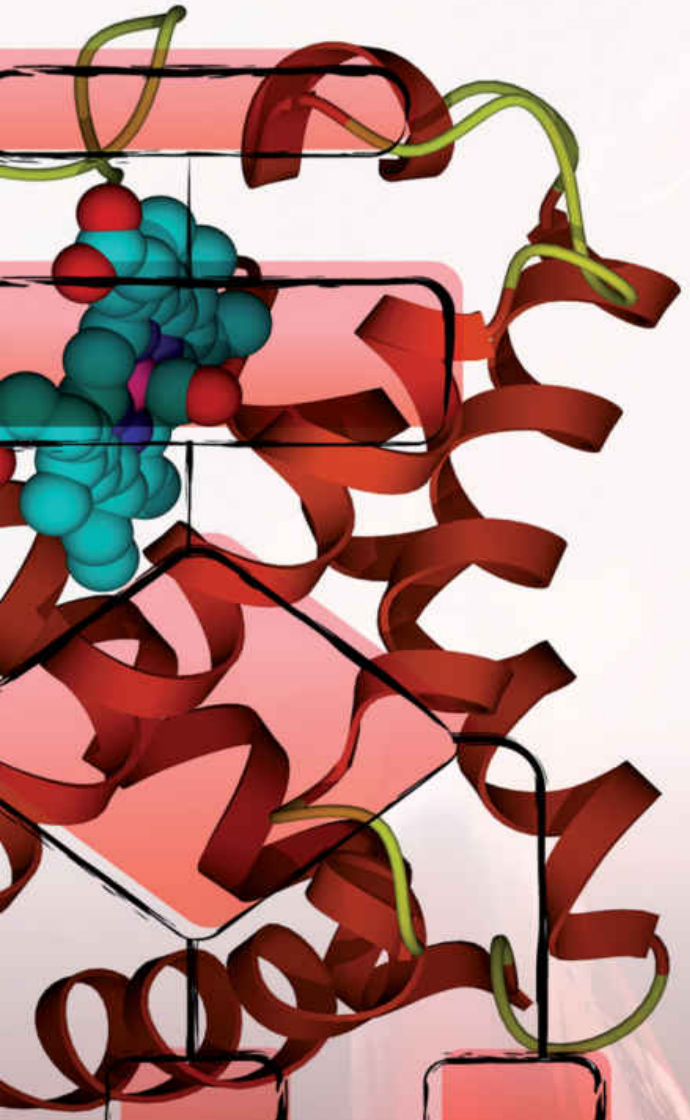


PRACTICAL GUIDE TO Laboratory Test Interpretation and Differential Diagnosis in Small Animals

HAEMATOLOGY AND BIOCHEMISTRY

Ignacio López Villalba
Ignacio Mesa Sánchez

SERVET

Practical Guide to Laboratory Test Interpretation and Differential Diagnosis in Small Animals

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Warning:

Veterinary science is constantly evolving, as are pharmacology and the other sciences. Inevitably, it is therefore the responsibility of the veterinary surgeon to determine and verify the dosage, the method of administration, the duration of treatment and any possible contraindications to the treatments given

to each individual patient, based on his or her professional experience. Neither the publisher nor the author can be held liable for any damage or harm caused to people, animals or properties resulting from the correct or incorrect application of the information contained in this book.

This book is dedicated to my parents, José and Encarni, and to my brother Daniel, for his daily love and unconditional support.

IGNACIO MESA SÁNCHEZ

This book is dedicated to Paula, to my parents, Ignacio and Benilde, and to my canine family (Tina and Kenny).

IGNACIO LÓPEZ VILLALBA

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The authors wish to thank each of our colleagues at the veterinary teaching hospitals of the University of Córdoba and the Autonomous University of Barcelona, with whom we have the opportunity to learn and enjoy each day we share together.

We also thank our families, partners, and friends for their support of our professional careers, which at times can be difficult to reconcile with personal responsibilities. None of this would be possible without their patience and understanding.

Finally, thanks to the entire editorial team at Servet for providing us with the opportunity to write this book, and for their excellent work in bringing this project to fruition.

The authors



Ignacio López Villalba

PhD in veterinary medicine from the University of Córdoba, Spain, in 2002. Professor of Internal Medicine and Propaedeutics at the Faculty of Veterinary Medicine of the University of Córdoba. Since 2003 he has worked in clinical practice at the Veterinary Teaching Hospital of the University of Córdoba, where he currently heads the Small Animal Internal Medicine Service.

He is a member of the PAIDI CTS-179 Veterinary Internal Medicine Research Group of the University of Córdoba and the Calcium Metabolism and Vascular Calcification Research Group of the Maimónides Biomedical Research Institute, Córdoba (IMIBIC). He is also a member of the Spanish Society of Veterinary Internal Medicine (SEMIV), the European Society of Veterinary Oncology (ESVONC), and the Founding Committee of the Veterinary Oncology Group of AVEPA (GEVONC).

He has been a visiting researcher at several prestigious veterinary hospitals in the United Kingdom (University of Bristol and Queen Mother Hospital of the Royal College of London), Germany (veterinary hospitals of the University of Hannover and the Free University of Berlin), USA (Ohio State University Veterinary Hospital), and South America (Institute of Feline Medicine, Santiago de Chile).

He has authored over 60 scientific publications in international journals in the fields of veterinary sciences, endocrinology and metabolism, and urology and nephrology, and has spoken at more than 100 national and international congresses and postgraduate events.

He has received numerous awards for his research in the fields of nephrology and mineral metabolism, including awards from the Spanish Society of Nephrology (2009 and 2013).

His clinical work focuses exclusively on small animal practice, specifically the fields of haematology, oncology, and nephro-urology.



Ignacio Mesa Sánchez

Degree in veterinary medicine (2008) and master's degree in Animal Medicine, Health, and Improvement (2009) from the University of Córdoba.

He has worked as a clinician at the Veterinary Teaching Hospital of the University of Córdoba (2009) and the San Marco Veterinary Hospital (Padova, Italy) (2010). From 2011 to 2014 he carried out his residency in internal medicine (ECVIM-CA) at the Veterinary Teaching Hospital of the Autonomous University of Barcelona (UAB), later joining the Internal Medicine Service at the Ars Veterinaria hospital. He currently carries out his clinical activities at the Internal Medicine Service of the Valencia Sur Hospital and is the clinical director of its Animal Blood Bank.

He is an educational collaborator at the Department of Medicine and Animal Surgery of the UAB and an honorary collaborator at the Department of Medicine and Animal Surgery of the University of Córdoba.

He has published in various national and international journals. His clinical work focuses exclusively on small animals, with a particular emphasis on internal medicine.

Collaborator



Carmen María Pineda Martos

PhD in veterinary medicine from the University of Córdoba (2014). She has authored and coauthored numerous scientific publications and lectured at national and international conferences within the fields of feline medicine, endocrinology, mineral metabolism, and nephrology.

Currently she works at the Department of Medicine and Animal Surgery of the University of Córdoba.

Foreword

It is a great honour for me to recommend this book on differential diagnoses and laboratory algorithms. It is written by two great authors, who without doubt will make names for themselves at the national level in the coming years.

This book provides clinicians with crucial diagnostic advice and assistance. It consists primarily of algorithms and tables, the aim of which is to provide the reader with rapid access to the most essential laboratory information. Moreover, specific tables focus on the diagnosis of certain hard-to-diagnose diseases. The layout is very simple, and the schematics provided are clear and self-explanatory.

The book structure has been carefully considered, an indication of the professionalism of the two authors. I will without doubt be consulting this manual, and I hope that it will become a reference text and a useful aid for those of us working in laboratory and clinical diagnosis.



JOSEP PASTOR MILÁN

Ldo Vet, PhD, ECVCP
Full Professor, Department of Animal Medicine and Surgery,
Faculty of Veterinary Medicine, Autonomous University of Barcelona.

Preface

Haematology and biochemistry are two of the main pillars of current veterinary medicine, and are among the most used diagnostic procedures in daily clinical practice. More and more veterinary practitioners routinely request these types of tests, which now provide more complete information thanks to the development and availability of new techniques. Adequate interpretation of the information they provide is therefore essential.

When planning this manual, we sought to create a detailed guide that was also practical and easy to understand from a clinical point of view. As such, the book is based on a series of decision-making algorithms that facilitate logical and systematic management of the main alterations found within this discipline. These algorithms are accompanied by diagrams, tables, and photographs providing basic information on sample acquisition and interpretation of the results of basic haematology and biochemistry tests.

This book provides basic information on alterations in the haemogram and blood smear and biochemical parameters related to liver and kidney function, as well as tips on advancing the diagnosis based on basic data obtained from the clinical history and general examination. In addition, it provides valuable information on how to perform different diagnostic and therapeutic techniques, including transfusion medicine techniques.

We would like to thank the Servet Editorial team at Grupo Asís for giving us the opportunity to create this book, and for their patience and dedication. We hope that this manual will prove useful to students, trainee veterinary surgeons, and veterinary clinicians in their daily work.

THE AUTHORS

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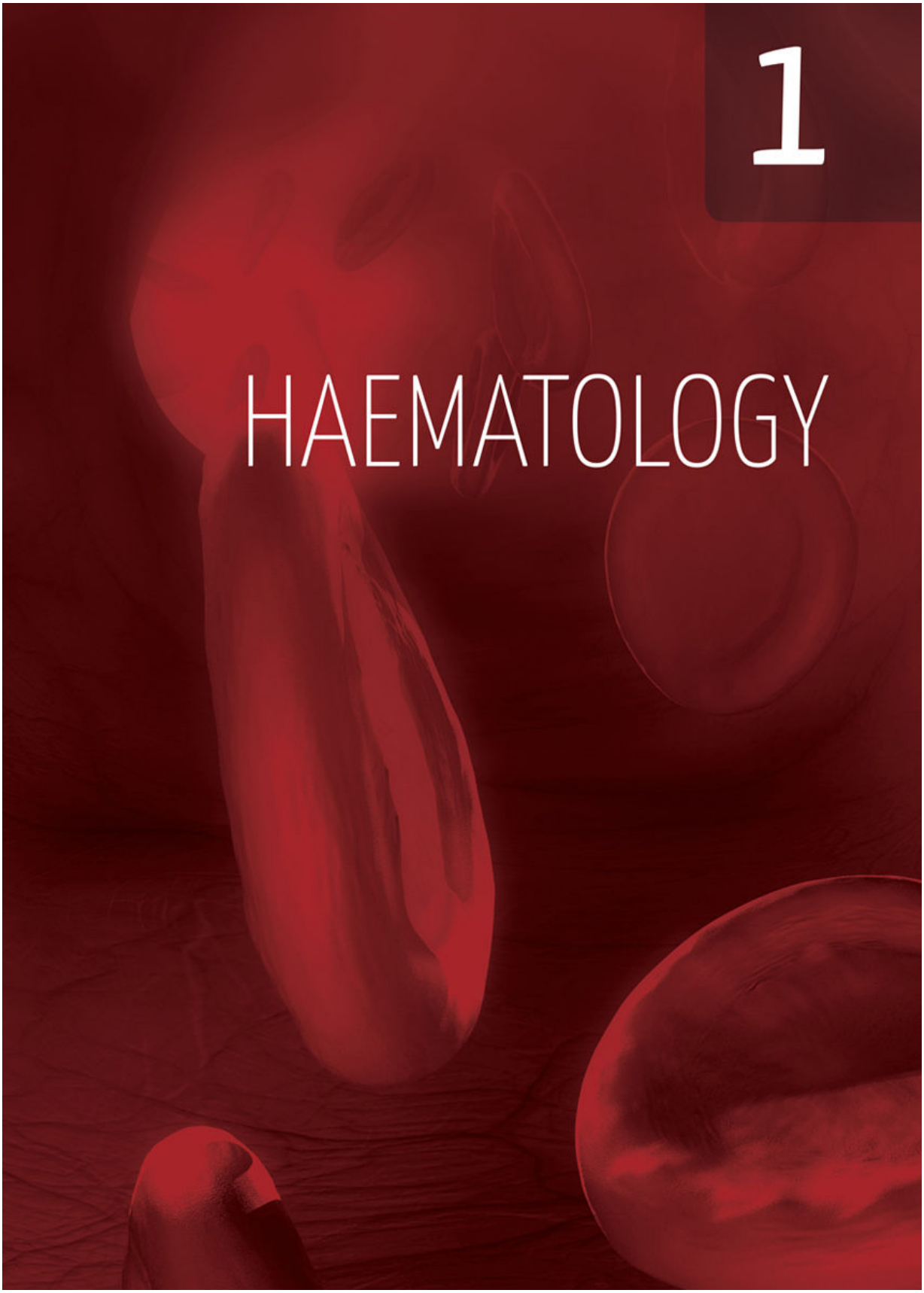
Index of abbreviations

Ab: antibody
ACEI: angiotensin-converting enzyme inhibitor
ACT: activated clotting time
ACTH: adrenocorticotropic hormone
ADH: antidiuretic hormone
Ag: antigen
ALL: acute lymphoblastic leukaemia
ALT: alanine aminotransferase
ANA: antinuclear antibody test
AP: alkaline phosphatase
aPTT: activated partial thromboplastin time
ARA-II: angiotensin II receptor antagonists
ARF: acute renal failure
AST: aspartate aminotransferase
AT: antithrombin
BE: base excess
BMBT: buccal mucosa bleeding time
BP: blood pressure
BUN: blood urea nitrogen
Ca: calcium
Ca_i : ionic calcium
cAMP: cyclic adenosine monophosphate
CAT: computed axial tomography
Ca_t : total calcium
cGMP: cyclic guanosine monophosphate
CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone
CK: creatine kinase

CKD: chronic kidney disease
Cl: chlorine
CLL: chronic lymphocytic leukaemia
CNS: central nervous system
Co: cobalt
COAP: cyclophosphamide, vincristine, cytosine arabinoside, and prednisone
COP: cyclophosphamide, vincristine, and prednisone
CRC: corrected reticulocyte count
CRF: cerebrospinal fluid
CRT: capillary refill time
Cu: copper
DEA: dog erythrocyte antigen
DIC: disseminated intravascular coagulation
DSH: domestic short hair
EBM: evidence-based medicine
ECG: electrocardiogram
EDTA: ethylenediaminetetraacetic acid
EPO: erythropoietin
FDPs: fibrin degradation products
Fe: iron
FeLV: feline leukaemia virus
FFP: fresh frozen plasma
FGF23: fibroblast growth factor 23
FIP: feline infectious peritonitis
FIV: feline immunodeficiency virus
FLUTD: feline disease of the lower urinary tract
FNA: fine needle aspiration
FP: frozen plasma
GFR: glomerular filtration rate
GGT: gamma glutamyl transpeptidase
GP: glycoprotein

Hb: haemoglobin
HCO_3 -: bicarbonate
Hct: haematocrit
HDL: high density lipoprotein
HMG-CoA: 3-hydroxy-3-methylglutaryl-coenzyme A
IBD: inflammatory bowel disease
IFN: interferon
Ig: immunoglobulin
IGF-1: insulin growth factor type 1
IL: interleukin
IM: intramuscular
IRIS: International Renal Interest Society
IV: intravenous
K: potassium
KCl: potassium chloride
LDL: low density lipoprotein
Li: lithium
Mg: magnesium
MRI: magnetic resonance imaging
Na: sodium
NaCl: sodium chloride
NH_3 : ammonia
NSAIDs: nonsteroidal anti-inflammatory drugs
P: phosphorus
Pb: lead
PCO_2 : partial pressure of carbon dioxide
PCR: polymerase chain reaction
PIVKA: protein induced by vitamin K absence
PLI: pancreatic lipase immunoreactivity
PMN: polymorphonuclear
PO_2 : partial pressure of oxygen

PRP: platelet-rich plasma
PT: prothrombin time
PTH: parathyroid hormone
PTHrp: parathyroid hormone-related protein
PTT: partial thromboplastin time
PU/PD: polyuria/polydipsia
RBC: red blood cell (erythrocyte)
RI: regeneration index
SaO: oxygen saturation of haemoglobin in circulating blood
SBP: systolic blood pressure
SC: subcutaneous
SCID: severe combined immunodeficiency
Se: selenium
SIRS: systemic inflammatory response syndrome
T_3 : triiodothyronine
T_4 : thyroxine
TCC: transitional cell carcinoma
TLI: serum immunoreactive trypsin
TNF: tumour necrosis factor
TP: total protein
TSH: thyrotropin
TT: thrombin time
UPC: protein:creatinine ratio
UTI: urinary tract infection
vWF: von Willebrand factor
WBC: white blood cell (leukocyte)
WM: Wisconsin Madison


1
HAEMATOLOGY

Additives used for blood sample collection

Additive	Effect	Properties	Indication	Format
Heparin Na or Li	Anticoagulant that inhibits the conversion of prothrombin to thrombin	Preserves blood for 10–12 hours without altering oncotic pressure	Biochemical tests	Green tube
EDTA	Anticoagulant Ca chelator	Preserves cell morphology	Haematology tests	Violet tube
Citrate	Anticoagulant Ca chelator	Prevents platelet aggregation	• Platelet count • Coagulation tests	Blue/black tube
Fluoride	Inhibits enolase	Prevents degradation of glucose and lactate	Determination of glucose and lactate	Grey tube
Serum tubes	Procoagulant action	Prevents interfering effect of fibrin	• Serology • Biochemistry	Red/brown tube

Blood smear examination

Reference ranges for blood smear examination

Platelet concentration

Estimation in a “counting window” in a 1000× field

Species	Marked decrease	Moderate decrease	Mild decrease	Reference range	Possible increase	Increased
Canine	≤3	4–7	8–9	10–25	26–30	>30
Feline	≤3	4–11	12–14	15–40	41–48	>48

