlled barn setting overnight. Partial reversal of this protocol with atipamezole should be avoided in most blackbuck because it can lead to rough recoveries.

Propofol, a nonbarbiturate, nonsteroidal hypnotic drug, is useful as a supplemental IV drug titrated to effect to facilitate intubation, for example, but can also be used as total IV anesthesia. It causes respiratory depression, and it is recommended that the animal be intubated (Berry 2015). It is advantageous in many settings because the animal may have a rapid return to consciousness.

Alfaxalone is a controlled, neuroactive steroid labeled for IV use in the United States in dogs and cats in a 10 mg/mL solution. Its IV use has also been investigated in sheep, camelids, and goats (Riebold 2015; Dzikiti et al. 2014; Oakleaf et al. 2019). It also provides effective sedation when administered intramuscularly in cats, dogs, rabbits, swine, bighorn sheep, reptiles, and amphibians alone or in combination with other drugs. One publication describing IM alfaxalone use in combination with medetomidine and azaperone in lowland nyala (*T. angasii*) reported hypoxemia but adequate anesthesia for minor procedures (Black et al. 2020). Due to alfaxalone's relatively low concentration, its volume limits its use for remote darting (Hector et al. 2020). It may be useful as supplemental anesthesia, especially when intravenous access has not yet been established or to supplement parenteral or inhalant anesthesia (Riebold 2015). A novel 40 mg/mL formulation of alfaxalone has been investigated but may not be commercially available yet (Patterson et al. 2021).

Pronghorn Anesthesia

The American pronghorn (*A. americana*) occupies its own family and genera. It is a small antelope species native to North America, and its horns consist of a bony core with a keratinized sheath that is shed annually (Ball & Hofmeyr 2014). Historically, this species has been challenging to anesthetize due to its unpredictable nature and susceptibility to stress hyperthermia, and there is a dearth of published literature (Yoakum et al. 2014; Wolfe 2015). A carfentanil 0.05 mg/kg and xylazine 1 mg/kg combination has been historically recommended (Yoakum et al. 2014). Thiafentanil, with and without xylazine, has been used with good success, although muscle rigidity and rapid, shallow respiration were observed, and it is recommended that xylazine should be reversed (Kreeger & Arnemo 2018; Kreeger et al. 2001). Recent fieldwork suggests that A2 agonists such as detomidine and medetomidine combined with Telazol®, butorphanol, azaperone, and/or ketamine may be a safe alternative (Lance 2008; M. Miller, pers. comm.) (Table 54.1).

Reversal and Recovery

Reversibility is an important factor when choosing immobilization drugs, and this is one of the advantages of UPOs. Naltrexone is the veterinary-approved reversal that is most widely used to reverse carfentanil, etorphine, and thiafentanil. Typically, it is used at a ratio of 100 times the carfentanil dose, 50 times the etorphine dose, and 10–30 times the thiafentanil dose (Table 54.2; Lance & Kenny 2012; Wolfe 2015). In one study, goats given IM naltrexone were standing within 3.5 minutes of administration, and IV administration did not offer any advantages (Mutlow et al. 2004). Other reversal agents that can be used are naloxone and diprenorphine. Naloxone is a human-approved drug, but it is short-acting and less potent than naltrexone. Renarcotization has been more commonly seen with diprenorphine reversal of UPOs (Allen 1989). Butorphanol and other mixed agonist-antagonist opioids can be used to partially reverse some of the effects of the UPOs (Meyer et al. 2018). With UPOs, even a partial reversal dose will rouse the animal, so caution is needed.

The reversal of the A2 agonists is not always necessary but is often used if returning the animal to a group, or if the animal is predisposed to A2 agonist side effects or otherwise compromised. A2 agonists can be reversed with tolazoline, yohimbine, and atipamezole, preferably given intramuscularly. Tolazoline reverses xylazine and may restore rumen activity sooner than yohimbine (Kreeger & Arnemo 2018). Both tolazoline and yohimbine are nonspecific, so at high doses they may cause unwanted effects; tolazoline can cause apnea, hypotension, and seizures at high doses or when given intravenously (Mortenson & Robison 2011; Riebold 2015; Wolfe 2015). Although atipamezole is more specific to reversing medetomidine, it is also effective at reversing the other, less specific A2 agonists such as xylazine. However, it may be more cost effective to use tolazoline or yohimbine.

Flumazenil reverses the effects of the benzodiazepines. It is not very potent and is labeled for IV use. However, both authors have used it intramuscularly to good effect. Lower doses of midazolam do not usually need to be reversed with flumazenil. However, if an animal is still sedated after other reversals have been given, administration of flumazenil should be considered, as total doses of midazolam over 15–20 mg can be associated with prolonged recovery.

It is important to note that ketamine is not reversible; as previously mentioned, adequate time must be given to allow its effects to dissipate prior to reversing other anesthetic drugs to avoid a rough recovery.

The length of time of the anesthetic procedure should be minimized, ideally limiting it to ~60 minutes to produce the best outcome. If the procedure is longer than that,

additional anesthetic drugs should be available, and the limbs should be flexed and extended to minimize post-anesthetic myopathy-neuropathy (Riebold 2015). Inability to rise after prolonged anesthesia is not uncommon in severely debilitated antelopes and may be fatal.

For recovery, the area should be cleared of any obstacles or hazards to make it as safe as possible. The head should be held up with the nose down and the animal in a sternal position. Alternately, the head can be placed on a bale of hay and the body can be rested against the wall in a barn setting to reduce the risk to personnel if the animal rouses quickly. Ear plugs should be removed and the blindfold loosened. Once reversals are given, the horn protection can be removed. Once the animal starts to hold its head, the blindfold can be removed and the handler can leave the animal. It is imperative for the capture team to have an exit strategy, especially when working in an enclosed space. Typically, at least two exit routes should be identified and cleared of hazards to allow the capture team to leave quickly and safely. Reversal can be rapid, especially if the procedure was long and no supplemental drugs were given.

Despite the complete reversal of UPOs, renarcotization is a risk. Renarcotization occurs when the agonist outlasts the antagonist on the receptors, causing the animal to become resedated after initial recovery. Renarcotization may be dose dependent (Mutlow et al. 2004). Clinical signs vary but may include lethargy, pacing, head pressing, bruxism, high-stepping gait, and recumbency, among other things (Allen 1989; Mutlow et al. 2004). It is usually observed 2–6 hours post immobilization but may occur up to 24 hours later. It is most commonly observed with carfentanil and etorphine, less so with thiafentanil. The use of naltrexone and IM administration of UPO reversal has made renarcotization less common. Although not renarcotization, resedation has occurred with potent medetomidine at higher doses (Delk et al. 2019).

Standing Sedation

Standing sedation can be considered for certain procedures with experienced personnel. Small to medium-sized antelopes may be manually restrained in addition to the sedation. Large antelopes that are debilitated and require frequent care such as IV fluid therapy or radiographs may be candidates. Detomidine (0.15–0.2 mg/kg) and butorphanol (0.13–0.15 mg/kg) were used to successfully provide standing sedation in bongo (*T. euryceros*) (Bouts et al. 2017). One author (H.J.H.) has used butorphanol (0.1 mg/kg) and detomidine (0.1 mg/kg) for standing sedation in addax (*A. nasomaculatus*), sable (*H. niger*), and roan (*H. equinus*) to facilitate loading from a holding pen onto a trailer.

Low-dose opioid combinations combine an UPO, typically thiafentanil, with medetomidine and azaperone, or sometimes midazolam, often resulting in standing sedation in wild African antelopes. Animals are then roped, blindfolded, and walked onto a transport crate or trailer (Burroughs et al. 2021). It is possible these combinations may prove useful in a captive setting.

Tranquilizers and Sedatives

Tranquilizers and sedatives can assist with habituation to a new situation and help calm an animal prior to immobilization, among other things (Wolfe & Miller 2016). They can be classified as short-acting (azaperone, midazolam), medium-acting (haloperidol, zuclopenthixol acetate), and long-acting (perphenazine enanthate, fluphenazine) and thorough reviews are available (Citino 2007; Ebedes 1993; Read 2002). Haloperidol, a butyrophenone, is one of the most commonly used neuroleptic drugs in antelopes and can be given orally or parenterally. The oral dose is larger than the parenteral dose (see Table 54.3). Parenteral formulations of haloperidol include the shorter-acting lactate and the longer-acting decanoate form. Although haloperidol is considered relatively safe, side effects, including extrapyramidal signs, have been reported in some antelope species (roan [*H. equinus*], blesbok/bontebok [*D. pygargus*]) given parenteral haloperidol (Burroughs et al. 2021). Bongo are also sensitive to parental administration or higher oral doses in the author's (H.J.H.) experience. Diphenhydramine and diazepam have been used to treat this condition (Ball & Hofmeyr 2014; Wolfe 2015; Zuba & Oosterhuis 2007). A parenteral slow-release formulation of zuclopenthixol acetate has been used in blue wildebeest (*C. taurinus*) for a calming effect with no side effects (Laubscher et al. 2016) (see Table 54.3). Giving a short-acting (haloperidol lactate) and long-acting tranquilizer (perphenazine enanthate or zuclopenthixol acetate) at the same time is advantageous, as the long-acting tranquilizers, like perphenazine enanthate, can take 12–18 hours for to take effect (Meyer et al. 2021). Some of the long-acting neuroleptics are not available in the United States.

Azaperone is a short-acting butyrophenone tranquilizer with minimal effects on thermoregulation; it is often used in combination with other drugs (e.g., BAM). It is often used in swine medicine and is relatively safe when given intramuscularly; IV injection may cause excitation and is contraindicated (Malavasi 2015). Acepromazine has properties similar to azaperone and offers excellent muscle relaxation. However, it decreases blood pressure so it is best to avoid this in compromised animals (Rankin 2015). It is not very effective in domestic ruminants when used

Table 54.3 Tranquilizers and sedatives for use in antelope.

Drug	Dose (mg/kg)	Route	Time to Effect	Effective Time	Comments	Common Name	Species	Reference
Azaperone tartrate	0.3	IM				Blue wildebeest	*Connochaetes taurinus*	Laubscher et al. (2016)
	0.1–0.56	IM			Extrapyramidal signs noted in two animals, resolved with diphenhydramine	Pronghorn	*Antilocapra americana*	Miller (pers. comm.)
	Species specific		15–20 minutes	2–4 hours	Total dose for species, sex, age class recommended			Meyer et al. (2021)
Gabapentin	5.0–10.0	PO		SID-BID	Anecdotal, doses extrapolated from Coetzee et al. (2014)			Coetzee et al. (2014)
Haloperidol	0.5–1.0	PO		8–12 hours	SID to BID	Bongo	*Tragelaphus eurycerus*	Mikota et al. (1999)
Haloperidol lactate	0.1	IM	5–10 minutes	8–12 hours	May cause extrapyramidal signs, which can be treated with diphenhydramine or diazepam			Ball & Hofmeyr (2014); Zuba & Oosterhuis (2007)
	Species specific				Total dose for species, sex, age class recommended			Ball & Hofmeyr (2014); Meyer et al. (2021)
	0.12–0.16	IM				Blue wildebeest	*Connochaetes taurinus*	Fick et al. (2006)
Haloperidol decanoate	50–75 mg total	IM		3–4 days	Use with haloperidol lactate and/or oral haloperidol	Blackbuck	*Antilope cervicapra*	Fossil Rim Wildlife Center
Fluphenazine decanoate		IM	3 days	21–28 days	Use with a shorter-acting, rapid onset tranquilizer			Wolfe (2015)
Perphenazine enanthate	0.4–0.7		12–18 hours	7–10 days	Total dose for species, sex, age class recommended; peak effect at 36 hours			Meyer et al. (2021)
	1.5–5.7	IM	~8–21 hours	7 days		Impala	*Aepyceros melampus*	Gandini et al. (1989)
	0.4–0.8	IM				Blue wildebeest	*Connochaetes taurinus*	Fick et al. (2006)

(*Continued*)

Table 54.3 (Continued)

Drug	Dose (mg/kg)	Route	Time to Effect	Effective Time	Comments	Common Name	Species	Reference
Perphenazine HCl	Species specific		5–10 minutes	4–6 days				Meyer et al. (2021)
Pipotiazine palmitate		IM	2–3 days	21–28 days	Use with a shorter-acting, rapid onset tranquilizer			Wolfe (2015)
	4.5	IM		16 days		Impala	*Aepyceros melampus*	Gandini et al. (1989)
Trazodone	15	PO			Decreased activity level, mild hyporexia, short-acting	Blue wildebeest	*Connochaetes taurinus*	Prud'homme et al. (2023)
Zuclopenthixol acetate	0.6	IM	1 hour	72 hours	Total dose for species, sex, age class recommended			Meyer et al. (2021)
	1–1.5	IM		48–72 hours		Nile lechwe	*Kobus megaceros*	Clippinger et al. (1998)
	0.4–0.8	IM				Blue wildebeest	*Connochaetes taurinus*	Fick et al. (2006)
Zuclopenthixol acetate SR	1.5	IM		72 hours	Slow release formula; no adverse effects	Blue wildebeest	*Connochaetes taurinus*	Laubscher et al. (2016)
Zuclopenthixol deconoate		IM	7 days	10–21 days				Read (2002)

BID, twice daily; IM, intramuscular; PO, per os (orally); SID, once daily; SR, sustained release.

alone and is often combined with xylazine or butorphanol for sedation (Seddighi & Doherty 2016).

Trazodone is a short-acting serotonin reuptake inhibitor and is currently not controlled in the United States (Schwasinger-Schmidt & Macaluso 2019). In one study using goats as a model for nondomestic bovid species, oral doses reduced stress in the goats (Prud'homme et al. 2020). This drug was found to safely decrease activity level in wildebeest (*C. taurinus*), but it did not significantly affect cortisol levels and caused mild hyporexia (Prud'homme et al. 2023). Doses could be extrapolated to other species. One author (H.J.H.) commonly uses oral trazodone to calm flighty antelopes when moved from large pasture to holding pens, sometimes in combination with oral haloperidol.

One author (E.H.) has used gabapentin in combination with operant conditioning to facilitate wound treatment in nondomestic ruminants. There is a commercially available, compounded formulation of gabapentin and trazodone, and further evaluation on the use of these drugs as sedation/tranquilization is warranted.

Maintenance Anesthesia

Maintenance anesthesia can be via inhalant or parenteral anesthesia. Small animal machines are adequate for antelopes up to 60 kg. Conventional human anesthesia machines or small animal machines with expanded CO_2 absorbent (soda lime) are adequate for animals up to 200 kg. Large animal anesthesia machines are recommended for animals >250 kg (Riebold 2015). Although cumbersome, portable gas anesthesia can be used in a field setting (Chinnadurai 2019). When in a controlled environment, a ventilator can maximize oxygen and carbon dioxide exchange, thus minimizing the side effects of anesthesia, especially in larger antelopes.

Constant Rate Infusions, Total Intravenous Anesthesia, and Partial Intravenous Anesthesia

Once immobilized, total or partial IV anesthesia (PIVA) can lower needed gas anesthesia levels and total drug amounts or replace inhalant anesthesia in field conditions. These drugs may also provide pain control, especially in situations where initial immobilizing drugs are not sufficient for surgical procedures. They can be titrated to effect, may be more cost effective, and reduce the risk of waste anesthetic gases to the anesthetist. Hypotension from inhalant anesthesia may be mitigated. Single drugs may be used, including propofol, alfaxalone, UPOs, lidocaine, and guaifenesin, or multiple drugs can be combined. IV anesthesia is often used in domestic animals, with ruminant "triple drip" (xylazine, ketamine, and guaifenesin) a common combination (Riebold 2015; Seddighi & Doherty 2016).

There are several reports of using PIVA and total IV anesthesia (TIVA) in zoo and wild animals (Auer et al. 2010; Fontenot et al. 2012, Siegal-Willott et al. 2019). However, investigations into their use for antelopes are limited, except in impala (*A. melampus*) (Gerlach et al. 2017; Zeiler et al. 2015; Zeiler & Meyer 2017a). Buck et al. (2017) found propofol-medetomidine-ketamine TIVA a good alternative to inhalant anesthesia in impala (*A. melampus*), but hypoxemia warranted oxygen supplementation. Propofol constant rate infusion (CRI) 0.4 mg/kg/min provided good maintenance anesthesia in Speke's gazelle (*Gazella spekei*) (Kleinschmidt et al. 2018), but due to respiratory depression, the author noted that the animals should be intubated with IPPV available. One author (H.J.H.) uses PIVA in longer field procedures in the absence of inhalant anesthesia. The combination of midazolam 0.028 mg/mL and ketamine 1.8 mg/mL at a rate of 1.1 mL/kg/h IV has been used in several antelope species. These antelopes are intubated and provided with oxygen supplementation. Mild ataxia can occur after recovery, so stopping the PIVA at least 10 minutes prior to reversal of immobilizing drugs is important. A portable infusion pump is helpful to avoid over- or underdosing, which may occur when simply estimating the IV drip rate.

Exertional (Capture) Myopathy

Capture myopathy is caused by a combination of stress, intense muscular exertion, and hyperthermia experienced by the animal during a capture, usually during induction but it can occur during the procedure or recovery. This can be caused by equipment and darting failure or underdosing of immobilization drugs, among other things. Certain species, such as pronghorn (*A. americana*), nyala (*T. angasii*), impala (*A. melampus*), and kudu (*T. strepsiceros*), may be more predisposed to developing capture myopathy, and vitamin E or selenium deficiency may contribute to its development (Wolfe 2015). Lactate accumulates in the tissues and causes a metabolic acidosis. Skeletal muscle cells may become dysfunctional or die (due to severe hyperlactatemia), which leads to the release of potassium, calcium ions, and myoglobin. Myoglobinuria can cause acute renal failure; red urine may be seen clinically. Hyperkalemia and acidosis can cause arrhythmias and circulatory collapse. There are four clinical syndromes associated with capture myopathy: acute death, delayed peracute death, ataxic-myoglobinuric, and muscle rupture; more detailed reviews can be found elsewhere (Ball & Hofmeyr 2014; Breed et al. 2019; Caulkett & Arnemo 2015; Wolfe 2015).

The clinical signs may be seen immediately or up to several weeks after the procedure. Capture myopathy is difficult to treat so prevention is key. The addition of hyaluronidase to the immobilization dart may decrease induction time, as seen in a study in blue wildebeest (*C. taurinus*) (Dittberner et al. 2015). Oral tranquilizers given prior to the immobilization may help keep the animal calm during induction (Johns et al. 2020). When safe to do so, the immobilization team should consider aborting a procedure if the animal is overexerting itself during the capture. Treatment of capture myopathy may include fluid therapy, pain medicine, sodium bicarbonate, dimethylsulfoxide, corticosteroids, midazolam, and dantrolene administration, along with supportive care (Breed et al. 2019).

Analgesia

Analgesic agents should be included whenever an antelope undergoes a painful procedure or shows signs of pain. Recognizing pain in a stoic antelope can be challenging as most will mask any sign of weakness as a survival mechanism. Some signs of pain in antelopes may include bruxism, abnormal gait, isolation, and decreased appetite and/or activity level (Depenbrock 2017). Most analgesic information is extrapolated from domestic ruminants, and doses can be found in Table 54.4.

Nonsteroidal anti-inflammatory drugs (NSAIDs) work by inhibiting prostaglandins and thromboxanes through the inhibition of cyclooxygenase (Apley 2010). Examples include phenylbutazone, flunixin meglumine, and ketoprofen, which are commercially available in formulations appropriate for large species (Apley 2010; Flecknell et al. 2015). Phenylbutazone binds to milk proteins and its use in dairy cattle older than 20 months is prohibited in the United States (Apley 2010). However, one author (E.H.) has given phenylbutazone to a dam to treat lameness in the nursing calf. IM flunixin has been reported to cause tissue sloughing in horses and should be used with caution in other species (Davis 2018). Anecdotally, one author (E.H.) has seen two suspected cases of acute renal failure in common eland (*T. oryx*) when flunixin was given parenterally. Ketoprofen has a short half-life in domestic cattle, so multiple doses may be needed for analgesia (Kleinhenz 2019). Analgesic effects improved when ketoprofen was paired with a local anesthetic. Aspirin is a cycloxygenase inhibitor with poor oral absorption in ruminants (Apley 2010). Meloxicam is another readily available, inexpensive NSAID with pharmacokinetic and clinical data in cattle available (Coetzee et al. 2011, 2014; Kleinhenz 2019). Meloxicam, using the 15-mg tablet formulation crushed on feed, is commonly used by the authors in antelopes. Other NSAID options include carprofen and firocoxib. Animals given NSAIDs should be well-hydrated to prevent renal side effects and monitored for gastrointestinal ulcers. Gastroprotectants, such as famotidine, can be given with prolonged NSAID use.

Opioids, such as morphine, butorphanol, buprenorphine, and tramadol, provide pain control for antelopes, but they may cause sedation at higher doses. There is a dearth of information regarding butorphanol's use as an analgesic in ruminants, but in cattle it has a short half-life and minimal analgesic effects (Coetzee 2013; Seddighi & Doherty 2016). Butorphanol and morphine have been reported to cause excitement in ruminants (Depenbrock 2017). Nalbuphine is a synthetic opioid similar to butorphanol with fewer sedative side effects. A sustained-release formulation of buprenorphine may be efficacious for animals that cannot be handled frequently. In sheep, it provided steady plasma concentrations and continuous analgesia in thermal nociception for at least 72 hours at a 0.27 mg/kg dose (Walkowiak & Graham 2015). This dose has been used by one author (H.H.) without apparent side effects in multiple antelope species. Tramadol is a newer, synthetic opioid with a short oral and intravenous half-life in goats, with a recommended dose of 4 mg/kg IV every 6 hours (Souza & Cox 2011). However, in sheep IV tramadol is reported to have no mechanical antinociceptive effects (Bortolomi et al. 2015). When opioids are paired with an UPO immobilization, the use of naltrexone or another antagonist may negate the analgesic effects of these drugs.

Gabapentin is a gamma-aminobutyric acid (GABA) analogue used to treat neuropathic pain and partial seizures in humans, and it may be regulated in some areas. Good pharmacokinetic levels were achieved in cattle at a dose of 10–15 mg/kg (Coetzee et al. 2011). When gabapentin was used at a dose of 15 mg/kg with meloxicam, there was a reduction in severity of lameness in calves (Coetzee et al. 2014; Coetzee 2021).

In addition to its anesthetic properties, ketamine is an N-methyl D-aspartate (NMDA) receptor antagonist and provides analgesic effects at subanesthetic doses (Stillman & Whittaker 2019). It has a short duration of action and may be more suitable as a CRI (Coetzee 2013).

Amantadine is a NMDA receptor antagonist used off-label in horses, dogs, and cats as an antiviral, and when used in combination with NSAIDS, opioids, or gabapentin, may help with chronic pain in these species. Little to no information is currently available on its use in ruminants for pain control.

Regional anesthesia can assist in the already anesthetized patient by lowering general anesthetic drug doses and providing additional pain control once recovered. Domestic ruminant landmarks and doses usually serve as guides for use in antelopes. Mixing sodium bicarbonate 1:10 with lidocaine can decrease pain on injection and enhance analgesia, but it may decrease duration of effect (Coetzee 2013; Depenbrock 2017).

Table 54.4 Domestic ruminant analgesics for extrapolation to antelope species.