Red blood cell abnormalities

Mean number of abnormal RBCs per 1000× field

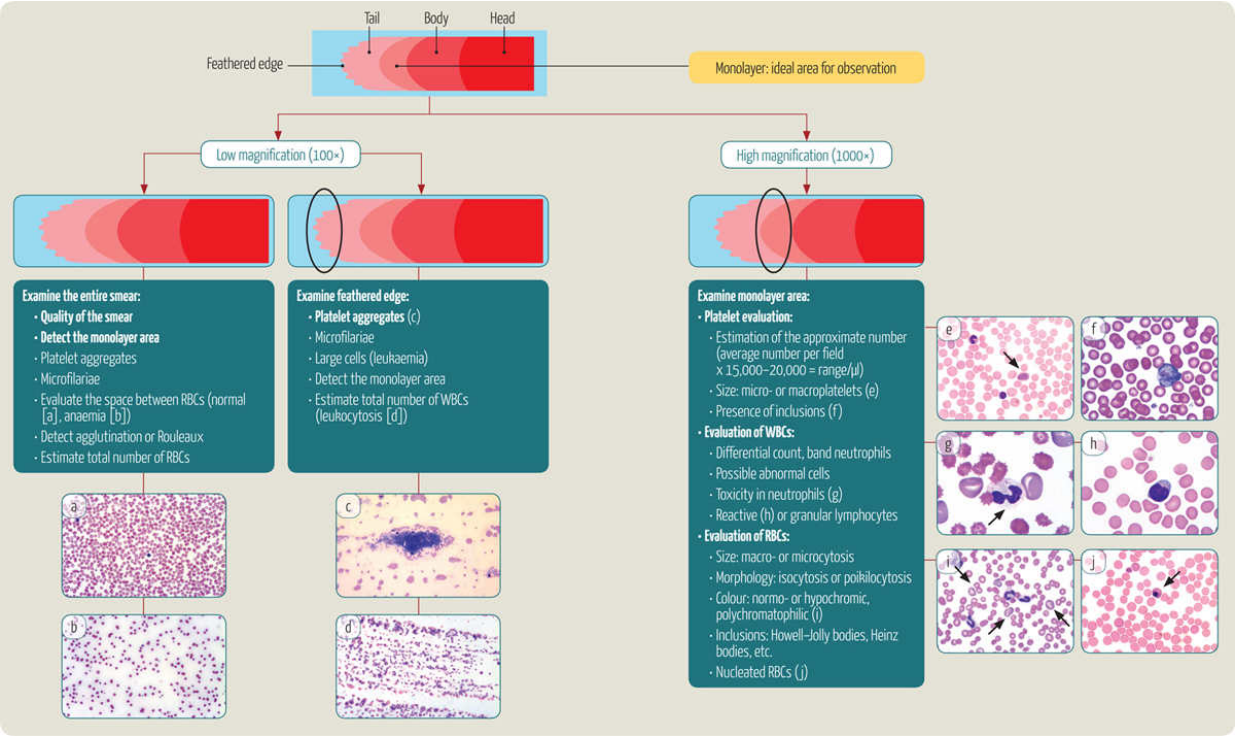
Polychromasia classification in dogs and cats			
Polychromasia	**Mild**	**Moderate**	**Marked**
Dog	2–7	8–14	>14
Cat	1–2	3–8	>8
Classification of other RBC alterations in all species			
Abnormality	**Mild**	**Moderate**	**Marked**
Hypochromia or poikilocytosis (any form)	1–10	11–50	>50
Codocytosis	1–5	6–15	>15
Spherocytosis, microcytosis, macrocytosis	1–10	11–50	>50
Schistocytosis, keratocytosis, acanthocytosis, elliptocytosis, Heinz bodies, Howell–Jolly bodies, basophilic stippling, or other poikilocytes	1–2	3–8	>8

White blood cell abnormalities

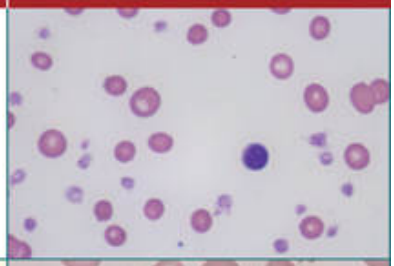
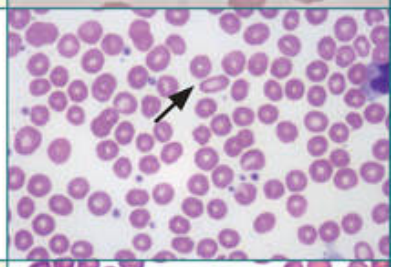
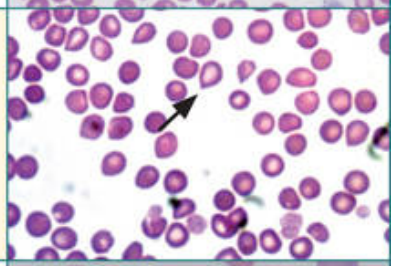
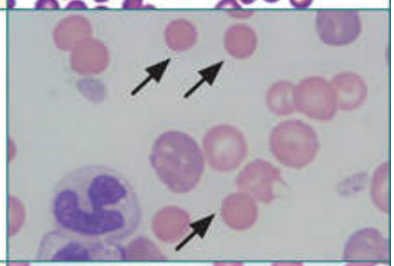
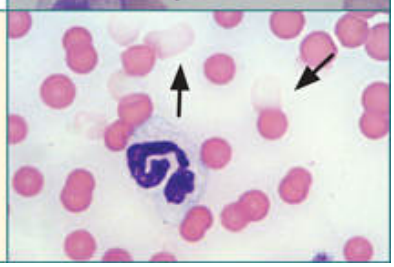
Severity	Toxic changes in neutrophils (classified according to the main change produced)	Frequency	Reactive lymphocytes, atypia, or other lymphocytic changes
Mild	Foamy cytoplasm or cytoplasmic basophilia in 25 % or more of neutrophils	Mild	1–10 %
Moderate	Mild changes + Döhle bodies* (focal cytoplasmic basophilia or giant neutrophils)	Moderate	11–50 %
Marked	Mild or moderate changes + cytoplasmic vacuoles in at least 10 % of affected neutrophils	Marked	51–100 %
Severe	Aforementioned changes + hyaline nucleus or toxic granules in 10 % of neutrophils		

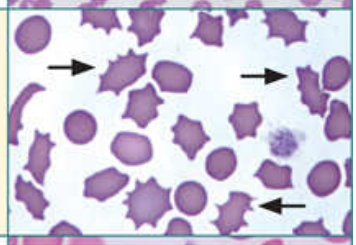
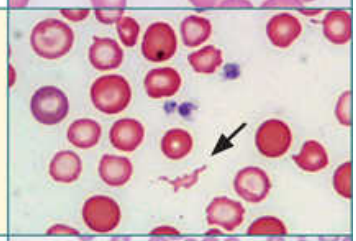
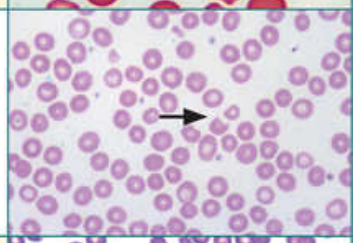
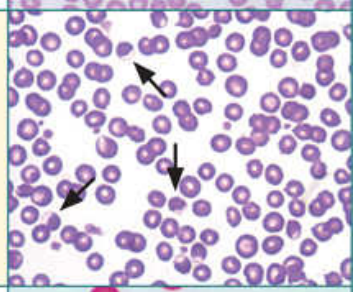
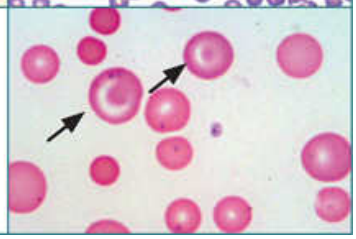
* Döhle bodies in cats are considered a mild toxic change.

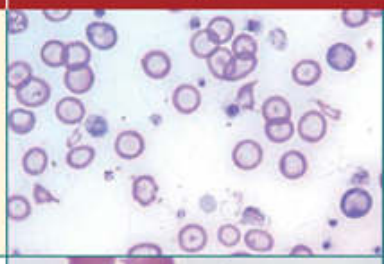
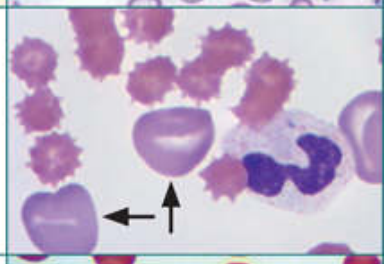
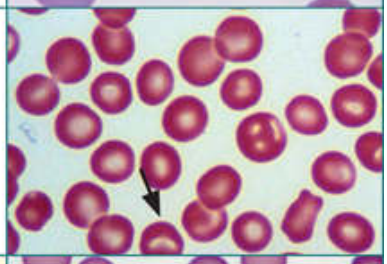
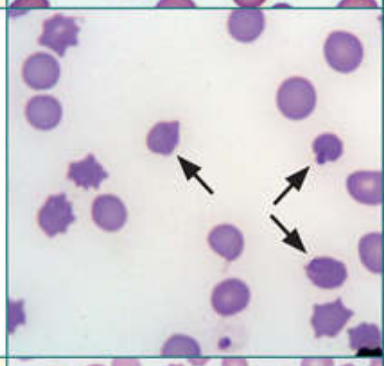
Systematic examination of blood smears



Red blood cell alterations in blood smears

Name	Mechanism	Association	Image
Microcytosis	Cytoplasmic maturation defects	• Iron-deficiency anaemia • Pb toxicity • Vitamin B6 deficiency	
Macrocytosis	Defects in nuclear maturation	• Folic acid deficiency • FeLV infection • Common in Poodles • Regeneration	
Elliptocytes	Alteration in RBC development in the bone marrow	• Spinal neoplasms • Hepatic lipidosis and portosystemic shunt • Hereditary diseases	
Dacrocytes	Alteration in RBC development in the bone marrow	• Spinal tumours • Glomerulonephritis and hypersplenism • Iron deficit (ruminants)	
Spherocytes	Plasma membrane loss	• Immune-mediated haemolytic anaemia • Hereditary diseases • Snake venom	
Ghost cells	Intravascular cell lysis	Haemolytic anaemias: immune-mediated, caused by oxidising agents, etc.	

Name	Mechanism	Association	Image
Echinocytes (crenation)	Alterations in RBC membrane phospholipids	• Artefact • Snake venom • Uraemia • Pyruvate kinase deficiency	
Echino-elliptocytes	Alterations in RBC membrane phospholipids	Renal impairment (glomerulonephritis)	
Acanthocytes	Alterations in lipid composition of plasma membrane	• Hepatic alterations • Glomerulonephritis • Haemangiosarcoma and DIC	
Schistocytes	RBC fragmentation	Microangiopathic haemolytic anaemia: DIC, haemangiosarcoma, dirofilariosis	
Keratocytes	Alterations of the plasma membrane	• Iron deficiency • Liver disease • Doxorubicin in cats	
Eccentrocytes	Oxidative phenomena that induce fusion of the plasma membrane	• Ketoacidotic diabetes • Intoxication with oxidising substances: onions, paracetamol, NSAIDs, etc.	
• **Target cells** • **Codocytes**	Alterations of the plasma membrane	• Low number (physiological) • Iron deficiency • Regenerative anaemias	

Name	Mechanism	Association	Image
• **Anulocytes** • **Hypochromasia**	Decrease in Hb content	Iron deficiency	
• **Polychromatophils** • **Polychromasia**	RBCs with nuclear remnants (reticulocytes)	• Low number (physiological) • Regenerative anaemias	
Stomatocytes	Alterations in osmotic pressure of RBCs	• Preparation artefacts • Hereditary diseases • Drugs	
Howell–Jolly bodies	Remnants of nuclear material	• Low number (physiological) • Regenerative anaemias • Splenectomy • Chemotherapy	
Heinz bodies	Oxidised Hb adhered to the membrane	• Up to 5 % in cats • Diabetes mellitus, hyperthyroidism, lymphoma • Oxidising agents: e.g. onions, paracetamol, vitamin K	
Nucleated RBCs	Immature cells (rubricytes and metarubricytes) with nuclear material	• Regenerative anaemias • Spinal tumours, myelodysplasia, myelophthisis	

Template for blood smear examination

Clinical history: **Species:** **Breed:**
Sex: **Age:**
Type of sample: EDTA blood ☐ Heparin blood ☐ Citrate blood ☐ Other ☐ Specify:
Date and time of collection:

Data of interest in clinical history:

Blood smear examination:

Red blood cells

	Mild	Moderate	Marked
Polychromasia	☐	☐	☐
Nucleated RBCs	☐	☐	☐
RBCn/100WBC			
Anisocytosis	☐	☐	☐
Acanthocytes	☐	☐	☐
Eccentrocytes	☐	☐	☐
Equinocytes (crenation)	☐	☐	☐
Keratocytes	☐	☐	☐
Ovalocytes	☐	☐	☐
Schistocytes	☐	☐	☐
Spherocytes	☐	☐	☐
Stomatocytes	☐	☐	☐
Anulocytes	☐	☐	☐
Target cells	☐	☐	☐
Agglutination	☐	☐	☐
Rouleaux	☐	☐	☐
Howell-Jolly bodies	☐	☐	☐
Heinz bodies	☐	☐	☐
Other inclusions, specify:	☐	☐	☐
Abnormal RBCs:			

Reticulocytes Aggregates ☐ Dotted ☐
Absolute reticulocyte count:
Corrected percentage of reticulocytes:
Red cell production index:

Platelets

	Mild	Moderate	Marked
Platelet aggregates	☐	☐	☐
Other abnormalities (specify):	☐	☐	☐
Macroplatelets	☐	☐	☐

Approximate count:

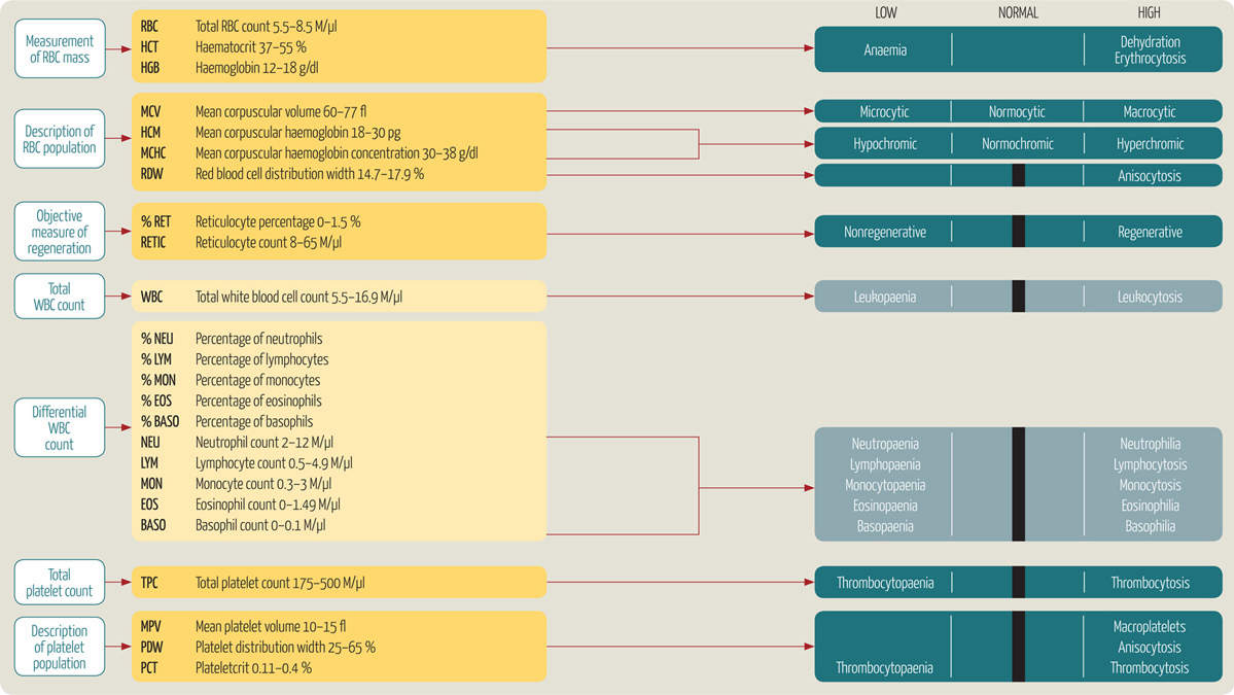
Observations and comments

White blood cells

Neutrophils (toxicity)	Mild	Moderate	Marked
Cytoplasmic basophilia	☐	☐	☐
Döhle bodies	☐	☐	☐
Cytoplasmic vacuolation	☐	☐	☐
Lymphocytes			
Reactive lymphocytes	☐	☐	☐
Granular lymphocytes	☐	☐	☐
Lymphoblasts	☐	☐	☐
Other abnormal findings:			

Differential WBC count
Neutrophils
Band:
Segmented:
Lymphocytes:
Monocytes:
Eosinophils:
Basophils:
Other (abnormal) cells:

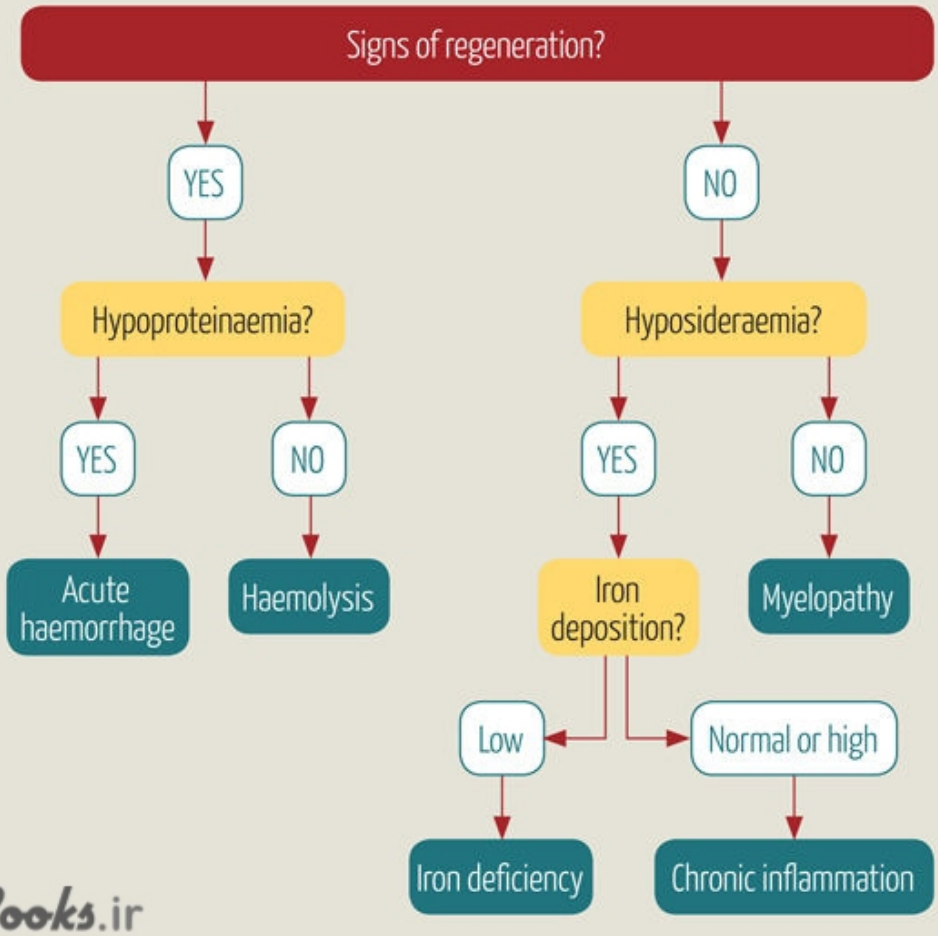
Interpretation of the haemogram



The reference ranges depend on the method used and, therefore, on the laboratory.

Anaemia

Differential diagnosis of anaemias



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Signs of regeneration

- Subjective: macrocytosis, polychromasia, anisocytosis, nucleated RBCs, etc.
- Objective: CRC >1 %

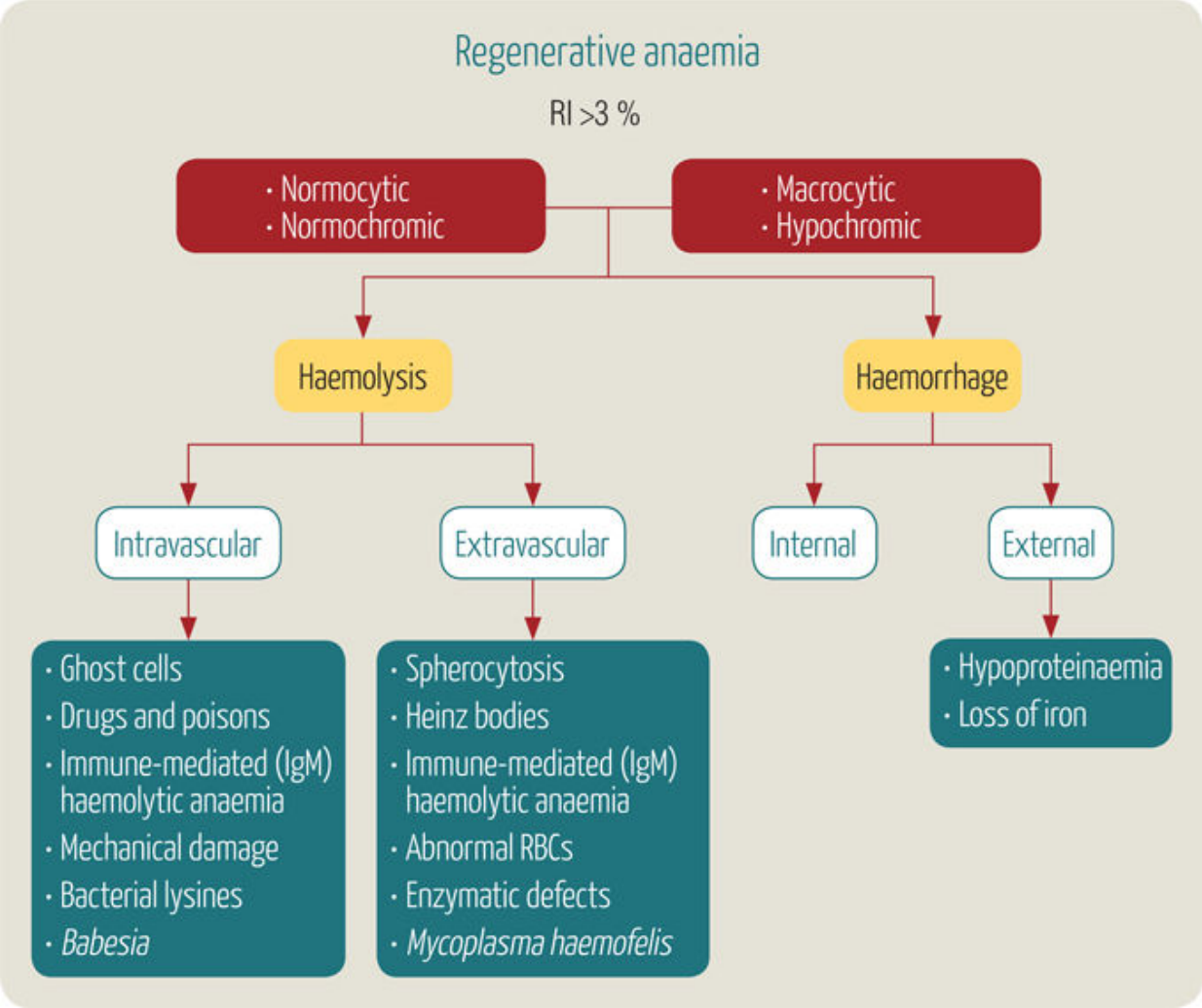
$$CRC = \frac{\%\ \text{Reticulocytes} \times \text{Observed Hct}}{\text{Ideal Hct}}$$

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Types of anaemia

According to degree of regeneration

Regenerative anaemias



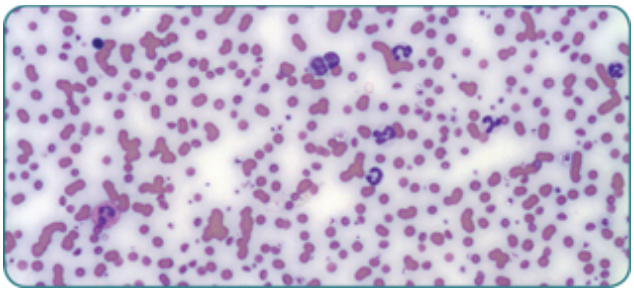


Figure 1. Immune-mediated haemolytic anaemia. Autoagglutination.

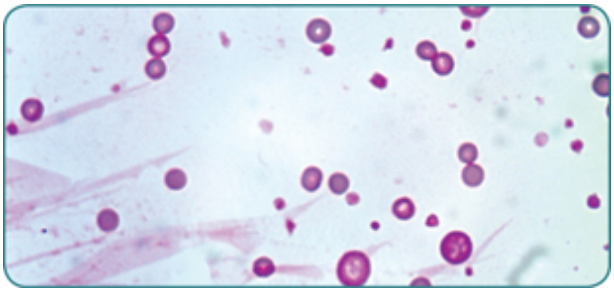
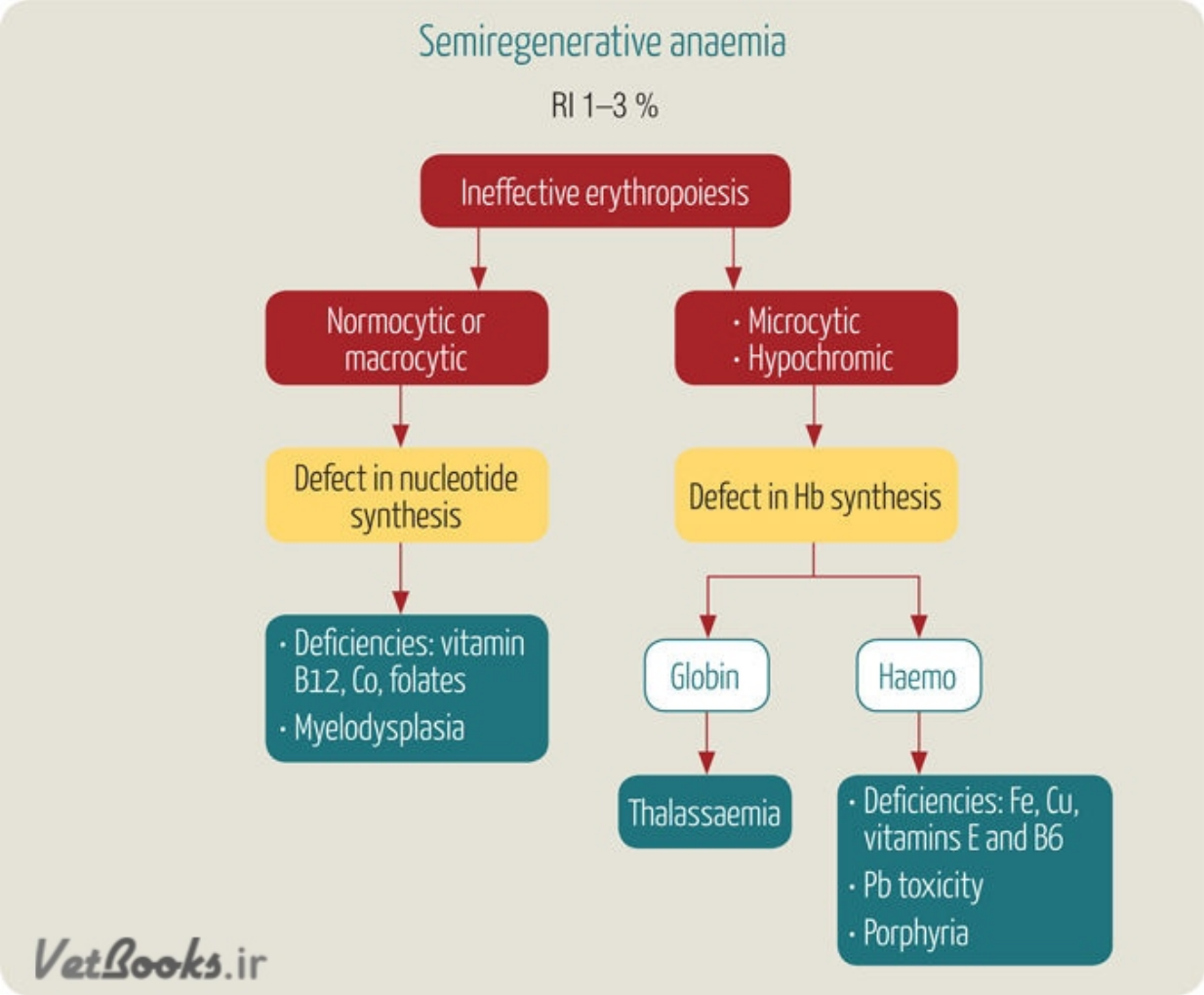


Figure 2. Immune-mediated haemolytic anaemia. Spherocytes.

Semiregenerative anaemias



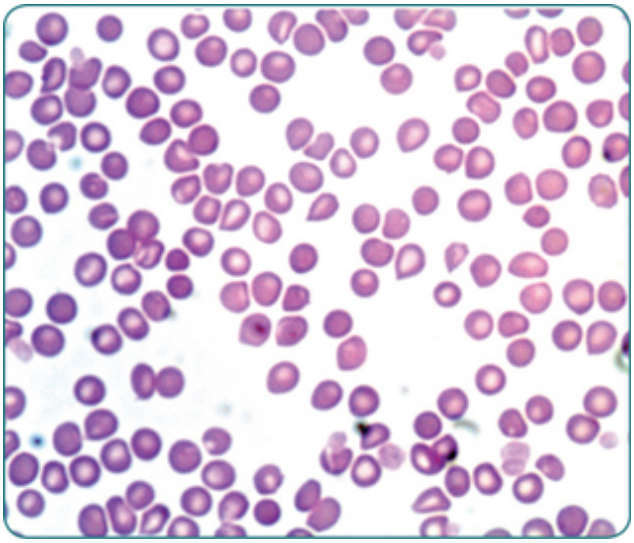


Figure 3. Iron deficiency anaemia. Dacryocytosis.

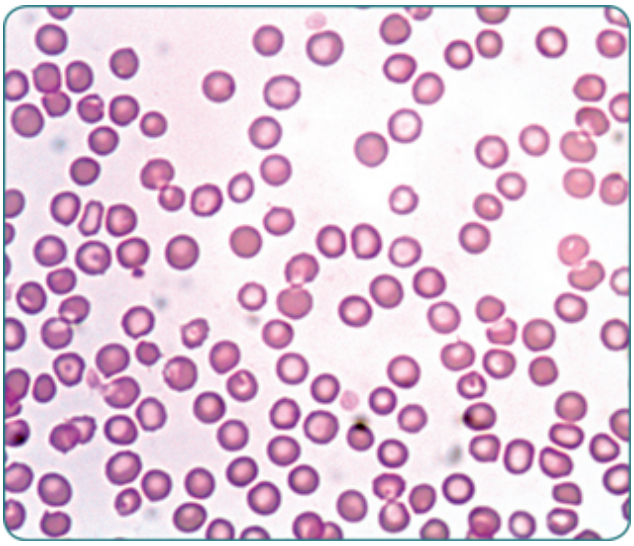
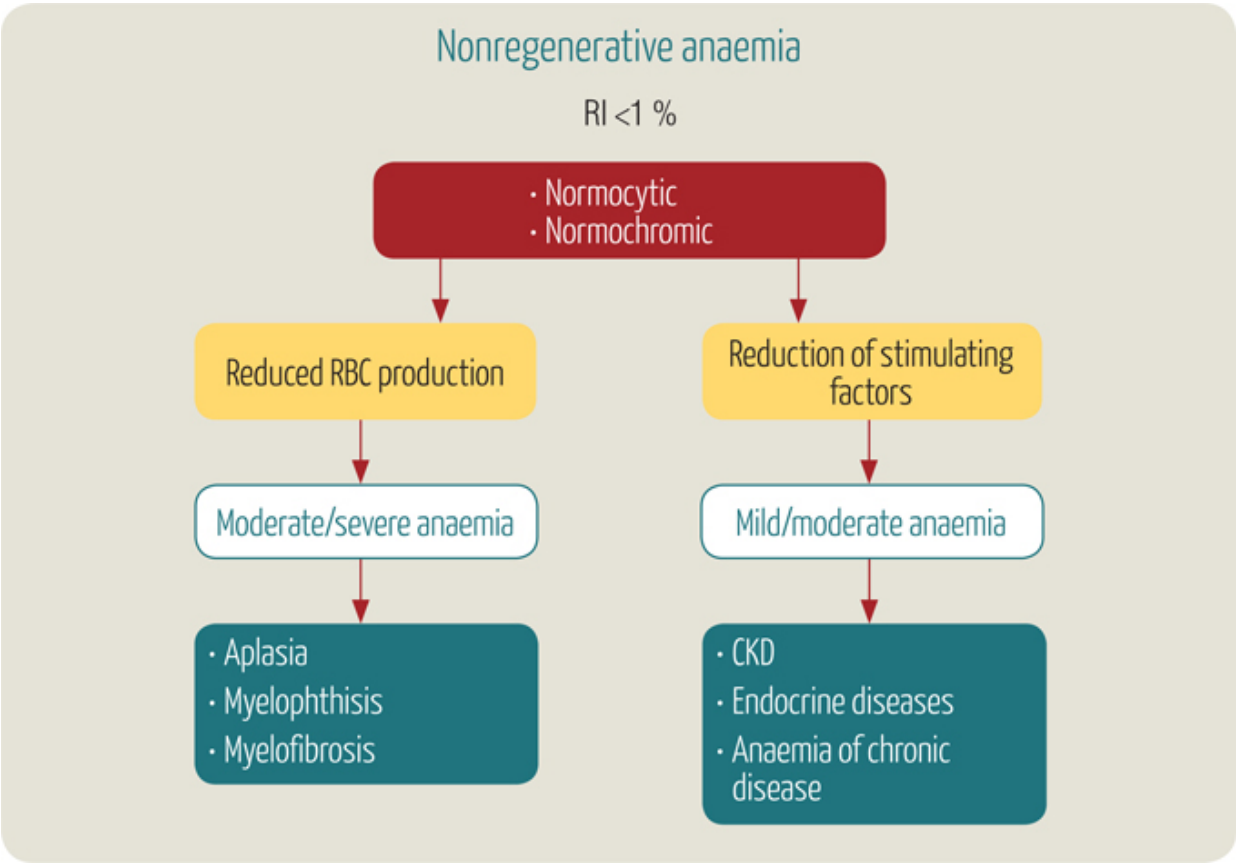


Figure 4. Iron deficiency anaemia. Hypochromy.

Nonregenerative anaemias



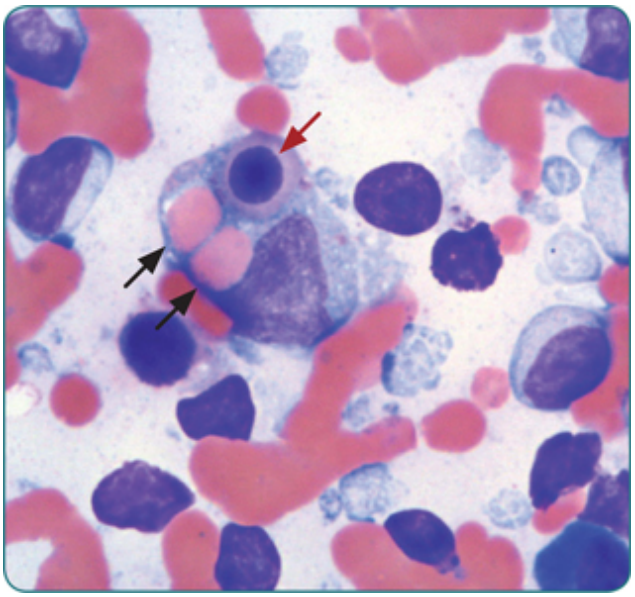


Figure 5. Image showing bone marrow of a dog with pure red cell aplasia. Erythrophagocytosis. Mature RBCs (black arrows) and nucleated RBC (red arrow).