Drug	Dose (mg/kg)	Route	Frequency (or Half Life)	Comments	Species	Reference
NSAIDs						
Aspirin	100	PO	q12h	Poor oral absorption in ruminants	Cattle	Apley (2010)
	Not stated	IV	0.5 hours		Cattle	Apley (2010)
Carprofen	1.4	PO, IV, SC	30.7 hours		Cattle	Coetzee (2013)
Firocoxib	0.5	PO	19 hours		Calves	Kleinhenz (2019); Stuart et al. (2019)
Flunixin meglumine	1.1–2.2	PO, IV, IM	SID	IM may cause myonecrosis, IV 3 hours half-life in cattle	Cattle	Coetzee (2013); Davis (2018); Kleinhenz (2019)
				Parenteral route suspected to cause renal failure in several in common eland (*Tragelaphus oryx*)		E. Hammond (pers. comm.)
	3.3	Transdermal		5 hours half life	Cattle	Kleinhenz (2019)
Ketoprofen	3	IV, IM	SID	Good for dosing larger species, short half-life in cattle	Cattle	Kleinhenz (2019)
Meloxicam	0.5–1.0	PO, IV, SC	SID to q48h		Cattle	Coetzee et al. (2011, 2014); Kleinhenz (2019)
Phenylbutazone	2.2–4.4	PO, IV		Good for dosing larger species, binds to milk proteins, prohibited to use in female dairy cattle 20 months of age and older due to concern for fatal blood dyscrasias in humans		Coetzee (2013)
Sodium salicylate	50	IV, IM	37 hours		Cattle	Kleinhenz (2019)
Opioids						
Butorphanol	0.02–0.04			Short half-life and minimal analgesia in cattle, may cause excitement in ruminants	Cattle	Depenbrock (2017)
	0.05–0.5	IM			Sheep/ goats	Riebold (2015)
	0.25	IV, IM	82 minutes		Dairy cows	Coetzee (2013)
Buprenorphine SR	0.27	SC	72 hours	Thermal nociception	Sheep	Walkowiak & Graham (2015)
Nalbuphine	0.5	IV		Xylazine-sedated goats, combined with ketamine 5 mg/kg for anesthesia and analgesia	Goats	Abouelfetouh et al. (2022)
Tramadol	4	IV	q6h	Lacks mechanical antinociceptive effects in sheep when given IV	Sheep, goats	Bortolomi et al. (2015); Souza (2011)
	2	PO		Short duration	Goats	Souza & Cox (2021)
Other						
Gabapentin	10.0–15.0	PO	15 hours	Study in cattle combined with meloxicam, enhanced analgesia when given with NSAID	Cattle	Coetzee et al. (2011); Coetzee (2013, 2021)
Ketamine	2.0–4.0	IV		Short duration	Calves	Coetzee (2013)
Regional analgesia						
Lidocaine	0.11–0.22	Epidural				Coetzee (2013); Ismail (2016)
				Mix 1:10 with sodium bicarbonate to decrease pain on injection, may enhance analgesia but decrease duration		Coetzee (2013)
Tramadol	1	Epidural	319 minutes		Sheep	Stillman & Whittaker (2019)
Xylazine		Epidural	253 minutes	Can mix with lidocaine to increase onset and duration, may cause ataxia	Cattle	Coetzee (2013)

q48h, every 48 hours; SC, subcutaneous; SR, sustained release.

Epidural analgesics can be useful during painful hind end procedures, like dystocia treatment, but large volumes or longer-acting local anesthetics may compromise recovery if motor control to the pelvic limbs is lost. Based on domestic ruminant literature, suggested drugs used for epidural analgesia include lidocaine, xylazine, bupivacaine, tramadol, and ketamine (Coetzee 2013; Depenbrock 2017; Ismail 2016; Stillman & Whittaker 2019).

It is important to note that field immobilization of antelopes is a dynamic process and may vary among individuals of the same species and within anesthetic events with the same individual. Some species have predilections for coexisting conditions, which may complicate anesthesia. Greater kudu (*T. strepsiceros*) may commonly have hypocalcemia and hypomagnesemia of unknown origin (Miller et al. 2010). These deficiencies may adversely affect anesthesia, and the clinician should have the ability to diagnose and supplement them. *Kobus* sp. (waterbuck) may present with elevated liver enzymes in clinically normal animals (Sadler et al. 2016). This may cause them to process drugs differently, especially drugs that are eliminated primarily by the hepatic route. In impala (*A. melampus*), hyperthermia has been reported to be caused by stress and is not necessarily related to ambient temperature, drugs use, or activity level (Meyer et al. 2008).

Antelope immobilization is an art, and no two anesthetic events are ever the same. Many doses are anecdotal, and the collegial sharing of information is encouraged.

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55

Wild Sheep and Goats

Nigel Caulkett and Chris Walzer

Body Weight

Body weight ranges for individual species can be found in Table 55.1. Weights are taken from Kreeger et al. (2023).

Physical Restraint

In the 1980s there were several excellent studies that critically evaluated capture methods in bighorn sheep (*Ovis canadensis*) (Kock et al. 1987a–c). This body of work evaluated a variety of outcomes to determine the safest capture method for this species.

The studies evaluated three methods of physical capture: drop net, drive net, and net gunning. They also evaluated chemical capture with narcotic-xylazine combinations. The studies compared capture outcome, biological, biochemical and hematological parameters, and long-term survival (Kock et al. 1987a–c).

Capture outcome was evaluated by categorizing the animals as normal, stress-induced compromise, and mortality from capture myopathy or trauma. Compromised animals were defined as having one or more of the following signs: body temperature >42.4°C, prolonged pursuit, excessive struggling, shock, or any other signs of physical compromise.

It was determined that net-gunning resulted in the lowest combined mortality rate at <2%, drop-netting had a 3% mortality, and drive-netting resulted in a 4% mortality rate. Chemical immobilization was associated with the highest mortality at 8%. Chemical immobilization was also associated with the greatest number of compromised animals at 19%, drop-netting resulted in 15% compromised animals, and drive-netting resulted in 16%. Net-gunned animals demonstrated the lowest incidence of compromise at 11% (Kock et al. 1987a). These studies clearly demonstrated that physical restraint was the preferred capture method for short procedures.

In the Alpine and Balkan regions of Europe, chamois (*Rupicapra* spp.) are routinely captured using modified elastic leg snares, drop-net systems, and box traps (Ballestros & Benito 1992; Struch & Baumann 2000). Snares pose a serious risk of digital frostbite in the winter months and thus this method should not be used in low temperatures (Delmas 1993). Box traps, which are also routinely used for Alpine ibex (*Capra ibex*) need to be well established with salt licks prior to actual capture attempts (Abderhalden et al. 1998). Drive nets have been used extensively in the Pyrenees to capture southern chamois (*Rupicapra pyrenaica*) and Spanish ibex (*Capra pyrenaica*). Significant mortality (3–10% and 18% in nonmonitored nets) has been associated with this method in chamois (López-Olvera et al. 2009). The use of acepromazine in conjunction with physically trapped chamois has been reported to reduce the stress response (López-Olvera et al. 2007). In contrast, drive nets appear to be suitable for the capture of the more docile ibex (López-Olvera et al. 2009). The use of azaperone and haloperidol has been reported in drive-net captured Iberian ibexes. While haloperidol at 0.17 mg/kg (intramuscular [IM]) did not prove beneficial, azaperone at 45–59 mg/kg (IM) was suitable to reduce the stress response to the capture event (Mentaberre et al. 2010).

Beyond the risk to the captured animals, these physical restraint methods also pose a significant risk of serious injury to the operators; this is especially true in the chamois, which has sharply pointed, backward-curved horns (López-Olvera et al. 2009).

In central Asia the capture of mountain goats and sheep is particularly difficult owing to the unavailability of helicopters because of the remoteness and general national security concerns about aircraft. However, argali sheep

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Table 55.1 Recommended drug combinations for immobilization of wild sheep and goats.

Species	Drug Combination	Reversal	Comments	Reference
Bighorn sheep (*Ovis Canadensis*) 65–150 kg	Etorphine 4.5 mg (total) Xylazine 50 mg (total)	Diprenorphine 9 mg total Yohimbine 0.125 mg/kg	Total dose for adult animal	Kreeger et al. (2023)
	Medetomidine 0.16 mg/kg Ketamine 4.0 mg/kg	Atipamezole at 3–5 times the medetomidine dose	Dose for free-ranging sheep Captive animals may be immobilized with half of this dose	Williams et al. (2018)
	Medetomidine 0.15 mg/kg Azaperone 0.2 mg/kg Alfaxalone 0.05 mg/kg	Atipamezole at 5 times the medetomidine dose		Williams et al. (2018)
	Medetomidine 0.17 mg/kg Azaperone 0.29 mg/kg Butorphanol 0.43 mg/kg			Smith et al. (2014)
Mountain goat (*Oreamnos americanus*) 46–140 kg	Medetomidine 0.08 mg/kg Ketamine 2 mg/kg	Atipamezole 3–5 times the medetomidine dose	Used in captive goats Free-ranging goats may require a higher dose	(Caulkett, pers. experience)
	Etorphine 4 mg total Xylazine 30 mg total	Diprenorphine 8 mg Yohimbine 0.15 mg/kg		Kreeger et al. (2023)
Markhor (*Capra falconeri*) 80–100 kg	Medetomidine 63 µg/kg Ketamine 1.6 mg/kg	Atipamezole 282 µg/kg		Jalanka (1989)
	Etorphine 56 µg/kg Acepromizine 0.25 mg/kg	Etorphine 76 µg/kg		Jalanka (1989)
Chamois (*Rupricapra rupicapra*) 24–50 kg	Medetomidine 60–100 µg/kg Ketamine 1.5–2 mg/kg	Atipamezole 0.4 mg/kg	The higher end of the dose range should be used in wild chamois to speed induction	Walzer (1997)
Alpine ibex (*Capra ibex*) 35–150 kg Argali Sheep (*Ovis ammon*) 40–330 kg	Medetomidine 80–100 µg/kg Ketamine 1.5 mg/kg	Atipamezole at 5 times the medetomidine dose		Walzer (unpubl.)
Barbary sheep (*Ammotragis lerevia*) 40–55 kg (female) 100–145 kg (male)	Medetomidine 100–140 µg/kg Ketamine 1.5 mg/kg	Atipamezole at 5 times the medetomidine dose		Jalanka & Roeken (1990)
Himalayan tahr (*Hemitragus jemlahicus*)	Medetomidine 80–100 µg/kg Ketamine 1.5 mg/kg	Atipamezole at 5 times the medetomidine dose		Jalanka & Roeken (1990)
Mouflon (*Ovis orientalis*) 20–32 kg	Medetomidine 125 µg/kg Ketamine 2.5 mg/kg	Atipamezole at 5 times the medetomidine dose		Jalanka & Roeken (1990)
Muskox (*Ovibos moschatus*) 200–401 kg	Etorphine 0.015–0.05 mg/kg Xylazine 0.1–0.15 mg/kg	20 mg naltrexone:1 mg etorphine 1 mg atipamezole:10 mg xylazine	The low end of the dose range was described in captive animals The high end of the dose range was used in capture of wild muskox	Blix et al. (2011) Lian et al. (2017)

Body weights are referenced from Kreeger et al. (2023).

(*Ovis ammon*) have been successfully captured using drive nets (Kenny et al. 2008).

Generally, all these methods require a significant amount of manpower and constant monitoring to reduce the time of physical restraint.

Drug Delivery Method

Helicopter darting and free-range stalking of animals are the major methods used to facilitate drug delivery in wild sheep and goats. Helicopter darting, which is generally not available in Europe outside Scandinavia, has been associated with increased mortality in bighorn sheep and mountain goats (Kock et al. 1987a; Jessup 1999). Free-range stalking and ground-based drug delivery can also be used (Festa-Bianchet & Jorgenson 1985; Merwin et al. 2000; Shury & Caulkett 2006; Caulkett et al. 2012). Stalking is strenuous and time-consuming, but is used routinely in the Alps to capture chamois and ibex. Some 25 hours of stalking on average were needed per captured chamois in an alpine protected area (Walzer et al. 1998). The recovery of darted animals can be problematic in the highly strung chamois and the use of radio-telemetry darts may be indicated. Ground-based stalking tends to be associated with fewer stress-related complications compared to helicopter darting (Fig. 55.1).