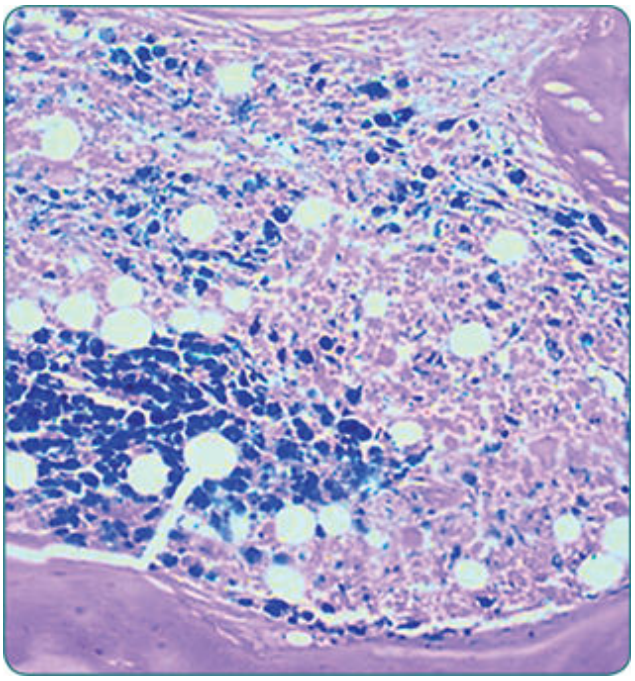
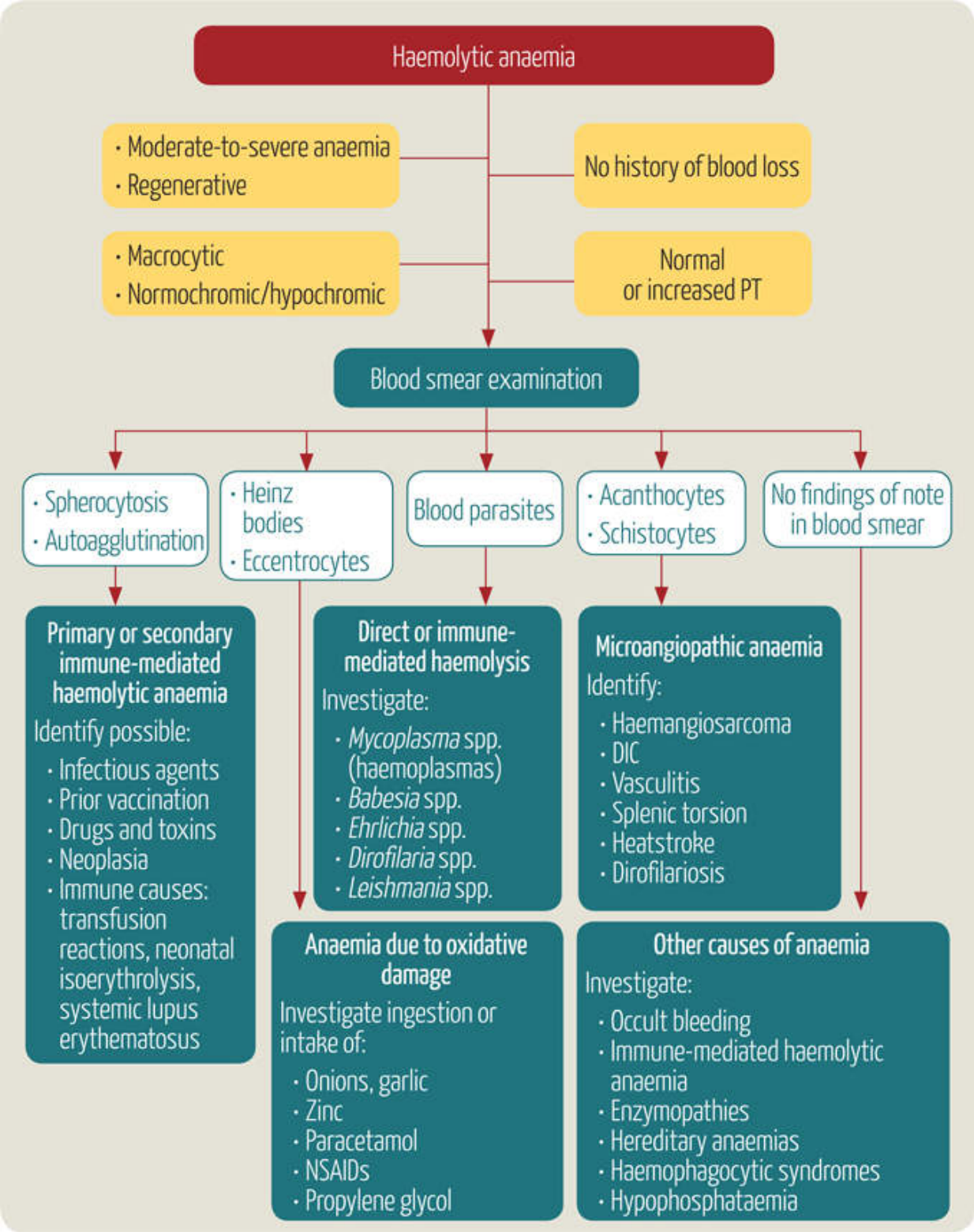


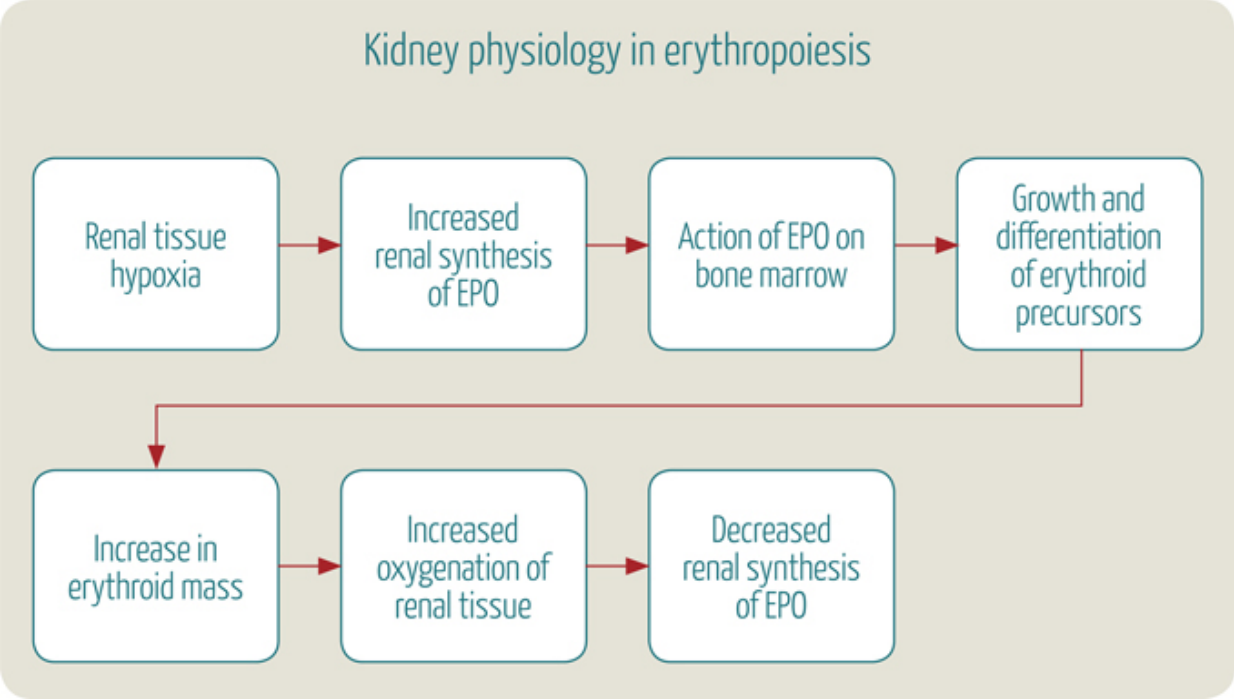
Figure 6. Deposits of Fe in bone marrow (blue). Anaemia of CKD. Staining with Prussia blue.

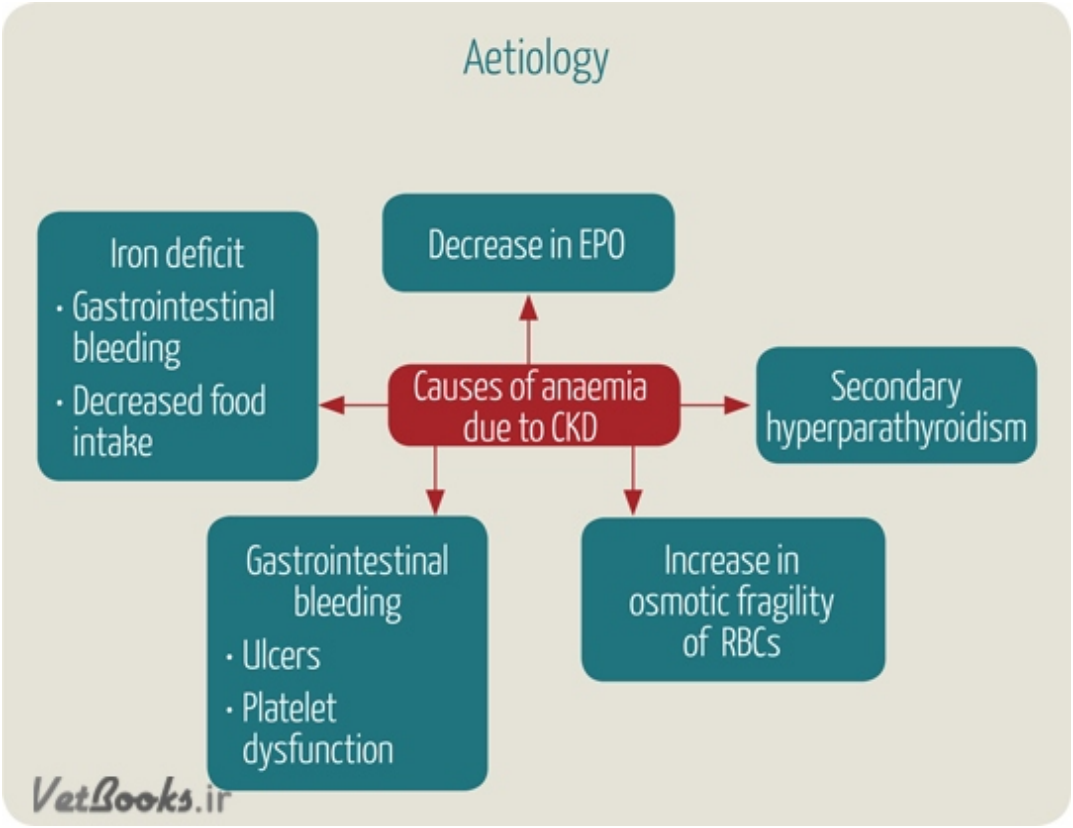
According to aetiology

Haemolytic anaemia



Anaemia due to CKD


Kidney physiology in erythropoiesis
Renal tissue hypoxia
Increased renal synthesis of EPO
Action of EPO on bone marrow
Growth and differentiation of erythroid precursors
Increase in erythroid mass
Increased oxygenation of renal tissue
Decreased renal synthesis of EPO


Aetiology
Iron deficit
• Gastrointestinal bleeding
• Decreased food intake
Decrease in EPO
Causes of anaemia due to CKD
Secondary hyperparathyroidism
Gastrointestinal bleeding
• Ulcers
• Platelet dysfunction
Increase in osmotic fragility of RBCs
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Infectious anaemias

Figure 7. *Babesia canis* .

Figure 8. *Ehrlichia canis* .

Figure 9. *Leishmania* spp.

Figure 10.*Dirofilaria immitis* .

Figure 11 *Mycoplasma haemofelis* .

Iron-deficiency anaemia

Anaemia of chronic disease

Differential diagnosis of iron-deficiency anaemia and anaemia of chronic disease

Erythrocytosis

Increases in RBCs, Hb concentration, and Hct value.

Aetiology

Diagnostic approach

Summary

Relative erythrocytosis: decrease in plasma volume

- **Differential diagnosis:** water deprivation, vomiting, diarrhoea, heat stroke, burns, passage of fluids into the interstitial space, splenic contraction.
- **Clinical signs:** dehydration, diarrhoea, vomiting.
- **Diagnosis:** signs of dehydration, increased Hct and PT with normal RBC. Normalisation after fluid therapy.
- **Treatment:** rehydration.

Absolute erythrocytosis: increase in number of RBCs

Primary (independent of EPO)

- **Differential diagnosis:**
  - **Congenital polycythaemia:** mutation in EPO receptors that results in hypersensitivity.
  - **Polycythaemia vera:** myeloproliferative disorder with clonal proliferation of erythroid precursors.
- **Clinical signs:** congestive and tortuous conjunctival vessels, hyperaemic mucosa, seizures, ataxia, blindness, epistaxis, hyphema, haematuria, haematemesis.
- **Diagnosis:** haemogram (Hct >70 %, reticulocytosis), thoracic radiography, abdominal ultrasound, blood gas analysis, ECG without alterations, normal or low EPO. Diagnosis by exclusion. Indistinguishable polycythaemia vera and congenital polycythaemia.
- **Treatment:** phlebotomy, hydroxyurea, radioactive P-32.

Secondary (increase in EPO)

- **Clinical signs:** similar to those seen in primary absolute erythrocytosis, together with clinical signs of the underlying disease (e.g. cyanosis, hyperaemia, heart murmur, dyspnoea, renomegaly).

Appropriate (with systemic hypoxia)

- **Differential diagnosis:** right-to-left cardiovascular shunt, chronic lung disease, upper airway obstruction, chronic exposure to carbon monoxide, methaemoglobin reductase deficiency, high altitude.
- **Diagnosis:** haemogram, chest radiography, ↓ PO_2 , ↓ SaO_2 , echocardiography, increased or normal EPO.
- **Treatment:** phlebotomy, resolve hypoxia, hydroxyurea if underlying aetiology cannot be corrected.

Inappropriate (without systemic hypoxia)

- **Differential diagnosis:** renal neoplasia, amyloidosis, pyelonephritis, renal cyst, hydronephrosis, paraneoplastic syndrome.
- **Diagnosis:** haemogram, ultrasound and abdominal radiograph, fine-needle aspiration, biopsy, increased or normal EPO.
- **Treatment:** phlebotomy, determine the primary aetiology, hydroxyurea if underlying aetiology cannot be resolved.

Leukogram alterations

Leukogram patterns

Neutrophilia

Figure 12. Toxic neutrophils in a dog with pancreatitis and peritonitis.

Figure 13. Hypersegmented neutrophil in a leukogram showing excess of corticoids in a dog.

Neutropaenia

Lymphocytosis

Lymphopaenia

Figure 14. Reactive lymphocyte.

Figure 15. Granular lymphocyte.

Monocytosis

Figure 16. Activated monocyte.

Figure 17. Myelomonoblastic leukaemia.

Eosinophilia

White blood cell alterations

Classification of leukaemias

Figure 18. Acute lymphoblastic leukaemia (ALL).

Figure 19. Chronic lymphoblastic leukaemia (CLL).

Lymphoma

Multiple myeloma

Pathophysiology	Systemic proliferation of malignant IgG-producing plasma cells or of Ig fragments (Bence Jones or heavy chain proteins)
Incidence	• <1 % of malignant tumours • 8 % of haematopoietic tumours
Aetiology	• Genetic predisposition? • Viral infection? • Chronic immune stimulation?
Clinical signs	Fever, apathy, PU/PD, haemorrhagic diathesis, bone pain, hepatosplenomegaly, lymphadenopathy, neurological signs, chronic infections
Diagnostic tests	Haemogram, serum biochemistry, urinalysis, clotting time, serum and urine protein electrophoresis, radiography, ultrasound, ophthalmological examination, cytology, and biopsy
Clinical-pathological alterations	• Normochromic normocytic anaemia (60 %), thrombocytopaenia (30–50 %), and leukopaenia (20–30 %) • Azotaemia (30–50 %) and hypercalcaemia (15–20 %) • Monoclonal gammopathy in serum and urine proteinogram (Bence Jones proteinuria, 25–40 %) • Increased clotting time (30–50 %) • Radiography showing osteolytic lesions, pathological fractures, diffuse osteopaenia, and osteoporosis in the long bones, vertebrae, and pelvis • Organomegaly and lymphadenopathy on ultrasound • Ophthalmological examination showing tortuous and dilated vessels and retinal detachment (20

	%) • Predominance of plasma cells in cytology and biopsy
Treatment	• Melphalan and prednisone • Supportive care: fluid therapy, FFP, antibiotic therapy, bisphosphonates • Rescue treatments: cyclophosphamide, chlorambucil, lomustine, doxorubicin, vincristine
Prognosis	• Complete remission, 43 %; partial remission, 49 % • Mean survival time: 540 days

Systemic lupus erythematosus (dog)

Pathophysiology	• Type III hypersensitivity reaction with formation of soluble Ag-Ab complexes, which diffuse into the vascular endothelial space, activate the complement cascade and attract inflammatory cells, producing membranous glomerulonephritis, necrotising vasculitis, and polyarthritis • Occasionally, type II hypersensitivity reaction caused by binding of Abs to surface Ags of RBCs, platelets, and WBCs	
Aetiology	Breed predisposition (Shetland Sheepdog, Collie, Beagle, Irish Setter, Poodle, and German Shepherd)	
Clinical signs	**Common**	Polyarthritis, fever, skin lesions
	Frequent	Lymphadenopathy, splenomegaly
	Rare	Polymyositis, CNS disorders, neuropathies
Diagnostic tests	Haemogram, blood smear, serum biochemistry, urinalysis, UPC, clotting time, serum protein electrophoresis, radiography, ultrasound, arthrocentesis, antinuclear antibodies	
Diagnosis	Sum of criteria (2 major and positive antinuclear Abs; or 1 major, 2 minor, and positive antinuclear Abs)	
	Major criteria	Nonerosive and nonseptic polyarthritis, polymyositis, dermatological lesions (erythema, erosions, ulcers, depigmentation), glomerulopathy or persistent proteinuria, and immune-mediated anaemia, leukopaenia, or thrombocytopaenia

	Minor criteria	Fever, oral, lingual, or nasopharyngeal ulcers, inflammation and effusion in body cavities, lymphadenopathy, seizures or neuropathies
Treatment	• Prednisone: 2 mg/kg/day in decreasing doses (minimum 6 months) • Supportive care: fluid therapy, antibiotic therapy, analgesics • Rescue treatments: azathioprine, cyclosporine, levamisole, mycophenolate mofetil, cyclophosphamide, or chlorambucil	
Prognosis	Guarded	

Most common hereditary immunodeficiencies

Hypersensitivity reactions

Alterations of the lymphoid organs and spleen

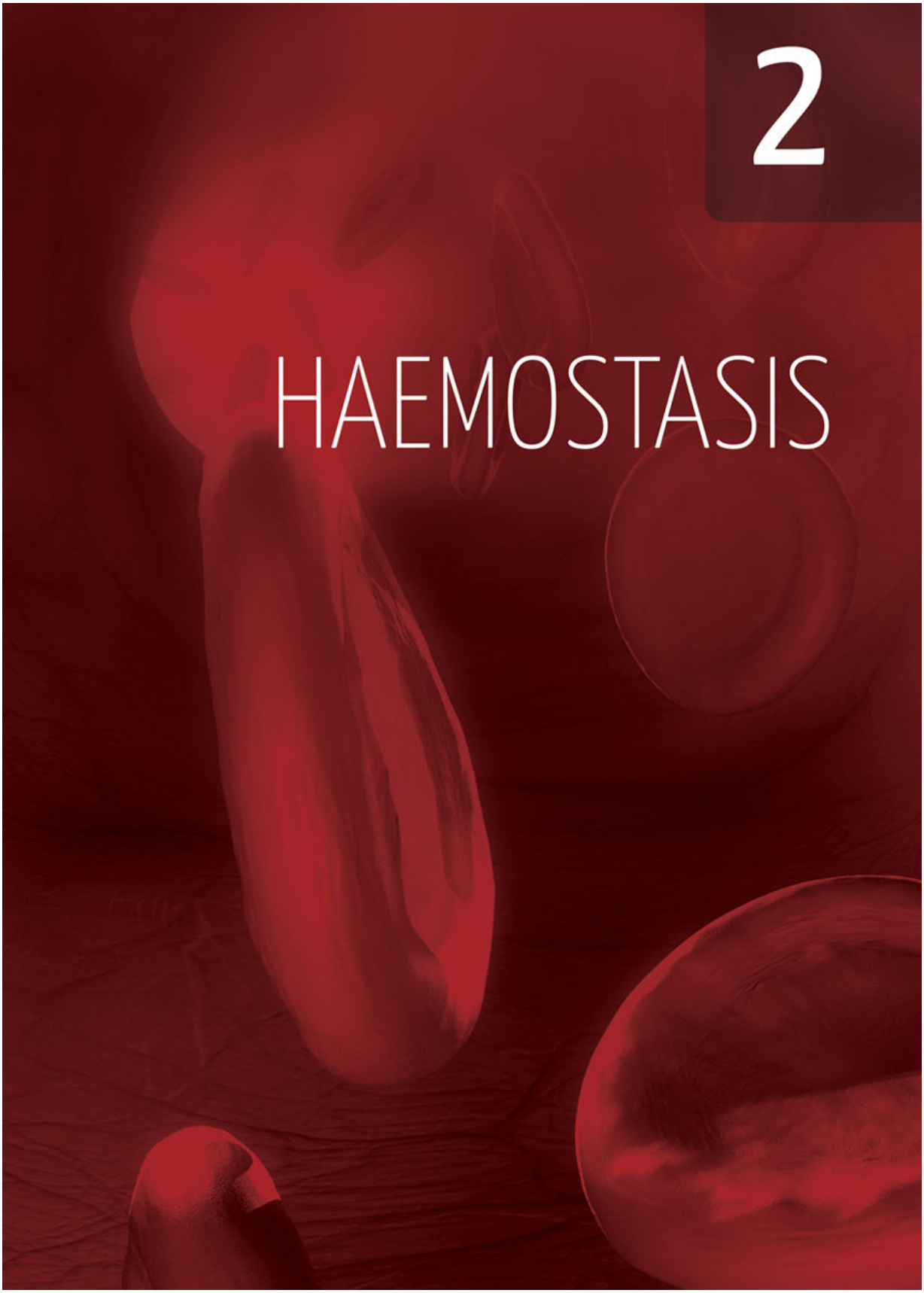
Lymphadenopathies

Fever of unknown origin

Aetiology

Splenomegaly

Aetiology


2
HAEMOSTASIS

Diagnostic techniques

Parameter		Alteration of reference value	Interpretation
Primary haemostasis	Platelet count	<175,000/µl	Thrombocytopaenia (FIV, FeLV, *Ehrlichia* spp., bleeding, DIC, bone marrow disorders, autoimmune destruction, sequestration)
		<30,000/µl	Severe thrombocytopaenia with risk of bleeding (usually with primary or secondary immune-mediated component)
	Mean platelet volume (in combination with thrombocytopaenia)	<12 fl	No bone marrow response
		>12 fl	Adequate bone marrow response
	BMBT	>1.5 min	Thrombocytopaenia, platelet dysfunction, von Willebrand disease
	Antiplatelet antibodies	Presence	Primary or secondary immune-mediated thrombocytopaenia (vaccines, drugs, infection, or neoplasia)
	vWF	<50 %	Von Willebrand disease
	PIVKA	Presence	Presence of proteins associated with vitamin K deficiency
Secondary haemostasis	PT	>10 seconds	Alterations in factors V, VII, X, prothrombin, or fibrinogen
	aPTT	>18 seconds	Alterations in factors V, VIII, IX, X, XI, XII, prothrombin, or fibrinogen (haemophilia)
	AT	<85 %	Hypercoagulable state (DIC, protein-losing nephropathy, protein-losing enteropathy, systemic inflammation, neoplasia)
Fibrinolysis	FDPs	>10 µg/ml	Increased fibrinolysis (DIC)
	D dimers	>250 ng/ml	Thromboembolism, DIC

Diagnostic approach

Rapid blood tests

	Platelets	ACT	BMBT	CRT
Angiopathy	N	N	N/I	N
Thrombopathy	D/N	N	I	I
Liver disease	N	I	N	N
Haemophilias	N	I	N	N
Von Willebrand disease	N	N	I	N
DIC	D	I	N/I	I

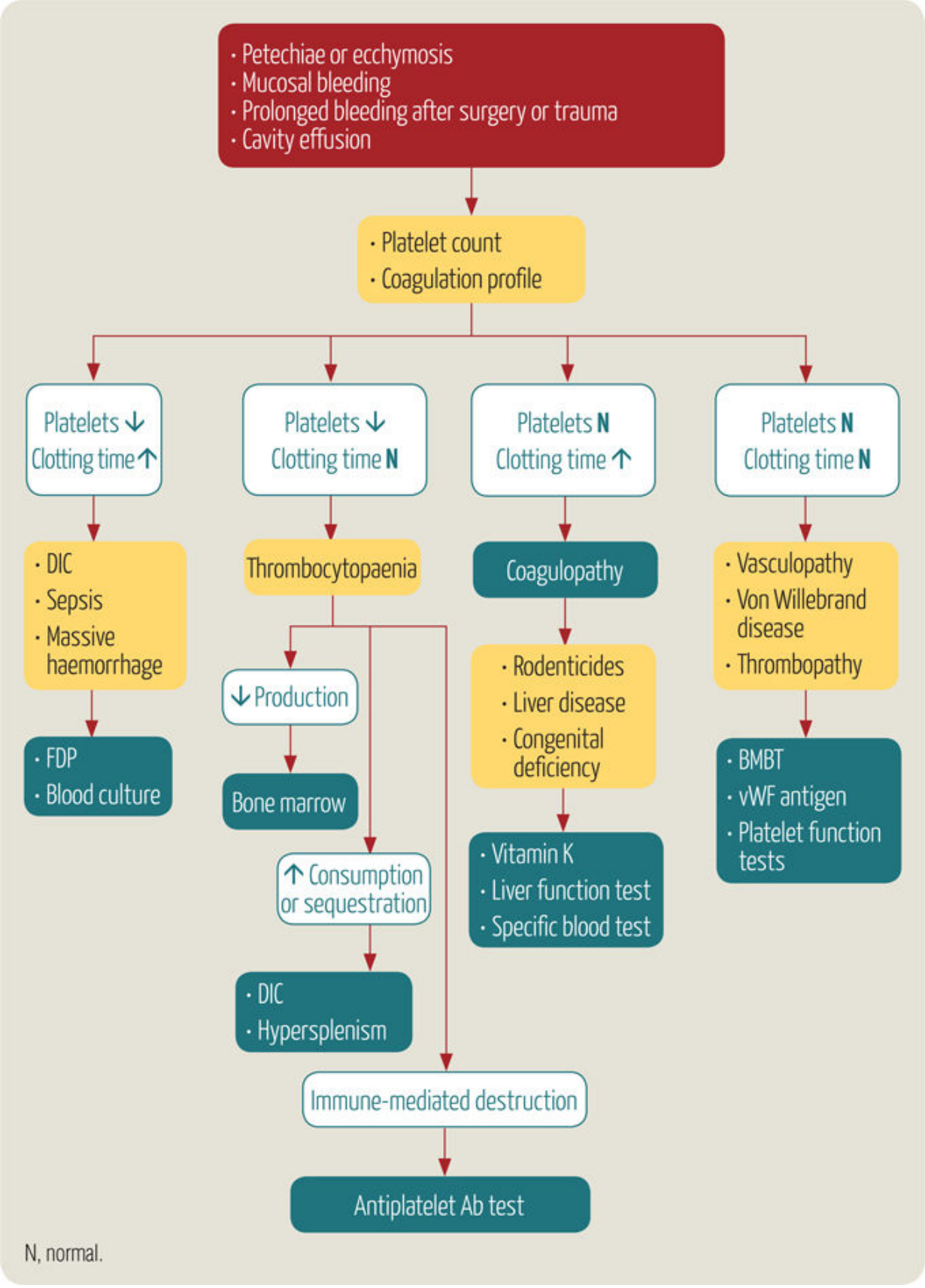
N, normal; I, increased; D, decreased.

Definitive tests

	aPTT	PT	TT	F	FDP
Liver disease	I	I	I	D	N
Vitamin K deficiency	I	I	N	N	N
Haemophilias	I	N	N	N	N
DIC	I	I	I	D	I
Excess heparin	I	I	I	N	N
Von Willebrand disease	I/N	N	N	N	N

N, normal; I, increased; D, decreased; F, fibrinogen concentration.

Diagnostic examination of patient with haemorrhages


• Petechiae or ecchymosis
• Mucosal bleeding
• Prolonged bleeding after surgery or trauma
• Cavity effusion
• Platelet count
• Coagulation profile
Platelets ↓
Clotting time ↑
Platelets ↓
Clotting time N
Platelets N
Clotting time ↑
Platelets N
Clotting time N
• DIC
• Sepsis
• Massive haemorrhage
Thrombocytopaenia
Coagulopathy
• Vasculopathy
• Von Willebrand disease
• Thrombopathy
• FDP
• Blood culture
↓ Production
Bone marrow
↑ Consumption or sequestration
• DIC
• Hypersplenism
• Rodenticides
• Liver disease
• Congenital deficiency
• Vitamin K
• Liver function test
• Specific blood test
• BMBT
• vWF antigen
• Platelet function tests
Immune-mediated destruction
Antiplatelet Ab test

N, normal.



Figure 1. Petechiae in a case of immune-mediated thrombocytopaenia.



Figure 2. Bleeding of the conjunctival mucosa in a case of immune-mediated thrombocytopaenia.



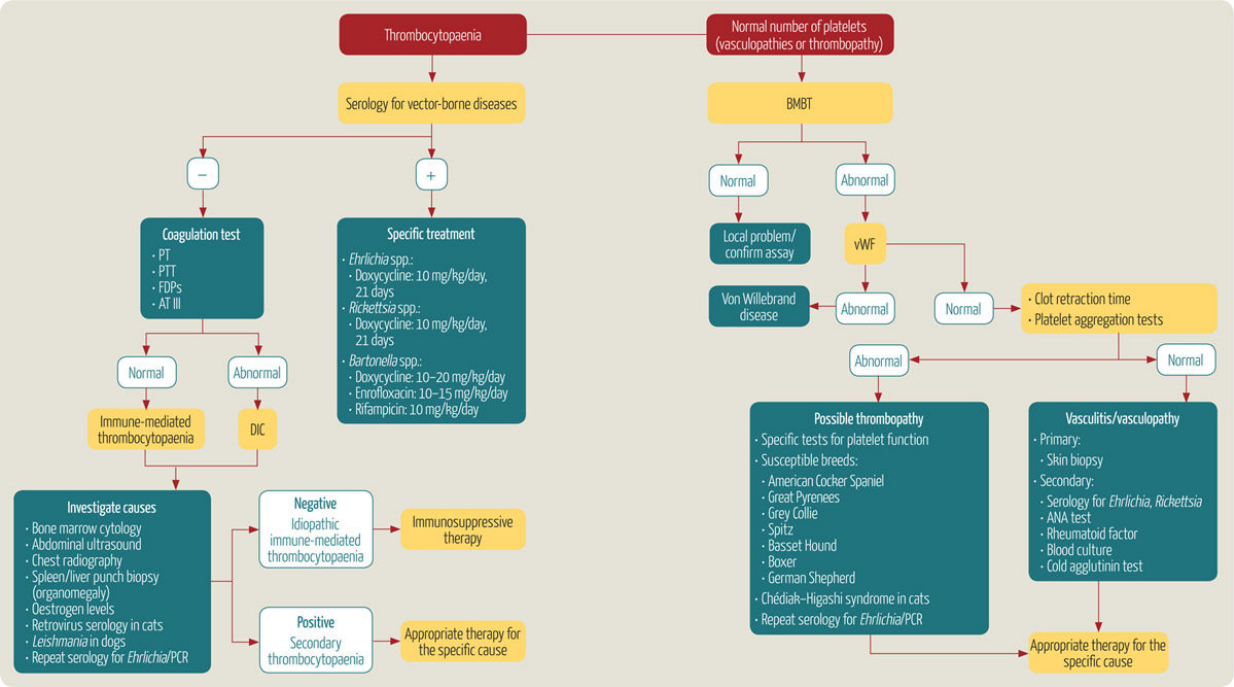
Figure 3. Hyphaema in a dog with severe thrombocytopaenia due to ehrlichiosis.



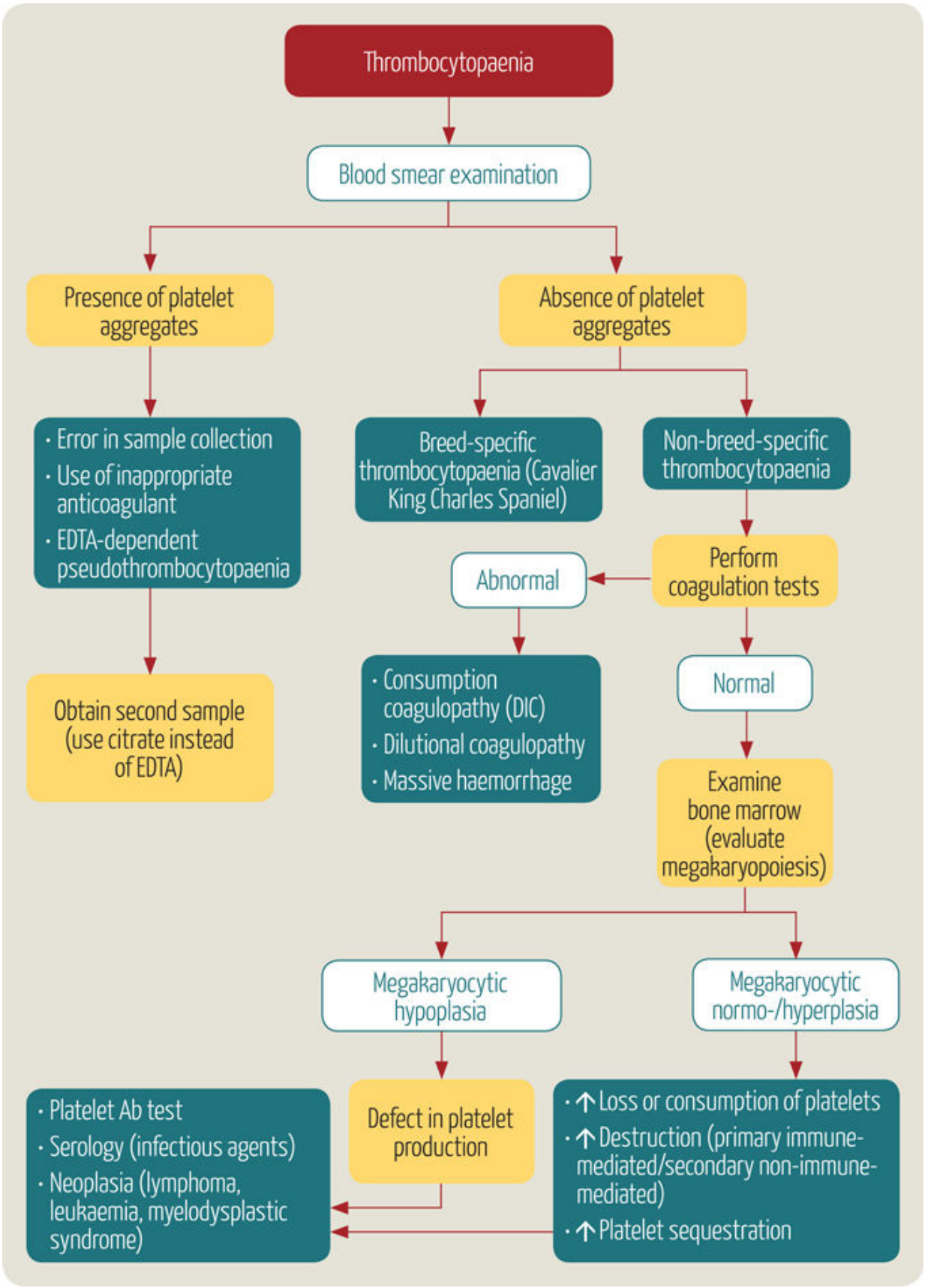
Figure 4. Profuse haematomas in a female dog with severe thrombocytopaenia due to Ehrlichia spp.