Vascular Access

Venous access is not difficult in sheep and goats. The cephalic vein, lateral saphenous vein (Fig. 55.2), and jugular vein can all be easily accessed. The auricular artery can be cannulated in some species for direct blood pressure monitoring or to facilitate sampling for arterial blood gas analysis. Arterial blood samples may also be obtained from the femoral artery when auricular arterial catheterization proves difficult.



Figure 55.1 Ground stalking of bighorn sheep in British Columbia, Canada.



Figure 55.2 Obtaining a blood sample from the lateral saphenous vein of a bighorn sheep. This vein is easy to access in anesthetized sheep and goats.

Endotracheal Intubation

Intubation is recommended during volatile anesthesia and in steep terrain when optimal positioning of the animal is compromised to minimize the risk of ruminal content aspiration. Intubation is not difficult in most sheep and goat species. The animal should be maintained in sternal recumbency with the head and neck extended towards the sky. The mouth is opened wide and gentle traction is placed on the tongue. A long flat-bladed laryngoscope is placed into the oral cavity. The tip of the laryngoscope is placed at the base of the epiglottis. The epiglottis is moved ventrally to reveal the glottis. A stylet should be placed inside the endotracheal tube to reduce the curvature of the tube. The tube is placed into the glottis and advanced into the trachea. Typically, the tube should not be fully deflated on extubation as this will help to prevent any rumen contents entering the trachea if regurgitation has occurred. Laryngeal mask airways (LMAs) have been used in bighorn sheep to provide airway protection during immobilization with medetomidine-azaperone-alfaxalone (Fig. 55.3). The LMA has the advantage of ease of placement that can be rapidly performed without the use of a laryngoscope (Hee et al. 2020).

Sedation/Tranquilization Techniques

A number of immobilization protocols have been used in wild sheep and goat species over the years. As many of these animals live in mountainous terrain it is advisable to



Figure 55.3 Laryngeal mask airways can be rapidly and easily placed to provide a patent airway in emergency situations.



Figure 55.4 Mountain goat in typical terrain. Capture personnel must be trained and prepared to work in steep, dangerous terrain.

use reversible protocols that confer a relatively complete recovery from immobilization. Potent opioids are still used in some of the larger species, such as muskox. Xylazine-ketamine mixtures have been used in the past but have largely been replaced by medetomidine-ketamine. Alpha-2-tiletamine-zolazepam mixtures have been described but they must be used cautiously due to the risk of ataxia on recovery. More novel combinations, such as butorphanol-azaperone-medetomidine and medetomidine-azaperone-alfaxalone, may prove to have some advantages in wild sheep and goats. Descriptions of immobilization techniques by species can be found in the species-specific section and recommended drug doses can be found in Table 55.1.

Complications and Other Considerations

Preanesthetic Concerns

Like all other ungulates, sheep and goats are prone to ruminal tympany and regurgitation during anesthesia. It is prudent to fast captive animals for 24 hours prior to anesthesia. Maintenance in sternal recumbency may help to prevent the onset of ruminal tympany.

Wild sheep and goats often inhabit mountainous terrain. Capture work in this type of terrain must be carefully planned to avoid trauma to the animal during induction of anesthesia (Fig. 55.4). Bighorn sheep are prone to capture myopathy (Kock et al. 1987c). Capture events must be carefully planned to avoid prolonged chase times in an effort to prevent capture myopathy.

Monitoring and Supportive Care

Sheep and goats are prone to hypoxemia during anesthesia, particularly if alpha-2 agonists have been used as part of the anesthetic protocol (Caulkett et al. 1994; Shury & Caulkett 2006; Jalanka 1989). Hypoxemia may be less severe if the animal is maintained in sternal recumbency (Caulkett et al. 1996). Oxygenation should always be monitored in anesthetized sheep. Pulse oximetry or arterial blood gas analysis should be used to monitor oxygenation. Oxygen should be available during anesthetic procedures to offset hypoxemia.

Hyperthermia is another potential complication that may be encountered during capture and anesthesia. Hyperthemia has been linked with stress-related complications and capture myopathy (Kock et al. 1987c). It is best to minimize the risk of hyperthermia by limiting pursuit times and planning capture events for cooler seasons when possible. Body temperature should be closely monitored during anesthesia. Body temperature in excess of 41°C should be treated by actively cooling the animal with a cold-water enema or snow. Antagonism of alpha-2 agonists should also be considered in emergent situations.

It is difficult to prevent ruminal tympany or regurgitation in free-ranging animals. Maintenance in sternal recumbency may help to prevent or treat ruminal tympany. A rumen tube, polaxalene (a surfactant) or alcohol ethoxylate (a detergent), and trocar should be carried to treat serious cases of ruminal tympany. Often it is most advisable to complete the procedure and antagonize alpha-2 agonists as ruminal tympany typically resolves following administration of an alpha-2 agonist.

Blood pressure monitoring should be considered if the animal is to be maintained with volatile anesthesia. Indirect blood pressure monitors can be used to monitor trends in blood pressure. The blood pressure cuff is typically placed midway between the carpus and the pastern joint (Fig. 55.5).

Free-ranging animals should be blindfolded to decrease stimulation during light

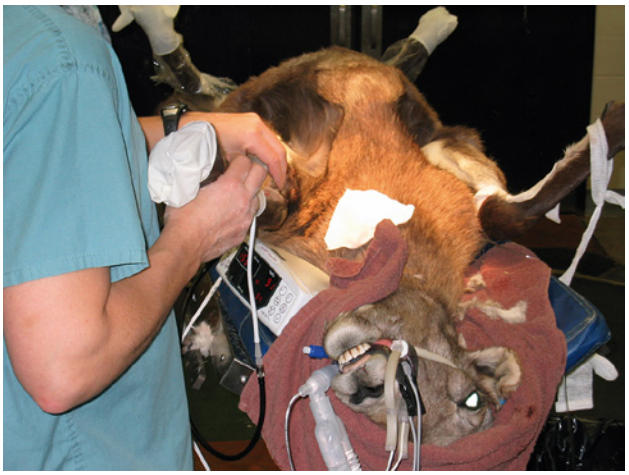


Figure 55.5 Placement of a blood pressure cuff over the metacarpus of a thinhorn sheep.

It is important to take care around the legs and horns of lightly anesthetized animals as they may kick and stab. The animal should be placed on a soft surface to avoid pressure points and supported in sternal recumbency for recovery following anesthesia.

Species-specific Considerations

Bighorn Sheep (*Ovis canadensis canadensis*) and Dall or Stone's Sheep (*Ovis dalli*)

Narcotic-based anesthesia with carfentanil-xylazine or etorphine-xylazine has been used for helicopter-based capture of bighorn sheep (Jessup 1999). Complications tend to occur with partial dosing or trauma during induction. This may reflect the method of capture (helicopter darting) more than an actual drug effect.

Xylazine-ketamine combinations have been used for the capture of bighorns (Festa Bianchet & Jorgenson 1985). Xylazine-ketamine combinations can be delivered using the Hellabrunner Mix (500 mg of xylazine dry powder dissolved in 4 mL of 10% ketamine) (Wiesner 1998) for low-volume delivery. The use of commercially available xylazine and ketamine results in relatively high volume requirements, therefore this mixture has been largely replaced by medetomidine-ketamine. A mixture of xylazine-tiletamine-zolazepam and hydromorphone has been used to capture bighorn sheep in flat terrain (Shury & Caulkett 2006). This mixture is administered at a dose of 1.64 mg/kg of tiletamine-zolazapam, combined with 1.1 mg/kg of xylazine and 0.22 mg/kg of hydromorphone. The mixture proved to be suitable for the capture of human-habituated sheep. Recovery was relatively rapid (10.3 minutes) following the administration of 0.11 mg/kg of atipamezole and 0.18 mg/kg of naltrexone.

The author (Caulkett) has used medetomidine-ketamine in captive and free-ranging bighorn sheep (Table 55.1). Free-ranging bighorns require a relatively high dose of this combination to induce immobilization (Williams et al. 2018). Medetomidine-azaperone-alfaxalone is a useful combination for the capture of bighorn sheep in steep terrain. Recoveries tend to be very smooth and reliable, with little ataxia (Williams et al. 2018. One of the major disadvantages of this combination is a relatively large volume because alfaxalone is only available in a 10 mg/mL dilution. Recently a 40 mg/mL formulation of alfaxalone was tested in bighorn sheep. It proved to be equally efficacious as the 10 mg/mL formulation and could be delivered at a significantly smaller volume (Patterson et al. 2021).

In our experience Dall and Stone's sheep are very similar to bighorn sheep. The combinations described above are equally effective in these species.

Mountain Goat (*Oreamnos americanus*)

Free-ranging mountain goats have typically been anesthetized with potent narcotics. Etorphine has also been used at a dose of 4–5 mg per animal (Jessup 1999). Medetomidine-ketamine can also be used to effectively immobilize mountain goats (Caulkett and Walzer, pers. obs.) (Table 55.1).

Markhor (*Capra falconeri megaceros*)

A detailed study exists that compares the efficacy and safety of medetomidine-ketamine and etorphine-acepromazine in captive Markhors (Jalanka 1989). Both combinations induced moderate hypoxemia. Medetomidine-ketamine induced slightly more respiratory depression, as evidenced by a significantly greater $PaCO_2$, compared to etophine-acepromazine. Medetomidine-ketamine produced better myorelaxation and a more complete immobilization than etorphine-acepromazine (Jalanka 1989). Both combinations were readily reversible (Table 55.1).

Chamois (*Rupricapra rupicapra*)

Various methods to chemically immobilize chamois have been described. In the German-speaking areas of Europe, the Hellabrunner Mix (125 mg of xylazine plus 100 mg of ketamine per milliliter) was until recently the method of choice. It is important to note that the required dose (0.27 mg/kg ketamine + 0.34 mg/kg xylazine) for chamois is extremely low when compared to other mountain ungulates (Wiesner & von Hegel 1985). The advantage of this combination is that very low dart volumes are possible. The combination of medetomidine and ketamine has proven to be a superior choice (Jalanka & Roeken 1990; Walzer et al. 1996) (Table 55.1). In wild chamois it is recommended to use the high end of the dose range to reduce the time to recumbency (Walzer et al. 1998). Other drugs/combinations that have been used include xylazine (Dematteis et al.

Alpine Ibex (*Capra ibex*)

Similar to other goat and sheep species, a combination of medetomidine and ketamine is recommended for the chemical capture of the ibex. For captive animals 80–140 μg/kg medetomidine combined with 1.5 mg/kg ketamine has been recommended (Jalanka & Roeken 1990) In free-ranging animals various combinations have been used: 100–120 μg/kg medetomidine and 3 mg/kg ketamine for the Iberian ibex; 80–100 μg/kg medetomidine, 1.5 mg/kg ketamine, 1.4–2.4 mg/kg xylazine, and 1.5–2.9 mg/kg ketamine for the alpine ibex have been reported (Dematteis et al. 2008; Casas-Díaz et al. 2011; Walzer, unpubl.). Alternate combinations include detomidine 190–270 μg/kg + 1.4–2 mg/kg ketamine or 6.8 mg/kg of tiletamine-zolazepam (Santiago-Moreno et al. 2011).

Argali Sheep (*Ovis ammon*)

Wild argali with an estimated weight of 90 kg have been captured using a combination of 4 mg of carfentanil, 50 mg of xylazine, and 100 mg of ketamine. Anesthesia was reversed with a combination of 500 mg of naltrexone and 15 mg of yohimbine (Kenny et al. 2008).

Barbary Sheep (*Ammotragus lervia*), Himalayan Tahr (*Hemitragus jemlahicus*), and Mouflon (*Ovis musimon*)

All of these sheep and goat species can be effectively immobilized with medetomidine-ketamine. The following doses have been used in captive animals (Jalanka & Roeken 1990): Barbary sheep 100–140 μg/kg medetomidine combined with 1.5 mg/kg ketamine, Himalayan tahr 80–100 μg/kg medetomidine combined with 1.5 mg/kg ketamine, and mouflon 125 μg/kg medetomidine combined with 2.5 mg/kg ketamine.