Alterations in haemostasis

Petechiae and ecchymosis



Thrombocytopaenia


Thrombocytopaenia
Blood smear examination
Presence of platelet aggregates
Absence of platelet aggregates
• Error in sample collection
• Use of inappropriate anticoagulant
• EDTA-dependent pseudothrombocytopaenia
Obtain second sample (use citrate instead of EDTA)
Breed-specific thrombocytopaenia (Cavalier King Charles Spaniel)
Non-breed-specific thrombocytopaenia
Perform coagulation tests
Abnormal
• Consumption coagulopathy (DIC)
• Dilutional coagulopathy
• Massive haemorrhage
Normal
Examine bone marrow (evaluate megakaryopoiesis)
Megakaryocytic hypoplasia
Megakaryocytic normo-/hyperplasia
• Platelet Ab test
• Serology (infectious agents)
• Neoplasia (lymphoma, leukaemia, myelodysplastic syndrome)
Defect in platelet production
• ↑Loss or consumption of platelets
• ↑Destruction (primary immune-mediated/secondary non-immune-mediated)
• ↑Platelet sequestration

Hereditary coagulopathies

	Defect	Cause	Breed	Diagnosis
Primary haemostasis	Glanzmann thrombasthaenia	GPIIa and GPIIb deficits	Otterhound, Pyrenean Mastiff	Breed and clinical history, platelet count, blood smear, mucosal bleeding time, vWF, flow cytometry for GP receptors, electron microscopy, and other specific platelet function tests
	Basset Hound thrombopathy	cAMP defect	Basset Hound	
	Unknown thrombopathy	Messenger defect	Boxer, Spitz	
	Dense granule deficiency	Dense granule deficiency	American Cocker Spaniel	
	Chédiak–Higashi syndrome	Dense granule deficiency and phospholipase C signalling deficit	Blue Persian	
	Cyclic haematopoiesis of Grey Collies	Serotonin uptake and storage deficit	Grey Collie	
	Von Willebrand disease	Deficit or abnormality of vWF	e.g. Pointer, Scottish Terrier, German Shepherd, Doberman	
Secondary haemostasis	Haemophilia A	Factor VIII deficiency	British Shorthair, Siamese	aPTT, factor VIII
	Haemophilia B	Factor IX deficiency	Siamese, domestic shorthair cat, American Cocker Spaniel	aPTT, factor IX
	Haemophilia C	Factor XI deficiency	German Shepherd, Pyrenean Mastiff	aPTT, factor XI
	Factor VII deficiency	Factor VII deficiency	Beagle, Alaskan Malamute	PT, factor VII
	Factor X deficiency	Factor X deficiency	Boxer, Cocker, Jack Russell Terrier, domestic shorthair cat	PT, aPTT, factor X
	Hageman's disease	Factor XII deficiency	Various cat breeds, Poodle	aPTT, factor XII
	Deficiency of vitamin K-dependent clotting factors	Deficiency of factors II, VII, IX, X	Devon Rex	PT, aPTT, factors II, VII, IX, X, PIVKA

Acquired coagulopathies

			Disease	Coagulopathy mechanism
Primary haemostasis	Thrombocytopaenia		Infection (e.g. distemper, parvovirus, FIV, FeLV, feline panleukopaenia, FIP, *Ehrlichia*, *Babesia*, *Leishmania*, *Borrelia*, *Dirofilaria*, bacteria)	• Decreased production and immune destruction • Ab-mediated decrease in adhesion and aggregation
			Neoplasia (e.g. myeloma, lymphoma, leukaemia, haemangiosarcoma)	• Deficit in production and consumption • Defective adhesion and aggregation
			Cytotoxic drugs and oestrogens	Decrease in production
			Primary or secondary immune-mediated thrombocytopaenia (drugs, infection, or neoplasia)	Immune-mediated destruction
			Hepatosplenomegaly	Sequestration
			Haemorrhage	Increased consumption
			DIC	Increased consumption
	Thrombocytopathy	Drugs	NSAIDs	Inhibition of prostaglandins
			Prostaglandins, nitric oxide, nitroprusside	Increase in cAMP and cGMP
			Diltiazem, verapamil	Ca antagonism
			Penicillin, ampicillin, gentamicin, phenothiazides, synthetic colloids, propranolol	Interference with platelet receptors
			Liver disease	Decreased aggregation
			Kidney disease	Decreased adhesion
			Pancreatitis	Decreased aggregation
			DIC	FDPs cover platelets and impair their function
			Dysproteinaemia (myeloma, *Leishmania*, *Ehrlichia*)	Adhesion and defective aggregation due to the presence of Igs coating the platelets

	Disease	Coagulopathy mechanism
Secondary haemostasis	Rodenticide poisoning	Vitamin K antagonism
	Malabsorption, exocrine pancreatic insufficiency, biliary obstruction	Vitamin K deficiency
	Liver disease	Deficiency in coagulation factors and inhibitors, lack of activation of vitamin K-dependent factors, defective clearance of activated coagulation factors
	DIC	Platelet consumption, coagulation factors, and AT
	Heparin	Inhibition of coagulation factors
	Lupus-type anticoagulant	Abs against coagulation factors

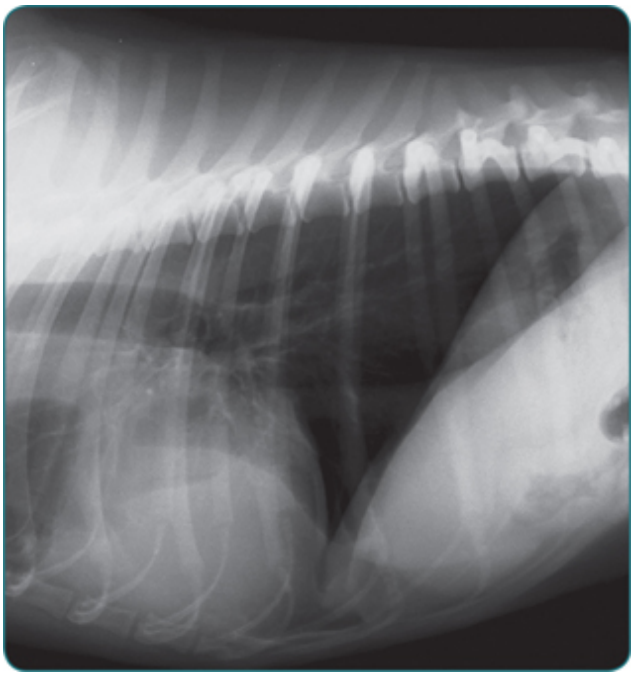


Figure 5. Chest radiography of a dog with haemothorax due to rodenticide poisoning.

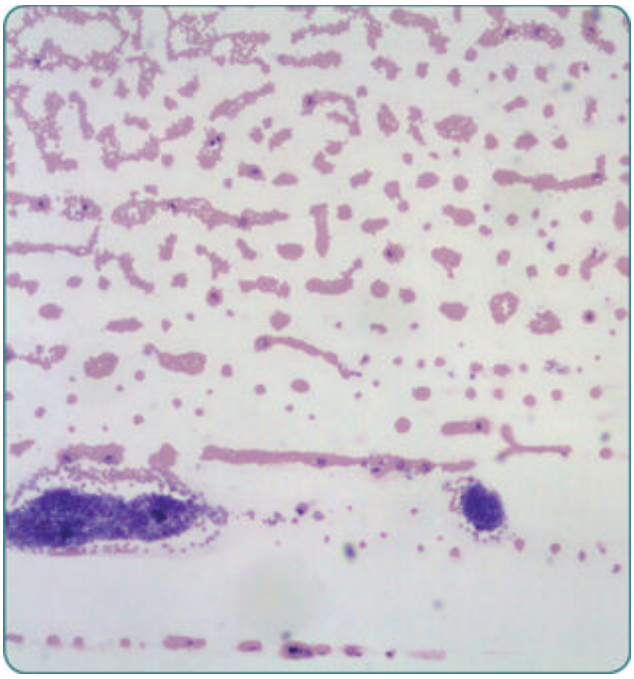
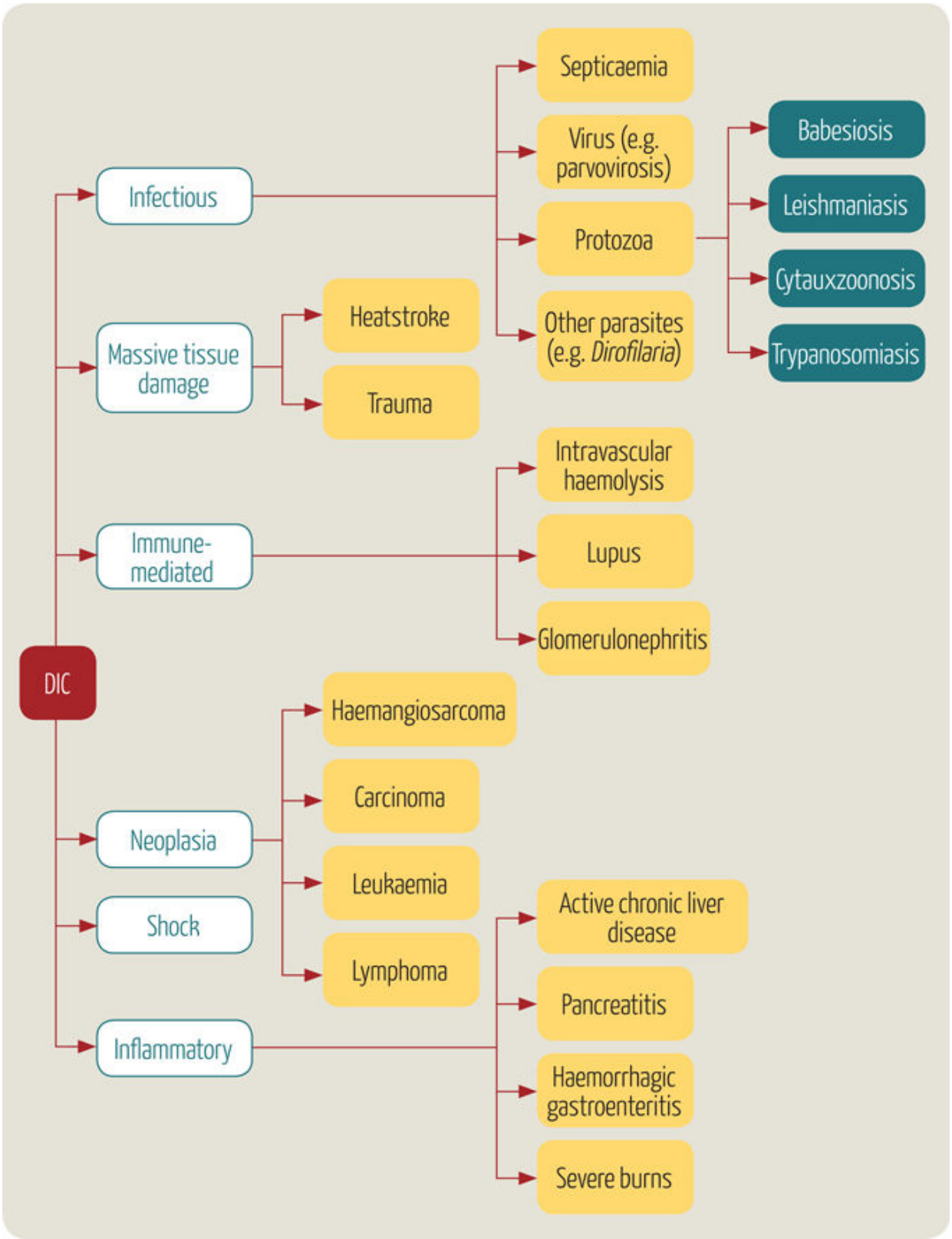


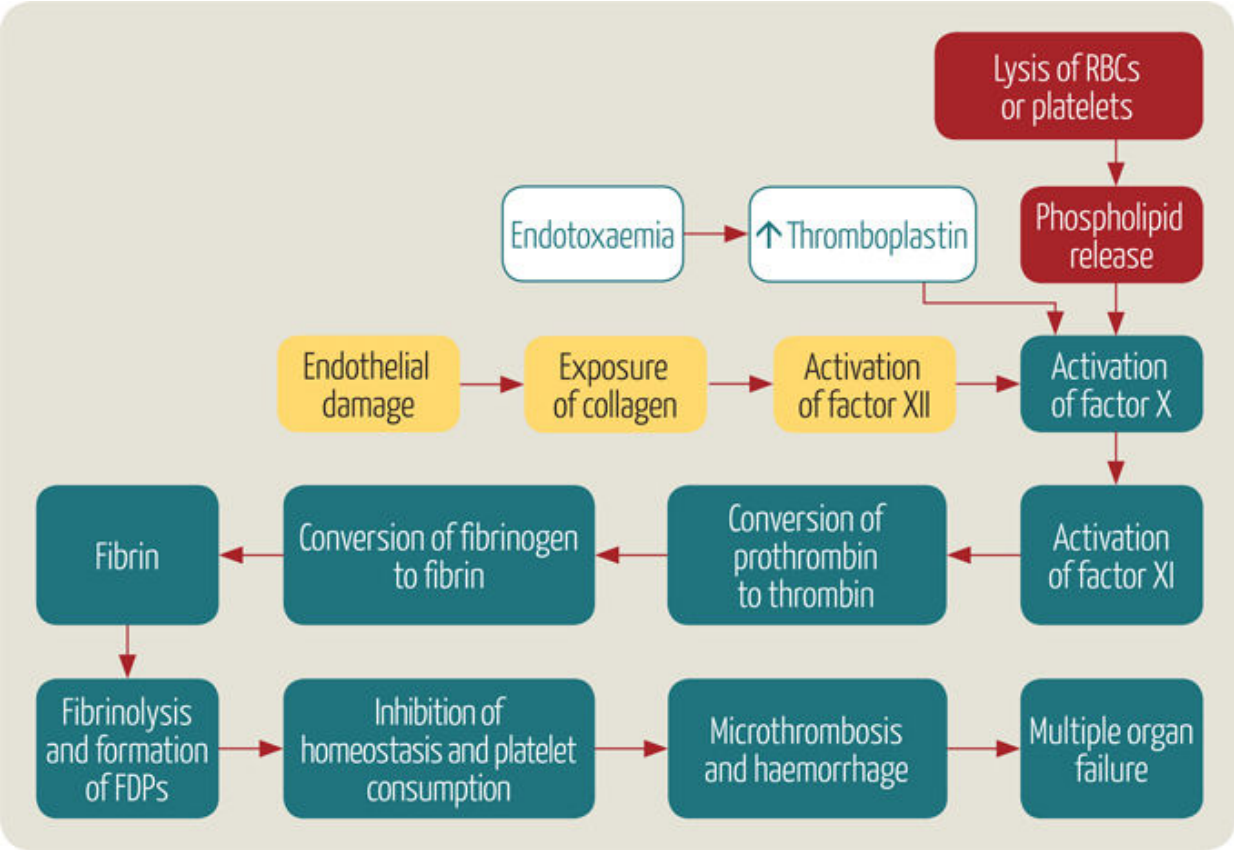
Figure 6. Blood smear of a cat with artefactual thrombocytopaenia due to platelet aggregation.

DIC

Aetiology


DIC
Infectious
Septicaemia
Virus (e.g. parvovirosis)
Protozoa
Babesiosis
Leishmaniasis
Cytauxzoonosis
Trypanosomiasis
Other parasites (e.g. Dirofilaria)
Massive tissue damage
Heatstroke
Trauma
Immune-mediated
Intravascular haemolysis
Lupus
Glomerulonephritis
Neoplasia
Haemangiosarcoma
Carcinoma
Leukaemia
Lymphoma
Shock
Inflammatory
Active chronic liver disease
Pancreatitis
Haemorrhagic gastroenteritis
Severe burns

Pathophysiology



Clinical signs, laboratory diagnosis, and treatment

DIC	Clinical signs	Laboratory diagnosis	Treatment
Chronic DIC	Subclinical	Clotting times, platelets, and D-dimers normal or slightly increased	• Aetiological treatment • Fluid therapy • Oxygen therapy • Transfusion of whole blood or plasma • Vasopressors (dopamine, dobutamine) • Anticoagulants/ platelet antiaggregants (heparin, aspirin, clopidogrel)
Subacute DIC	• Petechiae and ecchymosis • Tendency to bleed in response to trauma and venipuncture	• Moderate thrombocytopaenia • Clotting times, platelets, and D-dimers normal or slightly increased • AT normal or slightly diminished	
Acute DIC	Bleeding, oliguria, dyspnoea, jaundice, and multi-organ failure	• Severe thrombocytopaenia • Clotting times and D-dimers increased • AT decreased	

Donor selection

	Canine donor	Feline donor
Age	1–8 years	2–8 years
Weight	>25 kg	>4 kg
Hct	>40 %	>35 %
Absence of infectious diseases	Leishmania spp., Ehrlichia spp., Brucella spp., Babesia spp., Dirofilaria spp., Borrelia spp., Rickettsia spp., Bartonella spp.	FIV, FeLV, Mycoplasma spp., Bartonella spp., Dirofilaria spp., Babesia spp.
Other characteristics	Good temperament, no alterations in the physical examination, haemogram, biochemistry, urinalysis, or coprological examination. Properly vaccinated (over 10 days since the last vaccination) and dewormed. No pharmacological treatments or previous transfusions.	

Blood groups

Blood groups are defined by inherited antigens located on the surface of red blood cells. They are responsible for haemolytic transfusion reactions that occur in the presence of corresponding Abs, whether natural or generated in response to sensitisation after a previous transfusion.

Dogs

Group	Natural preformed alloantibodies	Transfusion reaction
1.1	No	Acute intravascular haemolysis
1.2	No	Intravascular haemolysis
3	Yes	Delayed extravascular haemolysis
4	No	Possible intravascular haemolysis
5	Yes	Delayed extravascular

		haemolysis
7	Yes	Delayed extravascular haemolysis

• “True” universal donor: A dog that is DEA 1.1, 1.2, 3, 5, and 7 negative and DEA 4 positive or negative.

• Possible donors: all DEA 1.1-negative animals.

Cats

In cats it is essential to perform blood typing of the donor and recipient before transfusing whole blood, red blood cell concentrate, or plasma products.

Compatibility tests

Verify the existence of Abs by evaluating agglutination and haemolysis.

• Major: detects the presence of Abs against the donor’s red blood cells in the recipient’s plasma. If the major compatibility test reveals agglutination the transfusion should not be performed.

• Minor : determines the presence in the donor’s plasma of Abs against the recipient’s red blood cells. In dogs, if the minor compatibility test reveals agglutination red blood cells can be transfused, but not plasma. In cats, if the minor compatibility test reveals agglutination the transfusion should not be performed.

Summary of the procedure

1. Collect blood from the donor and recipient in EDTA, and clearly label the tubes.

2. Centrifuge and separate the plasma from the red blood cells, and clearly label the tubes.

3. Label three slides: major, minor, and control.

4. Place one drop of red blood cells and two drops of plasma on each slide:

a. Major: donor RBCs + recipient plasma.

b. Minor: recipient RBCs + donor plasma.

c. Control: recipient RBCs and plasma.

5. Incubate for 2 minutes at room temperature.

6. Evaluate macroscopic and microscopic agglutination.

Blood products

Whole blood processing and different blood products (red blood cell concentrate and fresh frozen plasma).

Transfusion practice

Blood product indicated depending on the disease

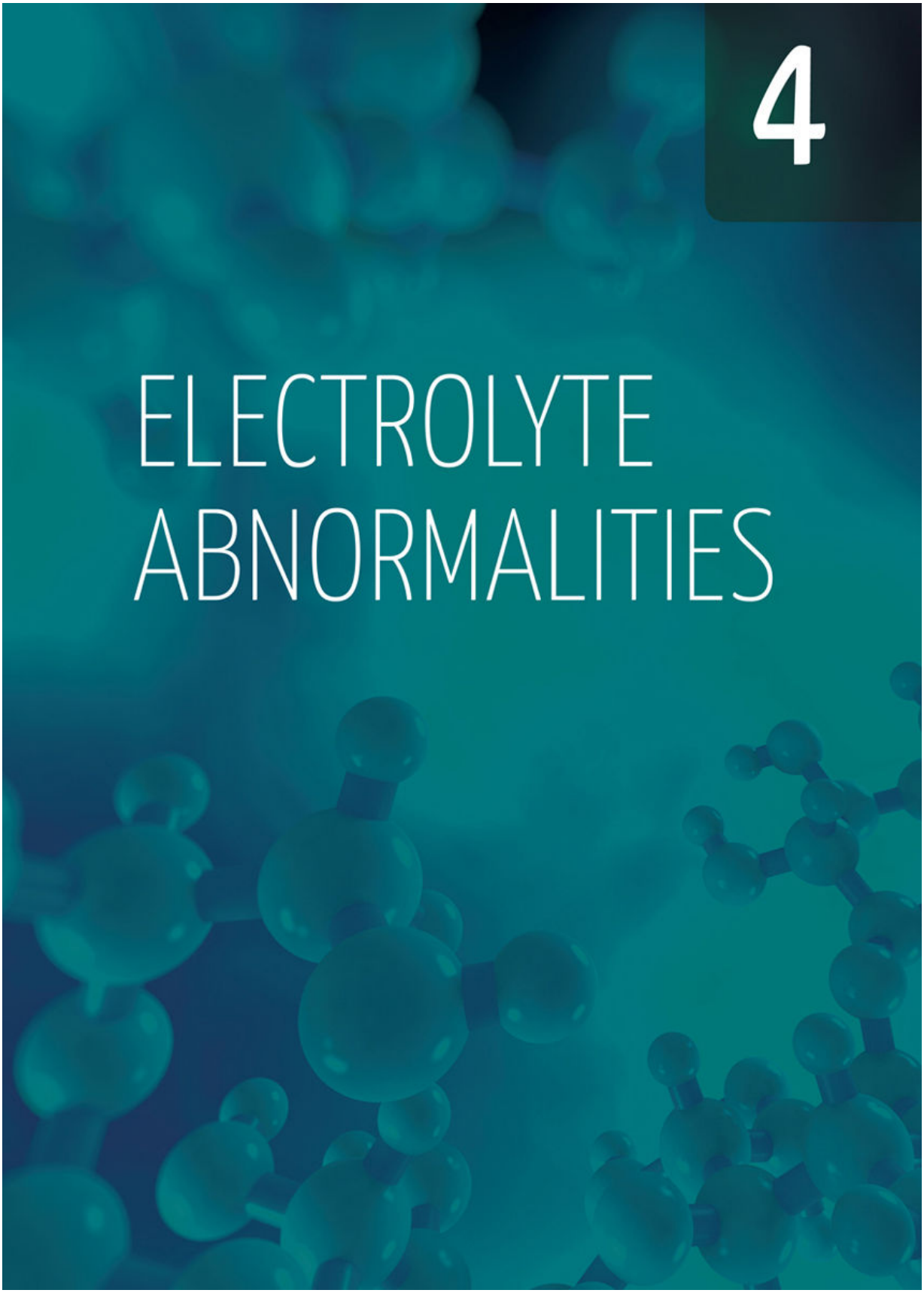
Transfusion reactions

• Nonspecific signs: tremor, vocalisation, dyspnoea, tachycardia, bradycardia, arrhythmias, hypotension, vomiting, diarrhoea, angioedema, urticaria.

• General treatment: stop transfusion and monitor patient.

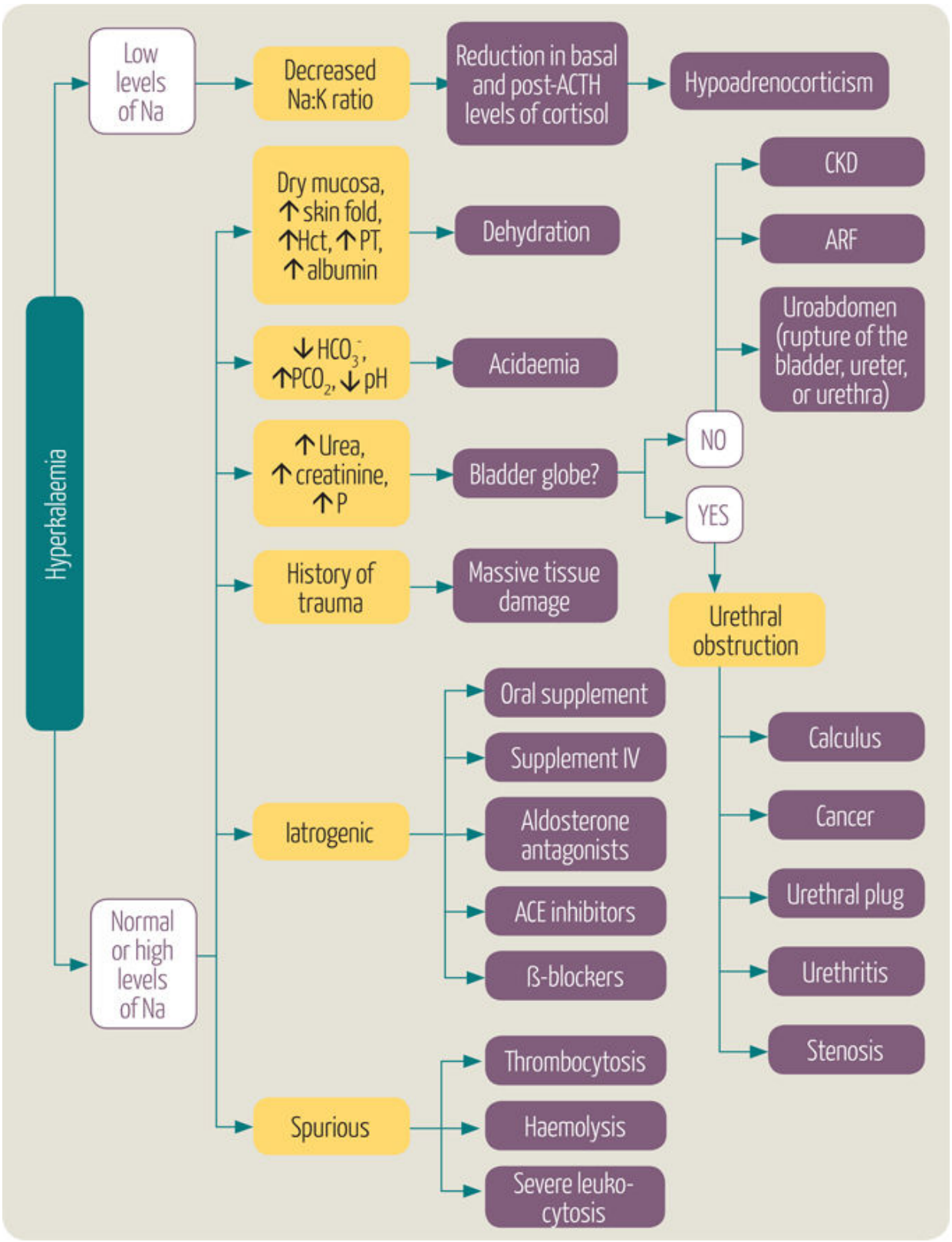
Immunological reactions	Specific signs	Treatment

Reaction to red blood cells	Haemolysis, haemoglobinuria, haemoglobin, acute renal failure, DIC	
Reaction to plasma proteins	Urticaria, angioedema, hypotension	Antihistamines, corticosteroids, fluid, oxygen, epinephrine, dopamine
Reaction to white blood cells	Fever, vomiting, noncardiogenic pulmonary oedema	
Reaction to platelets	Thrombocytopaenia	
Nonimmunological reactions	Specific signs	Treatment
Volume overload	Dyspnoea, pulmonary oedema, pleural effusion, ascites	Furosemide, oxygen
Hypothermia	Drop in temperature, tremor, arrhythmias	Warming
Citrate toxicity (hypocalcaemia)	Tremors, convulsions, vomiting, arrhythmia	Calcium gluconate
Thrombosis	Dyspnoea	Heparin
Microbial contamination	Vomiting, dyspnoea, fever	Antibiotic
Hypophosphataemia	Haemolysis	Phosphate salts
Acidosis	Acidosis	Bicarbonate

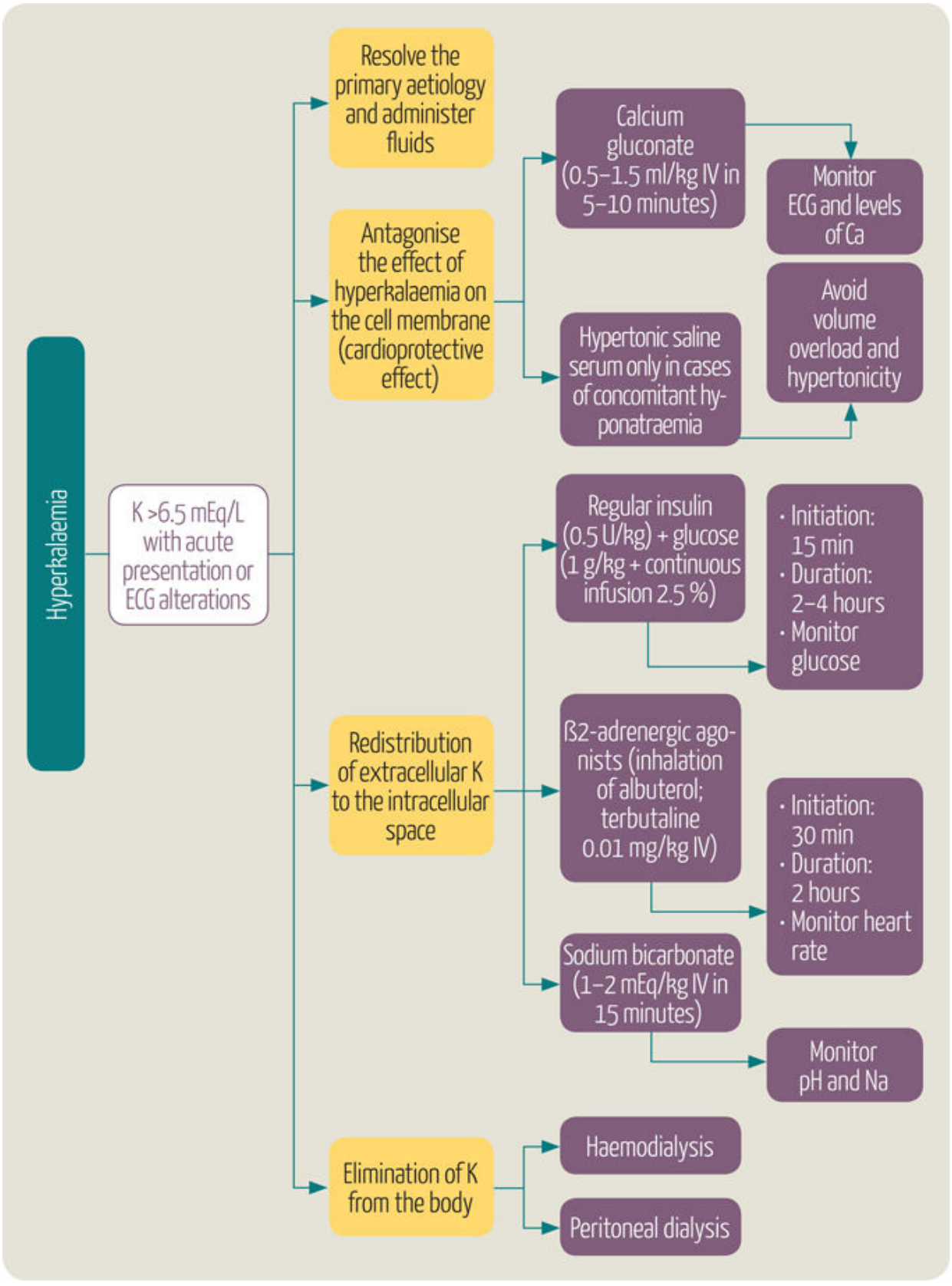

4
ELECTROLYTE
ABNORMALITIES

Potassium

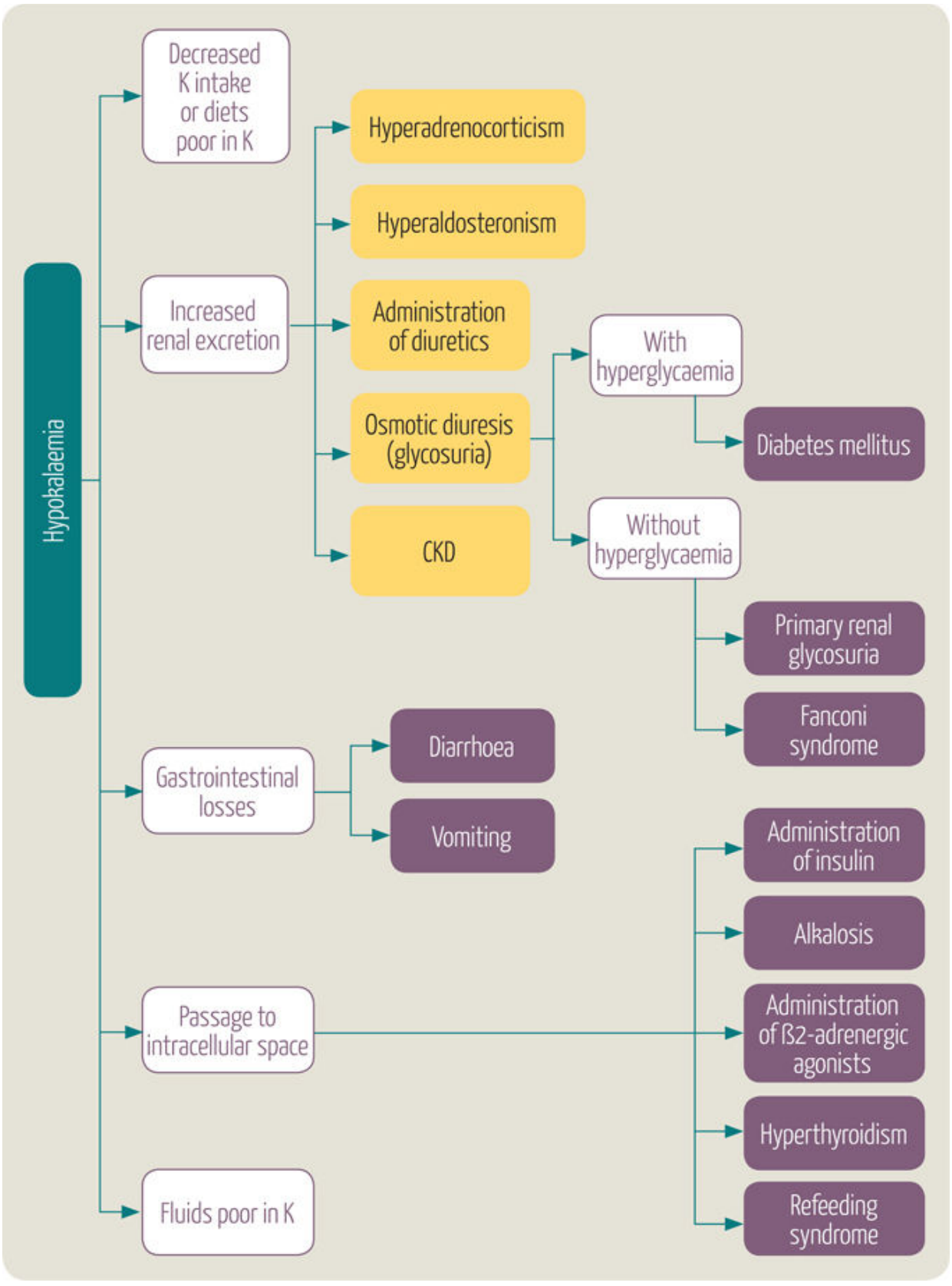
Hyperkalaemia


Hyperkalaemia
Low levels of Na
Decreased Na:K ratio
Reduction in basal and post-ACTH levels of cortisol
Hypoadrenocorticism
Normal or high levels of Na
Dry mucosa, ↑skin fold, ↑Hct, ↑PT, ↑albumin
Dehydration
↓HCO_3^-, ↑PCO_2, ↓pH
Acidaemia
↑Urea, ↑creatinine, ↑P
Bladder globe?
NO
YES
CKD
ARF
Uroabdomen (rupture of the bladder, ureter, or urethra)
Urethral obstruction
Calculus
Cancer
Urethral plug
Urethritis
Stenosis
History of trauma
Massive tissue damage
Iatrogenic
Oral supplement
Supplement IV
Aldosterone antagonists
ACE inhibitors
ß-blockers
Spurious
Thrombocytosis
Haemolysis
Severe leuko-cytosis

Management of hyperkalaemia


Hyperkalaemia
K >6.5 mEq/L with acute presentation or ECG alterations
Resolve the primary aetiology and administer fluids
Antagonise the effect of hyperkalaemia on the cell membrane (cardioprotective effect)
Calcium gluconate (0.5–1.5 ml/kg IV in 5–10 minutes)
Monitor ECG and levels of Ca
Hypertonic saline serum only in cases of concomitant hyponatraemia
Avoid volume overload and hypertonicity
Redistribution of extracellular K to the intracellular space
Regular insulin (0.5 U/kg) + glucose (1 g/kg + continuous infusion 2.5 %)
• Initiation: 15 min
• Duration: 2–4 hours
• Monitor glucose
ß2-adrenergic agonists (inhalation of albuterol; terbutaline 0.01 mg/kg IV)
• Initiation: 30 min
• Duration: 2 hours
• Monitor heart rate
Sodium bicarbonate (1–2 mEq/kg IV in 15 minutes)
Monitor pH and Na
Elimination of K from the body
Haemodialysis
Peritoneal dialysis

Hypokalaemia


Hypokalaemia
Decreased K intake or diets poor in K
Increased renal excretion
Hyperadrenocorticism
Hyperaldosteronism
Administration of diuretics
Osmotic diuresis (glycosuria)
CKD
With hyperglycaemia
Diabetes mellitus
Without hyperglycaemia
Primary renal glycosuria
Fanconi syndrome
Gastrointestinal losses
Diarrhoea
Vomiting
Passage to intracellular space
Administration of insulin
Alkalosis
Administration of ß2-adrenergic agonists
Hyperthyroidism
Refeeding syndrome
Fluids poor in K