All the above doses were used in captive animals. It may be necessary to increase the dose in free-ranging animals. It is important to allow adequate time for induction with medetomidine-based protocols as animals may rouse and flee if they are approached too early. Typically, the animal can be approached approximately 5 minutes post recumbency.

Muskox (*Ovibos moschatus*)

The author (Caulkett) has used 50–60 μg/kg medetomidine combined with 1.5 mg/kg ketamine for short-term anesthesia of captive muskox. Sedation can be provided with 0.5–1 mg/kg xylazine alone or combined with 1–2 mg/kg ketamine for deeper sedation. These animals were relatively tame and human-habituated, and these doses should not be extrapolated to wild muskox.

Muskox anesthesia can be somewhat more challenging than anesthesia of the smaller sheep and goat species. Their heads are relatively large and they have a small oral cavity, which can make intubation a challenge. We typically use a mouth gag to open the mouth and used a long flat laryngoscope blade to visualize the glottis. It is important to induce good muscle relaxation to facilitate intubation. We have used 0.05–0.1 mg/kg diazepam or 5% guaifenesin, given to effect, to induce muscle relaxation. Manual intubation may be attempted in large muskox. The endotracheal tube is guided into the trachea manually by placing a hand dorsally over the end of the tube and advancing the hand into the pharynx. Once the operator's hand is in the pharynx the epiglottis is reflected ventrally and the tube is advanced into the trachea

Free-ranging adult muskox have been immobilized with 0.05 mg/kg etorphine and 0.15 mg/kg xylazine. This combination was described for capture of 133 wild muskoxen (Blix et al. 2011). More recently a dose of 0.015 mg/kg etorphine combined with 0.1 mg/kg xylazine has been described for immobilization of captive muskoxen (Lian et al. 2017). The major side effect of this combination was hypoxemia. Hypoxemia was successfully treated with supplemental inspired oxygen (Fig. 55.6). The authors noted that hypercarbia became more pronounced during treatment with supplemental oxygen and careful titration of oxygen should be considered to prevent severe hypoventilation. Etorphine was antagonized with 20 mg of naltrexone per 1 mg of etorphine. Xylazine was antagonized with 1 mg atipamezole per 10 mg of xylazine.



Figure 55.6 Administration of supplemental inspired oxygen to a muskox. The pulse oximeter is used to titrate the oxygen flow to maintain hemoglobin saturation as close as possible to 95%.

Analgesia and Analgesic Techniques

Analgesic techniques have been extrapolated from domestic sheep and goats. Local anesthetic techniques can be used for intra and postoperative pain control.

Butorphanol at a dose of 0.02–0.05 mg/kg can also be used to provide intraoperative analgesia. Nonsteroidal anti-inflammatory drugs have been used in wild sheep. It is always best to be cautious as safety and efficacy data are not readily available in these species.

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56

Cattle and Buffalo

Julia E. Napier

Body Weight

Physical Restraint

Exotic ruminants vary greatly in behavior, temperament, and size (Table 56.1). These animals can be formidable and aggressive in nature. Most wild cattle have large horns and hooves, and a strong fight or flight response when approached. Careful planning is necessary when considering any kind of restraint, handling, or procedure. The primary concern should always be human and animal safety. Animals designated for a procedure should be separated from the group and held in a smaller enclosure or holding area whenever possible. Ideally, this area would be quiet and free of unnecessary stimulation.

Should physical rather than chemical restraint be utilized, there are several methods that can be used with wild cattle. Behavioral conditioning using positive reinforcement, such as food reward, can be used to move animals through walkways in buildings or to facilitate crate training. Manual restraint is possible with smaller exotic bovids and calves, but should not be attempted in animals in excess of 70 kg. Exceptional skill and experience, as well as the appropriate protective equipment, is necessary to handle some of the larger species, especially in a noncontrolled environment. Any animal under manual restraint should be monitored for stress and hyperthermia. Blindfolds will calm some but not all individuals (Citino 2003).

For most adult wild cattle, some type of mechanical or physical restraint device is required for minor procedures, such as trimming horns, tuberculin testing, venipuncture, administering medications, rectal and vaginal examinations, or brief physical examinations. Restraint chutes, including box chutes with or without a head gate and drop-floor types, have become more typical in zoo settings (Boever 1986; Fowler 1995).

Many of the current devices were designed for cattle- or game-farming businesses and have been successfully modified for use with exotic bovids. Some of the restraint devices available include manual squeeze chutes (Heavy-Duty Squeeze Chute, Powder River Livestock Equipment, Provo, UT, USA) (Read et al. 1989), drop-floor chutes (The Tamer and Tamer, Jr., Fauna Research, Red Hook, NY, USA), and hydraulic squeeze chutes (Hydraulic Tamer, Fauna Research) (Blumer & DeMaar 1993; Citino 2003). When an animal is in a drop-floor chute, the floor can be dropped or lowered, leaving the animal wedged in a v-shaped trough, suspended with the feet off the ground. Many animals will cease struggling once they have lost their footing. Most devices available have a variety of access panels and a mechanism to release the animal quickly should that become necessary.

Vascular Access and Urine Collection

The most commonly used vascular access site in wild cattle is the jugular vein. Other common sites for blood collection include the cephalic, medial and lateral saphenous, tail (coccygeal), and auricular veins. In larger ungulates, the jugular can be hard to palpate. Holding off the vein with the knee and using the fingertips to bounce along the neck to locate the vein when the animal is in sternal or lateral recumbency can be useful, as is following the line of the caudal ramus of the mandible to locate the jugular (Fig. 56.1).

Catheter placement can be done in the jugular, cephalic, or auricular vein. Alcohol applied topically to the ear in addition to pressure at the base of the ear can help the auricular vein be more easily visualized. Supplemental anesthesia, antagonists to anesthetic drugs, fluids, emergency drugs, or other medications are administered most commonly in the jugular or auricular

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Table 56.1 Average body weights of adult exotic cattle.[a]

Species	Body Weight (kg)
African buffalo	400–900
Ankole (Watusi)	400–725
Anoa (both species)	150–300
Asian water buffalo	700–1000
Banteng	400–900
Gaur (Seladang)	600–1000
Yak	400–1000
Zebu	300–600

[a] For both females (lower end of the range) and males (higher end of the range).



Figure 56.1 Jugular venipuncture in an adult gaur bull (*Bos gaurus*).

veins. Blood gas values require a smaller volume of blood and can be obtained from the medial or caudal digital artery just proximal to the fetlock (Fig. 56.2) or the auricular artery.

Urine can be collected via urethral catheterization in females but is generally not successful in males due to the sigmoid flexure of the penis. Ultrasound-guided cystocentesis is the easiest method for urine collection in most exotic bovids.

Endotracheal Intubation

For prolonged procedures or in animals that are prone to aspiration of regurgitated rumen contents, inhalation anesthesia via an endotracheal tube (ET) may be required. Tubes used in exotic cattle should have an inflatable cuff. Wild cattle can be intubated in lateral or sternal recumbency. Younger animals and smaller species should be intubated in sternal recumbency for easier elevation of the head. Endotracheal intubation can be accomplished by direct visualization via a laryngoscope or digital palpation. The tongue should be extended rostrally and to the side for easy insertion of the laryngoscope or the ET tube. Using either approach, the ET tube is guided through the oral cavity to the epiglottis, which is deviated ventrally to feed the tube into the trachea.



Figure 56.2 Obtaining a sample for blood gas values from the medial digital artery.

Drug Delivery Method

Free-ranging wild bovids are generally immobilized using remote delivery equipment. Captive, restrained bovids may be hand-injected. Injection sites include the gluteal muscle mass, quadriceps, or neck. Small volumes of drugs may be injected into the coccygeal vein. In well-restrained or sedated bovids large drug volumes may be injected into the jugular vein.

Sedation/Tranquilization/Anesthesia Techniques

Sedation and Tranquilization

There are short- and long-acting sedatives available for exotic bovids. Commonly used short-term sedatives include the alpha-2 adrenergic agents xylazine, detomidine, and medetomidine (Short 1992). The alpha-2 agents can produce a calming state that can be overridden in a highly excited animal. In cattle, standing sedation has been attained with intravenous (IV) xylazine (0.02 mg/kg) or

detomidine (0.01 mg/kg). The duration of effect can be extended with the addition of butorphanol to the protocol at a dose of 0.05 mg/kg (Lin & Riddell 2003). Another combination that has been used in cattle is xylazine administered IV or intramuscular (IM) at 0.05–0.2 mg/kg with detomidine at 0.0025–0.01 mg/kg IV (Caulkett 2003). In domestic cattle, IM detomidine can induce standing sedation at dosages of 0.04 mg/kg. Detomidine has been used to sedate domestic calves at doses of 0.01 mg/kg for lighter sedation and 0.02–0.04 mg/kg for deeper sedation. (Peshin et al. 1991). Calves have also been successfully sedated using xylazine at dosages of 0.025–0.05 IV or 0.1–0.2 IM (Caulkett 2003). Sedation has been achieved in free-ranging Norwegian cattle using xylazine (0.37–0.73 mg/kg) or medetomidine (0.029–0049 mg/kg) (Arnemo & Soli 1993). In yaks, medetomidine at 0.07 mg/kg produces deep sedation, whereas detomidine at 0.025 mg/kg produces light sedation (Sharma et al. 1998, 2001).

An intermediate-acting phenothiazine, acepromazine, has been used on its own and in combination with other drugs for anesthesia in domestic cattle. When used alone, IM doses of 0.05–0.10 mg/kg can produce a sedation effect in 10–20 minutes. The effect can last between 4 and 8 hours, with potential residual effect up to 12 hours in duration (Blumer 1991; Swan 1993).

Haloperidol has been used in a variety of ungulates. It has an onset of around 10 minutes and duration of effect can last from 6 to 18 hours (Blumer 1991). Twenty to 40 mg of haloperidol in combination with 50–350 mg of perphenazine enanthate can induce longer periods of tranquilization (Ebedes & Raath 1999). Perphenazine administered IM has been used in gaur to reduce stress-induced self-trauma and in African buffalo in quarantine. The sedation effect has an onset of 12–16 hours and can last as long as 7 days (Blumer 1991; Citino 2003; Ebedes & Raath 1995, 1999; Swan 1993). Extrapyramidal effects and anorexia have been noted in some animals after administration of haloperidol. It should be used with caution in very young or geriatric animals because the effect can be unpredictable (Ebedes & Raath 1999).

Azaperone at a dosage of 0.1 mg/kg had been used to successfully sedate African buffalo (Ebedes & Raath 1999). It can be combined with zuclopenthixol acetate at 1 mg/kg for a tranquilization effect. When administered IM, the onset of effect is 60 minutes with a duration lasting up to 3 days (Citino 2003; Ebedes & Raath 1995; Swan 1993). Zuclopenthixol and perphenazine may be used concurrently to get the initial effects of the zuclophenthixol and the longer-lasting effects of the perphenazine. Pipotiazine palmate has an onset of 48–72 hours with a duration of up to 30 days when given IM and can be used concurrently with zuclophenixol as well (Blumer 1991; Citino 2003; Ebedes & Raath 1995; Swan 1993). Extrapyramidal effects such as torticollis, tremors, muscle rigidity, head swaying, and akinesia can be seen with overdoses of perphanizine, azaperone, and zuclopenthixol. Administration of diazepam (10–20 mg) or xylazine (5–10 mg) have been used to control these symptoms (Quandt & Ebedes 1998). Newer antipsychotic drugs are also becoming more available to treat the extrapyramidal symptoms of neuroleptics. These include risperidone, olanzapine, ziprasidone, and olanzapine. These drugs are available in injectable form and can be administered at human doses as a starting point. There is no published information on the use of these agents in bovids, but they have been used successfully in cervids and rhino (Zuba & Oosterhuis 2007).

Benzodiazepine use for sedation has been reported in domestic and exotic bovids. Midazolam is more commonly used in combination with other drugs for general anesthesia. Diazepam has been used in domestic calves at 0.2 mg/kg in combination with other drugs for sedation and induction of anesthesia (Caulkett 2003). Diazepam should not be used alone in yak as it has been known to produce very rough inductions, paddling of the limbs, and the inability to rise after falling (Kumar et al. 1999).

Chemical Restraint and Capture

In many situations, physical restraint is not an option (i.e., field procedures, excessively long procedures, and surgeries). There are a variety of chemical agents available for use in wild cattle. Personal preference and experience, size, temperament and physiology of the species, and the environmental setting will help to determine what chemical restraint should be utilized.

General Anesthesia

There are a variety of techniques and chemical agents that have been used for general anesthesia in wild cattle (Table 56.2). The drug classes most commonly used include opioids, alpha-2 adrenoreceptor agents, and dissociatives. Most general anesthesia is administered IM. In close quarters, a pole syringe can be utilized. Injection via a remote darting system is the most common route of administration. Young animals, under the appropriate restraint, may be induced with inhalant anesthesia using a face mask. Commonly used inhalant anesthetics include isoflurane and sevoflurane. An African buffalo calf was induced with midazolam and ketamine prior to intubation for maintenance on an inhalant anesthetic (Stegmann 2004). Short-term anesthesia can be produced in adult cattle with xylazine as a preanesthetic, ketamine for induction, and a mixture of guaifenesin and ketamine for maintenance (Caulkett 2003).

Table 56.2 Recommended anesthetic agents and protocols for wild cattle.

Species	Drug (combination) (mg/kg)	Reversal (mg/kg)	Comment
African buffalo	Azaperone: 0.1		Sedation
	Zuclophenthixol: 1		Tranquilization
	Xylazine: 0.05–0.15		Sedation
	Xylazine: 0.20–0.40		Immobilization
	Xylazine: 0.10 Etorphine: 0.012	Diprenorphine: 0.024	Immobilization
	Xylazine: 0.08–0.18 Acepromazine: 0.02–0.03 Etorphine: 0.005–0.007	Diprenorphine: 0.010–0.014	Immobilization
	Azaperone: 0.15 Etorphine: 0.015	Diprenorphine: 0.030	Immobilization
	Azaperone: 0.06–0.07 Thiafentanil: 0.007–0.014	Naltrexone: 0.07–0.14	Immobilization
Ankole, Watusi	Xylazine: 0.14–0.70 Etorphine: 0.014–0.038	Atipamezole: 0.03 Diprenorphine: 0.028–0.076	Immobilization
	Acepromazine: 0.10–0.14 Etorphine: 0.024–0.034	Diprenorphine: 0.048–0.068	Immobilization
	Detomidine: 0.05–0.08 Butorphanol: 0.08–0.20	Atipamezole: 0.03–0.15 Naltrexone: 0.05–1.0	Sedation
	Detomidine: 0.019–0.029 Carfentanil: 0.006–0.010 Ketamine: 0.30	Atipamezole: 0.10 Naltrexone: 0.6–1.0	Immobilization
	Detomidine: 0.005 Acepromazine: 0.04–0.05 Etorphine: 0.016–0.019 Ketamine: 0.48–0.50	Atipamezole: 0.03 Naltrexone: 1.8	Immobilization
	Detomidine: 0.12 Ketamine: 0.40	Yohimbine: 0.33	Immobilization
Anoa	Xylazine: 1.0 Ketamine: 6.0	Atipamezole: 0.2	Immobilization
	Xylazine: 0.27–0.33 Acepromazine: 0.11–0.12 Etorphine: 0.027–0.033	Diprenorphine: 0.054–0.066	Immobilization
	Medetomidine: 0.025–0.100 Ketamine: 0.05–2.0	Atipamezole: 0.12–0.50	Immobilization
Banteng	Xylazine: 0.03–0.22	Yohimbine: 0.07–0.18	Sedation (♀)
	Xylazine: 1.5	Atipamezole: 0.04–0.08	Immobilization
	Xylazine: 0.05–0.09 Acepromazine: 0.06–0.10		Sedation (♀)
	Xylazine: 0.75–1.00 Ketamine: 1.5–2.0	Atipamezole: 0.06–0.08	Immobilization
	Xylazine: 0.056–0.125 Acepromazine: 0.02–0.05 Etorphine: 0.005–0.012 Ketamine: 0.15	Diprenorphine: 0.010–0.024	Immobilization
	Detomidine: 0.059–0.079 Butorphanol: 0.050–0.088	Yohimbine: 0.21–0.22 Naltrexone: 0.84–0.88	Sedation
	Detomidine: 0.069–0.104 Butorphanol: 0.071–0.083 Ketamine: 0.69–2.13	Yohimbine: 0.18–0.20 Naltrexone: 0.7–0.9	Immobilization
	Ketamine: 0.33–2.78		

Table 56.2 (Continued)

Species	Drug (combination) (mg/kg)	Reversal (mg/kg)	Comment
Forest buffalo	Xylazine: 0.09–0.33 Etorphine: 0.012–0.050	Atipamezole: 0.027–0.033 Diprenorphine: 0.024–0.10	Immobilization
	Acepromazine: 0.07–0.10 Etorphine: 0.018–0.024	Diprenorphine: 0.036–0.048	Immobilization
	Xylazine: 0.14–0.18 Acepromazine: 0.13–0.14 Etorphine: 0.031–0.036 Ketamine: 1.55–2.50	Diprenorphine: 0.062–0.072	Immobilization
Gaur	Xylazine: 0.12–0.22 Acepromazine: 0.04–0.09 Etorphine: 0.010–0.022 Ketamine: 0.06–0.09	Diprenorphine: 0.020–0.044	Immobilization
	Xylazine: 0.05–0.025 Thiafentanil: 0.011–0.018	Naltrexone: 0.11–0.18[a]	Immobilization
	Medetomidine 0.02 Thiafentanil 0.012	Atipamezole 0.1 Naltrexone 0.12[a]	Immobilization
Yak	Detomidine 0.025		Light sedation
	Medetomidine 0.07		Deep sedation
	Xylazine: 0.30		Sedation
	Xylazine: 0.6–1.0		Immobilization
	Xylazine: 0.04 Etorphine: 0.006	Diprenorphine: 0.012	Immobilization
	Xylazine: 0.05–0.20 Acepromazine: 0.025–0.10 Etorphine: 0.006–0.024	Diprenorphine: 0.012–0.048	Immobilization
	Xylazine: 0.40–1.67 Acepromazine: 0.04–0.05 Etorphine: 0.010–0.012 Ketamine: 0.04–1.67	Diprenorphine: 0.020–0.024	Immobilization
	Medetomidine: 0.10 Ketamine: 3.0	Atipamezole: 0.5	Immobilization

Notes: The dosages and protocols presented in this table are a compilation of information from the listed references, personal experience, and personal communication with staff from the following institutions: Denver Zoo, Denver, CO, USA; Disney's Animal Kingdom, Lake Buena Vista, FL, USA; Exotic Animal Service, Edinburgh University, Edinburgh, UK; Marwell Preservation Trust, Winchester, UK; Royal Zoological Society of Antwerp, Antwerp, Belgium; Omaha's Henry Doorly Zoo, and Aquarium, Omaha, NE, USA; Soffolk Wildlife Park, Edinburgh, UK; St. Louis Zoo, St. Louis, MO, USA; Whipsnade Wild Animal Park, Bedfordshire, UK; Zoological Society of London, London, UK.
[a] Naltrexone in Gaur can be administered 30–50% IV and 50–70% IM or 25% IV and 75% SQ, which may reduce renarcitization.

Where available, opioids are the most common group of drugs used to produce general anesthesia in wild cattle. They provide a smooth induction and a short recovery period. Carfentanil and etorphine were the most widely used; however, use of thiafentanil (A3080) is becoming increasingly common. It has been studied in various hoofstock (Citino et al. 2002; Janssen et al. 1991; Napier et al. 2011). Doses for etorphine range from 0.005 to 0.050 mg/kg. Doses for carfentanil range from 0.005 to 0.015 mg/kg. Thiafentanil doses range from 0.007 to 0.018 mg/kg. Inductions generally take longer with etorphine and are shortest with thiafentanil. In some species, such as gaur, induction times are quite similar with carfentanil and thiafentanil (1–4 vs. 1–6 minutes, respectively) (Napier et al. 2011). Hyaluronidase increases the rate of absorption of the opioid and may decrease induction times. Opioids are frequently used in conjunction with alpha-2 agents, including xylazine, medetomidine, and detomidine. They are also used in

combination with acetylpromazine, a phenothiazine. These combinations reduce the amount of opioid needed to produce the desired anesthetic effect and can increase muscle relaxation. They can be given with the opioid in a single injection or 15–20 minutes prior to the opioid. African buffalo have routinely been immobilized with etorphine (0.01 mg/kg) and azaperone (0.015–0.2 mg/kg) (Puffer et al. 2001). A combination of thiafentanil, medetomidine, and ketamine has been used successfully in bovids. This combination provided rapid onset and good muscle relaxation in field conditions (Citino et al. 2002). Gaur may be effectively immobilized with xylazine (0.08–0.10 mg/kg) and carfentanil (0.005–0.10 mg/kg) (Armstrong 1989; Napier et al. 2011; Wilson et al. 1993). The combination of thiafentanil (0.012 mg/kg) and medetomidine (0.02 mg/kg) was also used successfully in multiple electroejaculation procedures of gaur (Napier et al. 2011). If the initial immobilizing opioid dose is insufficient for adequate anesthesia, another IM dose of half of the initial dose can be given.

Because of their extreme potency in relation to morphine, etorphine, carfentanil, and thiafentanil are classified as ultra-potent opioids. It is imperative to take appropriate precautions when using these opioids. An emergency procedure should be in place in the event human exposure occurs with any of these substances. At the very least, personal protective equipment should include eye protection and impermeable gloves. It is advisable to have antagonists ready for injection prior to the preparation and use of these ultra-potent opioids. Accurate record keeping for all controlled substances is required by government and regulatory agencies.

When opioids are not available, dissociatives in combination with alpha-2 agents or benzodiazepines are commonly used (Barnett & Lewis 1990). Ketamine and the combination of tiletamine and zolazepam (Telazol and Zolatil) have been used. Adding an alpha-2 agent reduces the dose of the dissociative as it does with opioids. Medetomidine generally provides smoother inductions and recoveries compared with xylazine. Detomidine combined with tiletamine and zolazepam has been used successfully to immobilize wild banteng (Bradshaw et al. 2005). The quality of Telazol inductions and immobilizations is poor in gaur (Wilson et al. 1993). A detomidine (0.01 mg/kg), diazepam (0.01 mg/kg), and ketamine (3.0 mg/kg) combination has been used in Asian buffalo calves (Pawde et al. 2000). As with opioids, if the initial immobilization doses do not achieve the necessary level of anesthetic depth, lesser doses of these drugs can be given intravenously or intramuscularly.

In the majority of situations, intramuscular administration is the only route available for administering anesthetic agents; consequently, barbituates are not commonly used in wild cattle. This is also the case with glycerol guaiacolate, which is often combined with dissociatives and barbituates in IV administrations in domestic cattle. If venous access is available, these drugs can be given using domestic cattle doses. Propofol may also be used for IV induction at doses of 2.0–40 mg/kg (Jalanka et al. 1992).

If procedures are going to last in excess of an hour, inhalant anesthetic can be utilized. Sevoflurane and isoflurane can be administered following protocols used in domestic cattle.

Complications and Other Considerations

Preanesthetic Considerations

Ruminants are prone to ruminal tympany and regurgitation, which can lead to aspiration and subsequent pneumonia, especially in recumbent anesthesia. A rumen tube should be part of the standard equipment to help prevent or treat ruminal tympany. Animals should be fasted for a period of 18–36 hours prior to induction. Water access should be discontinued 8–12 hours prior. Maintaining the animal in sternal recumbency can reduce the possibility of rumen regurgitation, especially in field conditions, when the animal cannot be fasted. When sternal recumbency is not possible, as in an electroejaculation or surgical procedure, when access to the ventrum is necessary, the head should be positioned or propped so the mouth and nose are pointed in a downwards direction. This will allow flow from the oral cavity of any rumen contents, reducing the chances of aspiration. In either lateral or sternal recumbency, the head and neck should be extended to maintain a patent airway. To greatly reduce the occurrence of aspiration of regurgitated rumen contents, an animal can be intubated with an endotracheal tube, as described.

Anesthetic Monitoring

The same monitoring standards and equipment that are used in other mammals under anesthesia can be used in wild cattle. Depth of anesthesia can be assessed by several methods. Although most animals will go into sternal recumbency on their own, some animals will head press against a wall or remain standing with the legs positioned in a wide stance. Through manual manipulation, they can be moved into sternal recumbency after placing a towel or cloth over the eyes (Fig. 56.3).

Other animals, such as the gaur, will maintain a dog-sitting position prior to sternal recumbency (Figs 56.4 and 56.5). Once in sternal recumbency, depth of anesthesia can be monitored by response to the ear pinch, response



Figure 56.3 Field immobilization of an African buffalo (*Syncerus caffer*), moved into sternal recumbency with a blindfold placed over the eyes.



Figure 56.4 Gaur bull (*Bos gaurus*) in typical dog-sitting position prior to going into sternal recumbency.



Figure 56.5 Gaur bull (*Bos gaurus*) in sternal recumbency.

to tactile stimuli in the extremities or most accurately by manipulating the globe of the eye. The eye rotates ventromedially during a light plane of anesthesia. In deep anesthesia, it will rotate back to a central position (Reibold et al. 1982).

Normal heart and respiratory rates can vary greatly among wild cattle, depending on species, size, age, and the level of excitement attained prior to immobilization. Heart rate can be obtained using a stethoscope. Pulses can be palpated at the base of the tail and the facial artery in younger and smaller species, as well as the caudal auricular artery and the common digital arteries. To assess cardiovascular function and peripheral perfusion, capillary refill time can be utilized. This involves blanching the gums of the oral mucosa for several seconds then releasing and monitoring refill time, which should not exceed 2 seconds. The cardiovascular system should be monitored at regular intervals throughout anesthesia.

A pulse oximetry probe can be placed on the tongue, ear, or vulvar or preputial skin folds (Fig. 56.6). Many pulse oximetry units will measure pulse rate as well as oxygen saturation of hemoglobin (SaO_2), providing another set of data for anesthetic monitoring. The color of the oral mucus membranes can also be utilized as an indicator of oxygenation. If hypoxemia is present, the intranasal route is an easy way to administer supplemental oxygen. Respiratory rate is generally monitored visually by watching the movement of the thorax and abdomen.

Hyperthermia is common in immobilized wild cattle, especially if the animal goes into a hyperexcited state due to under dosing. Excessive running, high-stepping, or pacing occurring prior to induction can lead to very elevated body temperatures (Citino 2003). Normal wild cattle body



Figure 56.6 Pulse oximeter probe placed on the tongue to assess oxygen saturation of hemoglobin (SaO_2) as well as pulse rate.



Figure 56.7 Obtaining indirect systemic blood pressure values by placing an oscillometric cuff just proximal to the fetlock.

temperatures range from 37 to 39°C (99 to 102°F). If temperatures exceed this range, topical application of cold water or cold-water enemas are quite useful in bringing down the body temperature, although enemas will initially preclude accurate follow-up rectal thermometer temperature readings.

Indirect systemic blood pressure values can be acquired by placing an oscillometric cuff just proximal to the fetlock on most species or at the base of the tail in some smaller species (Fig. 56.7). The bladder of the cuff should be positioned on the medial aspect of the leg and on the ventral aspect of the tail for accurate measurements. Direct measurement requires catheterization, usually of the caudal auricular artery.

Complications

Hypoxemia occurs frequently with the use of potent opioids and should be treated with ventilation and intubation, if necessary. If the animal is not intubated, nasal oxygen can be given. Hyperthermia can occur in immobilized animals and can be treated as previously discussed.

Excess gas in the rumen can lead to tympany. A stomach tube should be passed in an attempt to reduce the gas. This problem can be seen in animals that have not been fasted but is infrequent in animals that were fasted previous to the procedure.

Capture or exertional myopathy has been reported in numerous bovid species. Since this condition is difficult to treat, especially in a free-ranging setting, it is important to keep pre-immobilization stress and activity to a minimum. This can be accomplished by selecting drugs and doses that will facilitate a rapid induction, limiting chases under free-ranging conditions, and removing anything that might contribute to stress, such as excess personnel and loud noises (Schumacher 2008). Pressure myopathy should be considered with heavy-bodied cattle under anesthesia for extended periods of time.

Renarcotization has also been reported in numerous cases in animals immobilized with potent opioids, particularly with carfentanil citrate (Allen 1989; Schumacher 2008). Studies have shown some species are more prone to this phenomenon than others and animals given a lower dose of reversal will have a greater tendency to experience renarcotization (Allen 1989; Haigh & Gates 1995; Mutlow et al. 2004; Wilson et al. 1993). Wild cattle that have been immobilized with potent opioids should be monitored for 72 hours post procedure. Clinical signs usually occur around 12–24 hours after the administration of the reversal and include circling, high stepping, agitation or mild excitement, recumbency paddling, and dulled mentation. IM administration of 50% of the initial antagonist dose should be given if any of these signs are noted. Repeated doses may be needed if the clinical signs of renarcotization do not subside.

Recovery

One of the advantages of using opioids for immobilizations is the ability to reverse the drugs and provide a safe, smooth, and rapid recovery. Naltrexone is the preferred antagonist for both carfentanil and thiafentanil. For carfentanil, the dosage of naltrexone is 100 mg per 1 mg of carfentanil given. For thiafentanil, a dose as low as 10 mg per 1 mg of thaifentanil can be given. The dose for naltrexone is usually split between IV, IM, and subcutaneous (SC) administration. The recommended label dose is one-fourth IV and three-fourths SC. A study was done that did not find any advantage to splitting the dose when reversing carfentanil (Mutlow et al. 2004).

Reversals for alpha-2 agonists include yohimbine for the reversal of xylazine and detomidine and atipamezole for medetomidine. Atipamezole can be used to reverse xylazine and detomidine if yohimbine is not available.

If supplemental drugs have been given during the procedure, such as ketamine, antagonists should not be given for at least 20 minutes after the ketamine has been administered to allow for a smooth recovery.

If an animal has been intubated, the endotracheal tube should not be removed until there is evidence of pharyngeal activity. It is not necessary to completely deflate the cuff of the tube in order to remove it. Keeping the cuff partially inflated will help clear the mouth of any oral secretions or regurgitated material that may have accumulated during the procedure.

In a herd situation, animals should be returned to the group as soon as possible if conspecifics do not pose an immediate threat to the recovering individual.

Analgesia

In any situation where an animal may be expected to experience pain, analgesia administration should be considered. These agents include opioids, alpha-2 adrenergic agents, and nonsteroidal anti-inflammatories (NSAIDs). Opioids and alpha-2 agents, which have already been discussed as common agents used for sedation and general anesthesia, provide analgesia during those periods. Detomidine has demonstrated analgesia comparable with epidural administration in domestic cattle when given IM at 0.04 mg/kg (Prado et al. 1999). Unless animals are going to be held in some kind of enclosure, opioids and alpha-2 agents are not generally used outside of anesthesia due to their potent sedative effects.

NSAIDs produce analgesia without the complication of sedation. There are no recent publications on the effectiveness of these drugs in wild cattle, but there are numerous publications on the effect of NSAIDs in domestic bovids. Ketoprofen given at 3.0 mg/kg IV produces analgesia in calves undergoing horn debudding and domestic bulls undergoing castration (Faulkner & Weary 2000; Ting et al. 2003). Ketoprofen is used less frequently in domestic cattle as it does not offer an advantage over drugs that are labeled for use in bovids or are less expensive (Smith et al. 2008). Phenylbutazone has been used in domestic cattle at doses of 10–20 mg/kg orally, then 2.5–5 mg/kg every 24 hours or 10 mg/kg every 48 hours (Jenkins 1987), and oral doses of 9 mg/kg with maintenance doses of 4.5 mg/kg administered every 48 hours (Eberhardson et al. 1979). Flunixin meglumine has been given IV, IM, and orally to dairy cows and beef cattle at doses of 1.1–2.2 mg/kg (Anderson et al. 1986; Smith et al. 2008).

Numerous studies have been conducted using meloxicam alone or in combination with other drugs in domestic cattle. Gabapentin capsules or powder, given orally at 10 mg/kg with meloxicam at 0.5 mg/kg, has been used for management of neuropathic pain in cattle (Coetzee et al. 2010). Meloxicam alone, at a dose of 0.5 mg/kg, has demonstrated nonimmunosuppressive and anti-inflammatory benefits in cattle with respiratory disease and in calves that have been dehorned (Heinrich et al. 2010; Smith et al. 2008).

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57

Bison

Nigel Caulkett

Body Weight

Wood bison (*Bison bison athabascae*) are the largest subspecies of bison, with adult males weighing up to 1200 kg and adult females weighing 500–600 kg. Adult male plains bison (*Bison bison*) weigh up to 1000 kg, with adult cows weighing up to 500 kg. Adult male European bison weigh up to 1000 kg while adult females weigh up to 500 kg.

Physical Restraint

Captive bison may be handled in facilities that are relatively similar to cattle-handling facilities. Bison are very powerful and it is vital that the chute system and squeeze are built from material that can accommodate rough handling. Ideally the chute system should be enclosed and there should be no right-angle turns, as the animal may run directly into the wall and injure itself. Typically, a hydraulic squeeze is used to capture and restrain the animal. It is not uncommon to include a crash gate at the end of the squeeze as the animal may enter the squeeze very rapidly and a physical barrier is required to stop the animal at the end of the squeeze. Restraint time must be kept to a minimum to decrease the risk of stress-related complications. Physical capture of free-ranging bison is typically achieved with a net gun. An experienced crew can potentially capture and handle cows and calves with this method. Mature bulls are more challenging and typically chemical immobilization is required.

Drug Delivery Method

Wild bison and unrestrained captive bison are generally drugged with remote delivery equipment, typically using dart sizes of 3–5 mL. Captive, restrained bison may be hand-injected. Injection sites include the gluteal muscle mass, quadriceps, or neck. Small volumes of drugs may be injected into the coccygeal vein (similar technique to domestic cattle).

Vascular Access

The two most common sites for vascular access are the jugular vein and the coccygeal vein. The coccygeal vein can be used to obtain small-volume blood samples and to top-up anesthetic or immobilizing drugs, but it is not a good location to place an indwelling catheter. The jugular vein is a good location to obtain large-volume blood samples or to place indwelling catheters, but it can be challenging to locate in large males. The size of the head also makes it difficult to manipulate the head and neck in sternally recumbent animals. Catheter selection is similar to domestic bovids, either over-the-needle or through-the-needle catheters may be used, and a typical gauge is 10–14, with a typical length of 10 cm. A small, full-thickness incision of the skin overlying the vein will facilitate catheter placement. In the laterally recumbent animal the lateral saphenous may also be used. Caution should be exercised as lightly anesthetized bison may suddenly kick with their hindlimbs. Arterial samples may be obtained from the coccygeal artery or the femoral artery, as auricular arteries are typically difficult to locate.

Endotracheal Intubation

Intubation is not typically performed in field settings, but it is recommended if the bison is to be maintained on volatile anesthesia. The technique is the same as for cattle. The bison is maintained in sternal recumbency. A mouth gag is placed prior to intubation. The tongue is pulled forward and the distal end of the tube is held. The person

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performing the intubation will advance their arm into the oral cavity and guide the tube to the epiglottis. The epiglottis is displaced ventrally with a finger and the tube is advanced into the glottis. A mature bison will require a size 24–30 endotracheal tube. The head will need to be elevated to facilitate intubation, which can be difficult in large, mature animals as the head can be heavy.

Sedation/Tranquilization Techniques

Sedation and Anesthesia of Captive Bison

Bison restrained in a head gate and squeeze can be sedated with intravenous xylazine. The coccygeal vein is useful for the injection of small volumes. Xylazine can be used as the sole agent at a dose of 0.1–0.2 mg/kg IV for standing sedation. Sedation may be enhanced by the addition of 0.05 mg/kg of acepromazine or 0.05 mg/kg of butorphanol administered IV. All three drugs may also be combined to produce deep sedation and possibly recumbency. If short-term general anesthesia is desired 0.2–0.5 mg/kg of xylazine can be administered IV, via the tail vein, to produce recumbency. This is followed by 2 mg/kg of ketamine, via the jugular vein. If the jugular vein is used the head must be adequately restrained to avoid injury to handlers.

Anesthesia may be prolonged with 5% guaifenasin and additional 1 mg/kg boluses of ketamine administered to effect. Use guaifenasin cautiously as we have observed guaifenasin toxicity in two bison at what appeared to be a relatively low dose. It would be premature to say these animals are overly sensitive to the drug, but it should be used cautiously until more information is available. Guaifenasin must be administered via a jugular catheter as it will cause severe tissue irritation and damage if it is administered perivascularly.

Xylazine should be antagonized at the end of the procedure. If IV ketamine has been used, the antagonist should not be administered for 10–15 minutes to avoid the undesirable effects of the ketamine.

Bison calves can be induced to anesthesia with IV ketamine 2–4 mg/kg plus diazepam 0.2 mg/kg. This combination will give 5–10 minutes of light anesthesia. In depressed calves diazepam 0.2 mg/kg + 0.1 mg/kg of butorphanol can be used IV for sedation. If the calf is difficult to work with 0.1–0.2 mg/kg of xylazine + 0.1 mg/kg of butorphanol can be administered IM prior to induction with ketamine-valium.

Immobilization of Free-ranging Bison

Bison may require immobilization for a variety of reasons. Remote delivery of immobilizing agents necessitates the use of potent agents that can be delivered in relatively small volumes. Recommended drug combinations can be found in Table 57.1.

Table 57.1 Recommended drug combinations for anesthesia of bison.

Species	Drug Combination	Reversal	Comments	Reference
Plains bison (*Bison bison*) and wood bison (*Bison bison athabascae*)	Medetomidine 60 µg/kg Telazol 1.2 mg/kg	Atipamezole at 5 times the medetomidine dose	Captive bison, increased dose requirements in free-ranging animals Hypoxemia	Caulkett et al. (2000)
Plains bison (*Bison bison*) and wood bison (*Bison bison athabascae*)	Xylazine 1 mg/kg Telazol 2 mg/kg	Tolazoline 2–3 mg/kg half IV, half IM	Captive bison, increased dose requirements in free-ranging animals Hypoxemia	Caulkett et al. (2000)
Plains bison (*Bison bison*) (immobilization of adult cow bison)	Butorphanol 95.6 mg Azaperone 31.9 mg Medetomidine 38.1 mg	Atipamezole 4.6 mg/1 mg medetomidine + 1 mg naltrexone/1 mg butorphanol	Captive and free-ranging bison, supplemental doses were sometimes required when heliopter-darting	Harms et al. (2018)
Plains bison (*Bison bison*)	Nalbuphine 0.4 mg/kg Azaperone 0.08 mg/kg Medetomidine 0.08 mg/kg	Atipamezole at 5 times the medetomidine dose + 150 mg of naltrexone (total dose)	Captive animals, more anxious animals difficult to sedate Hypoxemia	Wolfe et al. (2017)
European bison (*Bison bonasus*)	Medetomidine 0.08 mg/kg Ketamine 2.5 mg/kg	Atipamezole at 5 times the medetomidine dose	Limited number of animals ($n = 3$)	Jalanka & Roeken (1990)
Bison sp.	Etorphine 0.01 mg/kg Xylazine 0.05 mg/kg	Diprenorphine 0.02 mg/kg Yohimbine 0.125 mg/kg		Kreeger et al. (2023)

Potent Opioids

Carfentanil-xylazine has been used for capture of free-ranging wood and plains bison (Haigh & Gates 1995; Kock & Berger 1987). Carfentanil is administered at a dose of 4–8 μg/kg and combined with xylazine at a dose of 0.05–0.1 mg/kg. Given the lack of availability of carfentanil, etorphine can be considered as a substitute at a dose of 10 μg/kg (Kreeger et al. 2023). Bison, like other ungulates, will demonstrate increased activity and excitement during induction. If the animal demonstrates head and/or limb movement when approached after becoming recumbent, an additional 0.05–0.1 mg/kg of xylazine may be administered IV to improve muscle relaxation. Following the procedure opioids should be antagonized with naltrexone at an appropriate ratio.

Butorphanol-Azaperone-Medetomidine and Butorphanol-Azaperone-Nalbuphine (NalMed-A)

Limited access to ultra-potent narcotics has necessitated the development of alternative combinations. Butorphanol-azaperone-medetomidine (known as BAM) has been used at a total dose of butorphanol 95.6 mg, azaperone 31.9 mg, medetomidine 38.1 mg to immobilize adult cow bison. The drug combination was delivered either from the ground or via helicopter. The authors found this combination to be relatively reliable but suggested that higher doses may be required for helicopter-based immobilization to increase reliability (Harms et al. 2018). The combination was antagonized with 4.6 mg of atipamezole per 1 mg of medetomidine and 1 mg of naltrexone per 1 mg of butorphanol. Recovery was rapid and reliable. Butorphanol-azaperone-medetomidine (NalMed-A) has been evaluated in captive bison at a mean dose of 0.4 mg/kg of nalbuphine, 0.08 mg/kg of medetomidine and 0.08 mg/kg of azaperone (Wolfe et al. 2017). The combination was antagonized with 5 mg/kg of atipamezole per 1 mg of medetomidine and 150 mg of naltrexone (total dose per animal). The combination induced relatively reliable immobilization and recovery in captive animals but the authors noted subjectively that more anxious animals were more difficult to sedate. The authors recommend that this combination may be most suitable for captive animals or ground darting. Hypoxemia was the major side effect and supplemental inspired oxygen was recommended

Xylazine-Telazol

A dose range of 0.75–1.5 mg/kg of xylazine combined with 1.5–3 mg/kg of telazol is generally effective to immobilize bison (Caulkett et al. 2000). The low end of the dose is often effective in calm animals. The high end of the dose range may be required in fractious or wild animals. A 400-kg cow could require a dose volume of up to 7 mL, which can decrease dart accuracy and increase tissue trauma. Large-volume requirements decrease the utility of this mixture for wild animals, but it is still very useful in captive or game-farmed animals.

The mixture will produce approximately 1 hour of anesthesia and will provide adequate analgesia for minor procedures. The major complications that can be encountered with this combination are hypoxemia, bloat and/or regurgitation, and hyperthermia.

Xylazine should be antagonized to hasten recovery and stimulate ruminal motility. Since the telazol dose is relatively low, recoveries are generally smooth. Rougher recoveries may be noted if a high dose of telazol was used for induction. Tolazoline or atipamezole should be used to antagonize xylazine in bovids. Tolazoline can be administered at a dose of 2–3 mg/kg. This dose may be split between IV and IM administration. Yohimbine will not effectively antagonize xylazine-induced sedation in bovids and should not be used as the reversal agent (Klein & Klide 1989).

Medetomidine-Telazol

The immobilization characteristics of this combination are similar to those of xylazine-telazol (Caulkett et al. 2000). The major advantage of medetomidine-telazol is that it can be administered at approximately half the volume of xylazine-telazol. This quality greatly increases its utility in free-ranging animals. Another major advantage is that a lower dose of telazol is required and arousal from sedation is significantly faster than recovery following antagonism of the xylazine in the xylazine-telazol mixture.

A dosage of 60 μg/kg of medetomidine + 1.2 mg/kg of telazol can be used to immobilize captive and free-ranging bison. Medetomidine can be antagonized with 180–300 mg/kg of atipamezole. Caution should be observed following antagonism of the medetomidine as arousal from anesthesia can be very rapid, and IV administration of atipamezole should be avoided unless the condition of the animal is seriously compromised.

Complications are similar to those of xylazine-telazol and include hypoxemia, hypercarbia, and rumenal tympany. Steps should be taken to prevent or treat these complications.

Complications and Other Considerations

Bison are similar to domestic cattle in many respects, and anesthesia of an animal with a full rumen pack typically results in bloat or regurgitation. Xylazine or general anesthesia with volatile agents will lead to decreased rumen



Figure 57.1 Aerial darting of a plains bison. Pursuit times should be limited to less than 2 minutes whenever possible.

motility, bloat, and regurgitation. These can be fatal complications and tend to be more severe in large, mature animals (Caulkett et al. 2000).

Bison become stressed very quickly. Stressed animals tend to over-ride the sedative effects of alpha-2 agonist drugs (Wolfe et al. 2017), necessitating the use of relatively high dosages of these agents to produce immobilization. Bison are prone to capture myopathy. It is extremely important to keep chase times to a minimum and to try to avoid excitement prior to induction (Fig. 57.1).

Trauma during induction of anesthesia is not uncommon. It is particularly important to control the rest of the herd during induction as other members of the herd may traumatize the drugged animal. There is no information concerning the abortogenic effects of xylazine in bison cows. The risk of abortion in the last third of pregnancy may be increased with this drug.

Bison are prone to hypoxemia during general anesthesia. Positioning in dorsal or lateral recumbency will exacerbate hypoxemia (Caulkett et al. 2000). Alpha-2 agonist drugs such as xylazine or medetomidine will also exacerbate hypoxemia (Caulkett et al. 2000; Wolfe et al. 2017).

Inspired oxygen should be considered in hypoxemic bison and a flow rate of 10–15 L/min is typically required.

Arterial blood gas analysis will provide the most accurate means of assessing oxygenation. The femoral artery may be used in laterally recumbent animals. It is prudent to exercise caution when working near the legs of anaesthetized bison as they may spontaneously kick. The coccygeal artery can be used to facilitate arterial blood sampling in sternally recumbent bison (Fig. 57.2).



Figure 57.2 Collection of an arterial blood sample from the coccygeal artery of a bison.

Heart rate and pulse quality should be monitored every 5 minutes. The auricular pulse is difficult to palpate in bison. The facial artery or the femoral artery may be used. Bison anesthetized with xylazine-telazol or medetomidine-telazol have an average heart rate of approximately 60 beats

per minute (bpm) (Caulkett et al. 2000). Bison anesthetized with NalMed-A demonstrated mean heart rates of 54 bpm (Wolfe et al. 2017).

Rectal temperature should be monitored every 5–10 minutes. Bison are prone to hyperthermia, particularly following a long pursuit. Rectal temperatures greater than 40°C are cause for concern, and attempts should be made to cool the animal; cold water sprayed on the animal or snow packed into the inguinal and axillary regions may help. Rectal temperature in excess of 41°C is an emergency and should be treated aggressively. It is difficult to actively cool large animals and often the best option with severe hyperthermia is to antagonize the immobilizing agents and allow the animal to recover. Hyperthermia greatly increases metabolic oxygen demand. Hyperthermia, in the face of hypoxemia, is a particularly serious complication. Hyperthermic animals should receive supplemental inspired oxygen to offset hypoxemia.

Maintenance in sternal recumbeny will help to prevent the development of rumenal tympany (Fig. 57.3). If rumenal tympany is a problem the animal may be rocked gently to stimulate eructation. A rumen tube can be used, but may predispose to regurgitation and aspiration. Generally, if rumenal tympany is severe, it is advisable to finish the procedure quickly and antagonize the anesthetic agents. If alpha-2 agonists have been used, the administration of tolazoline or atipamezole will stimulate rumenal activity and relieve rumenal tympany.



Figure 57.3 Plains bison positioned in sternal recumbency.

Analgesia and Analgesic Techniques

Given the similarity of bison to domestic cattle, many analgesic techniques for bison can be extrapolated from cattle. Local anesthetic techniques should always be considered for intraoperative and postoperative pain control. The author has utilized butorphanol at a dose of 0.02–0.05 mg/kg for intra- and postoperative analgesia and meloxicam at a dose of 0.5 mg/kg for postoperative analgesia. It is important to note that the efficacy and safety of these drugs have not been critically evaluated in this species.

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