Management of hypokalaemia: parenteral K supplementation

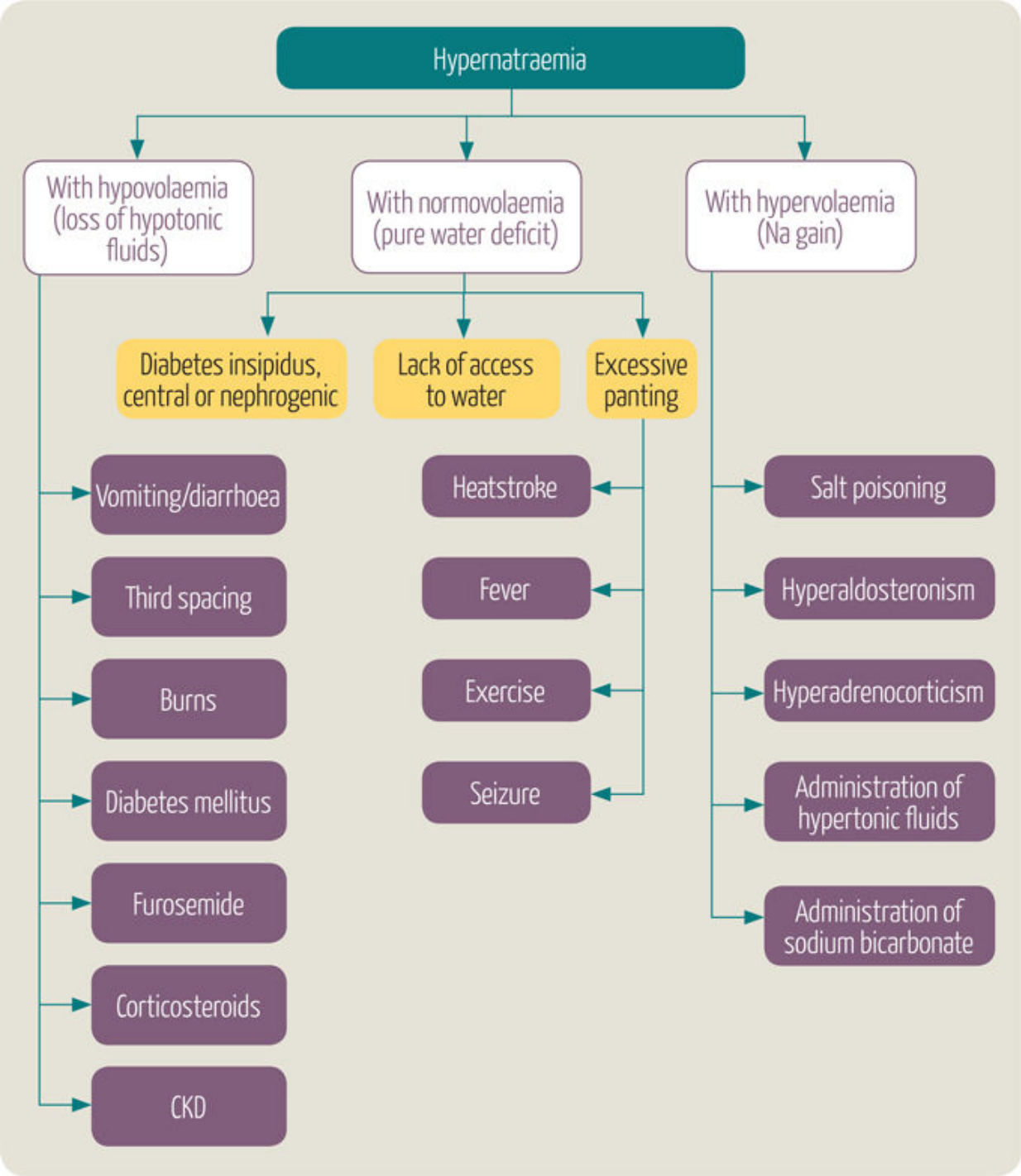
Parenteral K supplementation	
Serum K (mEq/l)	**Required K supplementation (mEq/l)**
3.5–5	20
3–3.4	30
2.5–2.9	40
2–2.4	60
<2	80



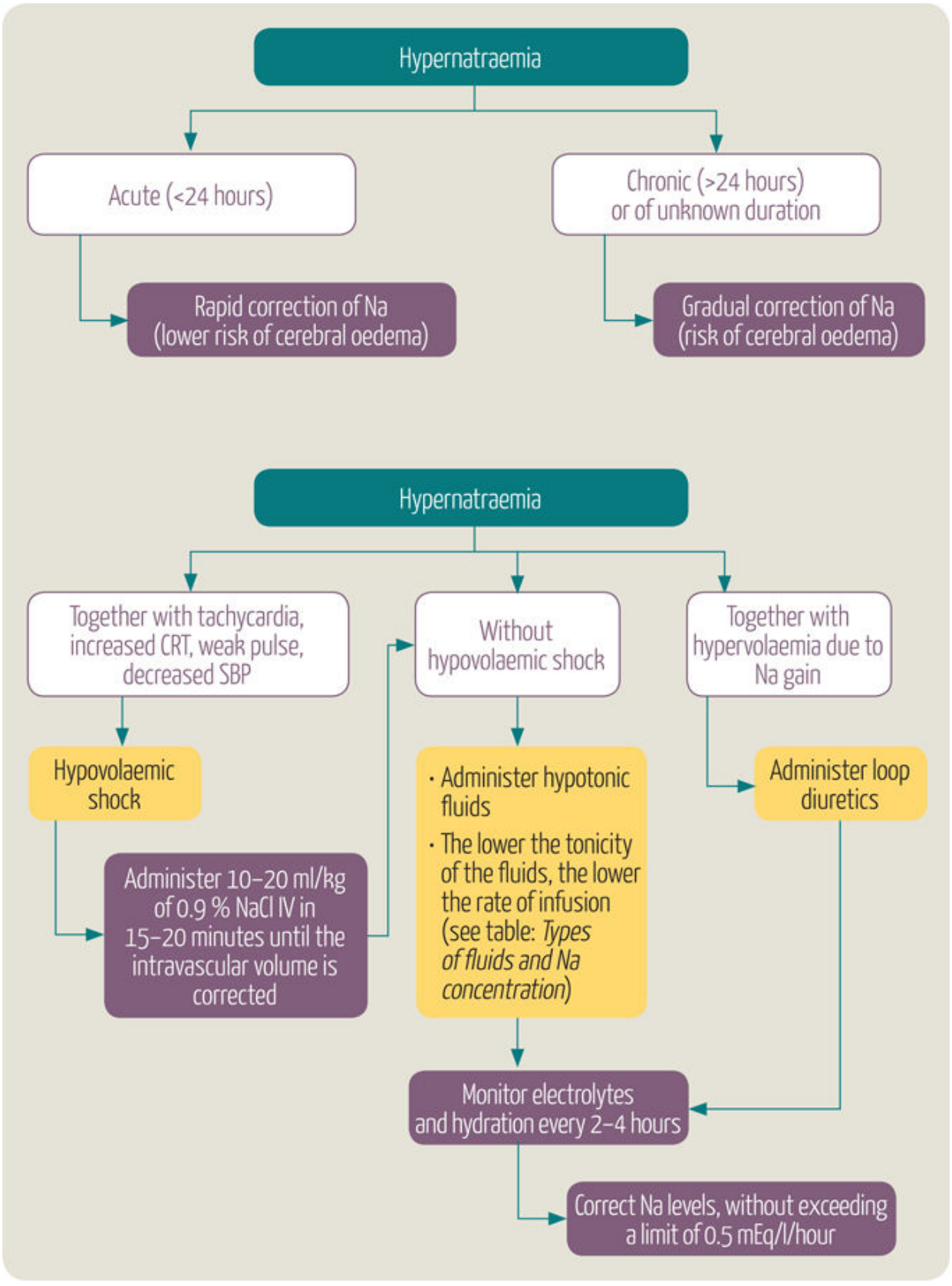
Figure 1. (a) Cat with ventroflexion of the neck due to hypokalaemia.
(b) Same cat after treatment.

Sodium

Hypernatraemia



Management of hypernatraemia


Hypernatraemia
Acute (<24 hours)
Chronic (>24 hours) or of unknown duration
Rapid correction of Na (lower risk of cerebral oedema)
Gradual correction of Na (risk of cerebral oedema)
Hypernatraemia
Together with tachycardia, increased CRT, weak pulse, decreased SBP
Without hypovolaemic shock
Together with hypervolaemia due to Na gain
Hypovolaemic shock
Administer 10–20 ml/kg of 0.9 % NaCl IV in 15–20 minutes until the intravascular volume is corrected
• Administer hypotonic fluids
• The lower the tonicity of the fluids, the lower the rate of infusion (see table: *Types of fluids and Na concentration*)
Administer loop diuretics
Monitor electrolytes and hydration every 2–4 hours
Correct Na levels, without exceeding a limit of 0.5 mEq/l/hour

Types of fluids and Na concentration

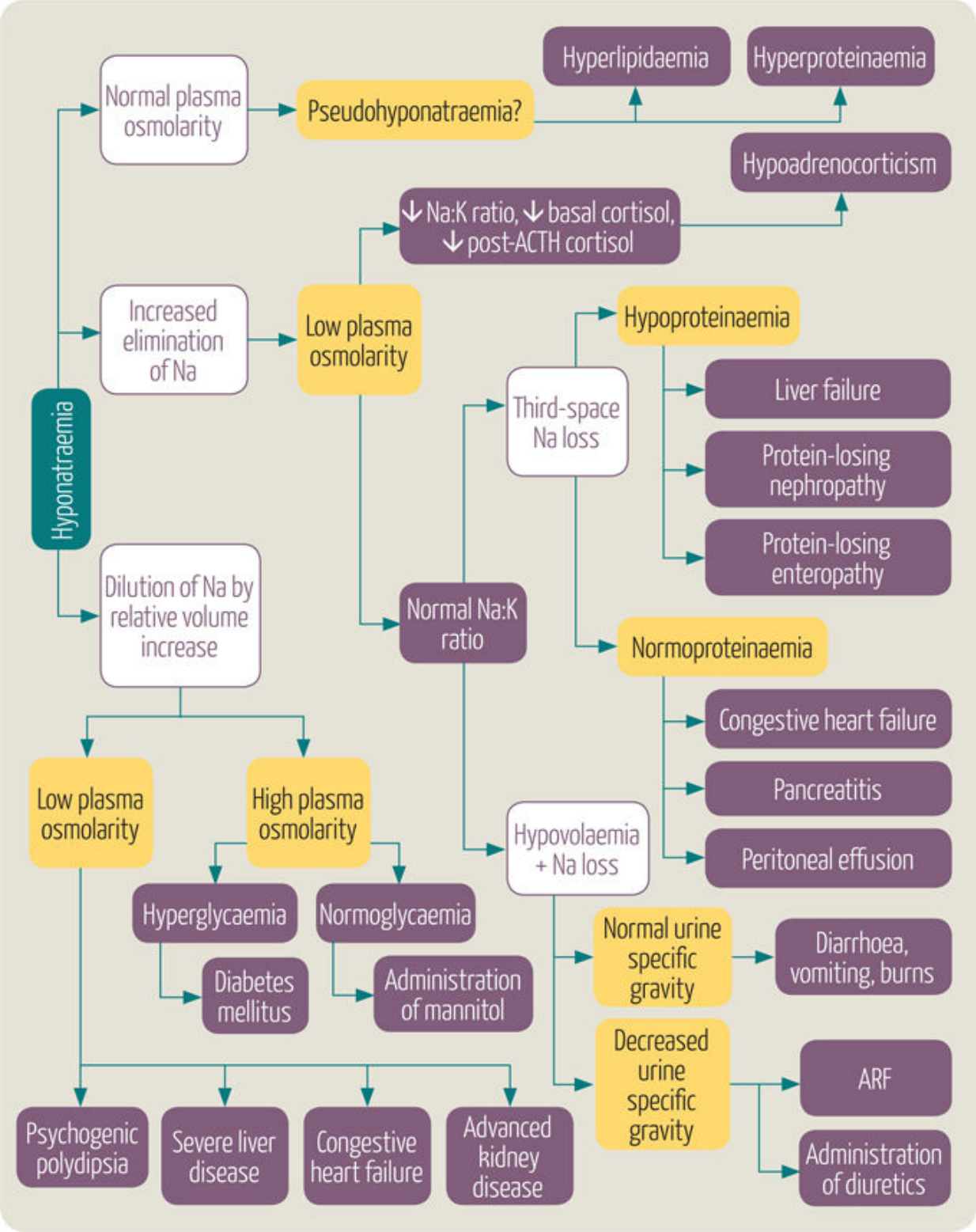
Fluids	Na concentration (mEq/l)	Osmolarity (mOsm/kg)
0.9 % NaCl	154	308
Normosol R	140	295
Plasmalyte A	140	294
Ringer's lactate	130	273
0.45 % NaCl	77	154
0.45 % NaCl + 2.5 % dextrose	77	280
5 % Dextrose in water	0	252



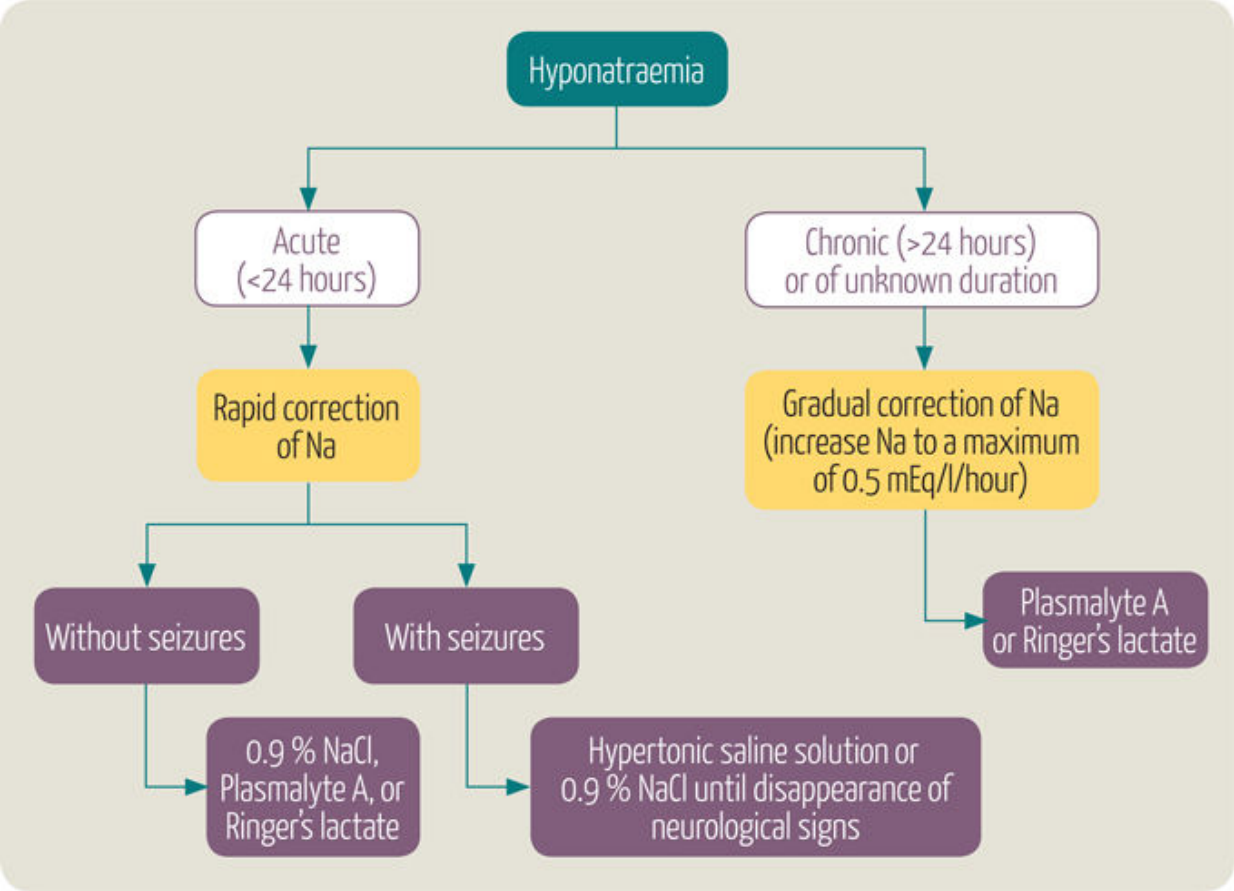
Figure 2. Patients receiving fluid therapy.

Hyponatraemia

- Calculate serum osmolarity = 2(Na + K) + BUN/2.8 + glucose/18.
- Normal osmolarity = 290–310 mOsm/kg (dogs); 308–335 mOsm/kg (cats).

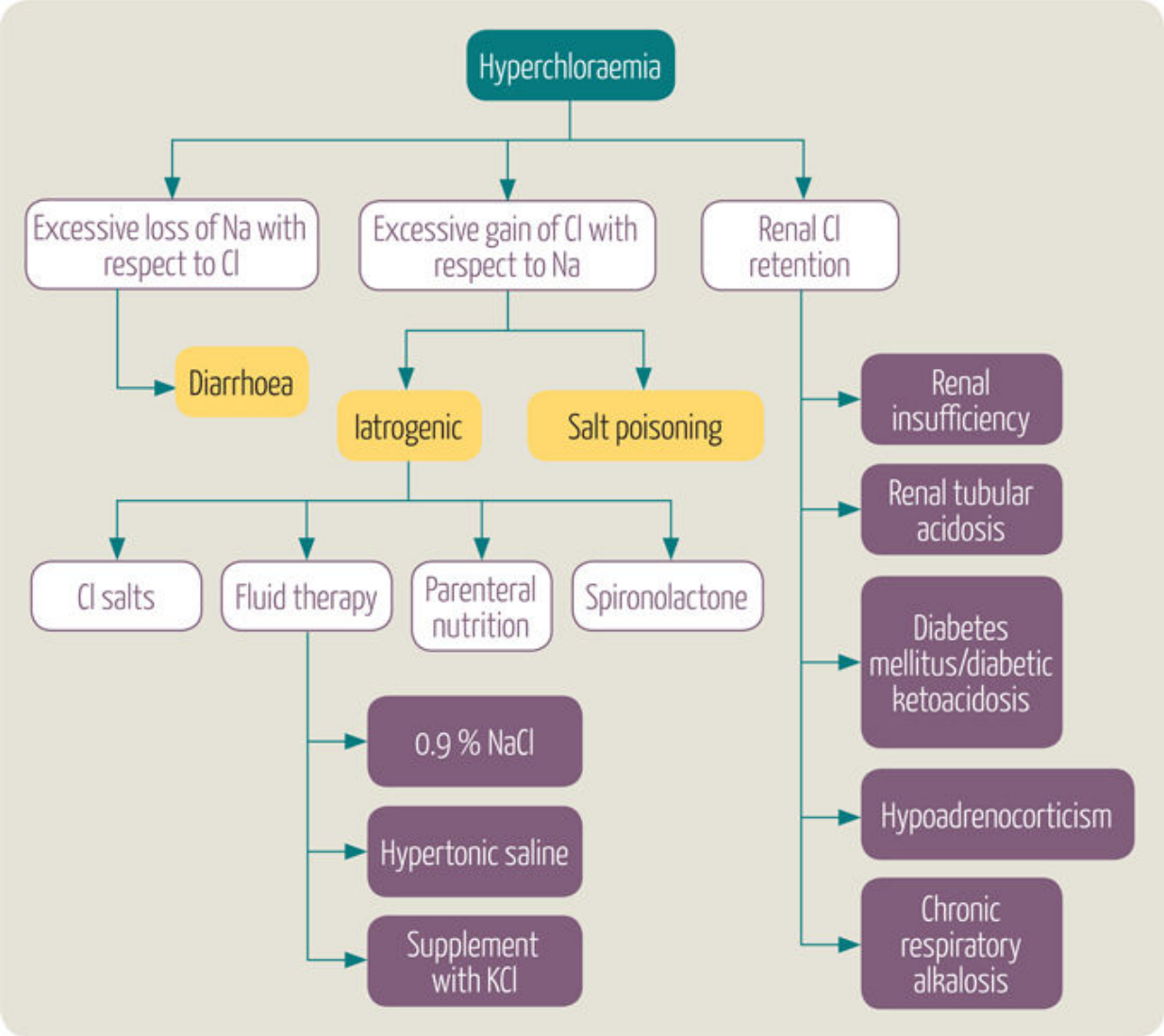


Management of hyponatraemia

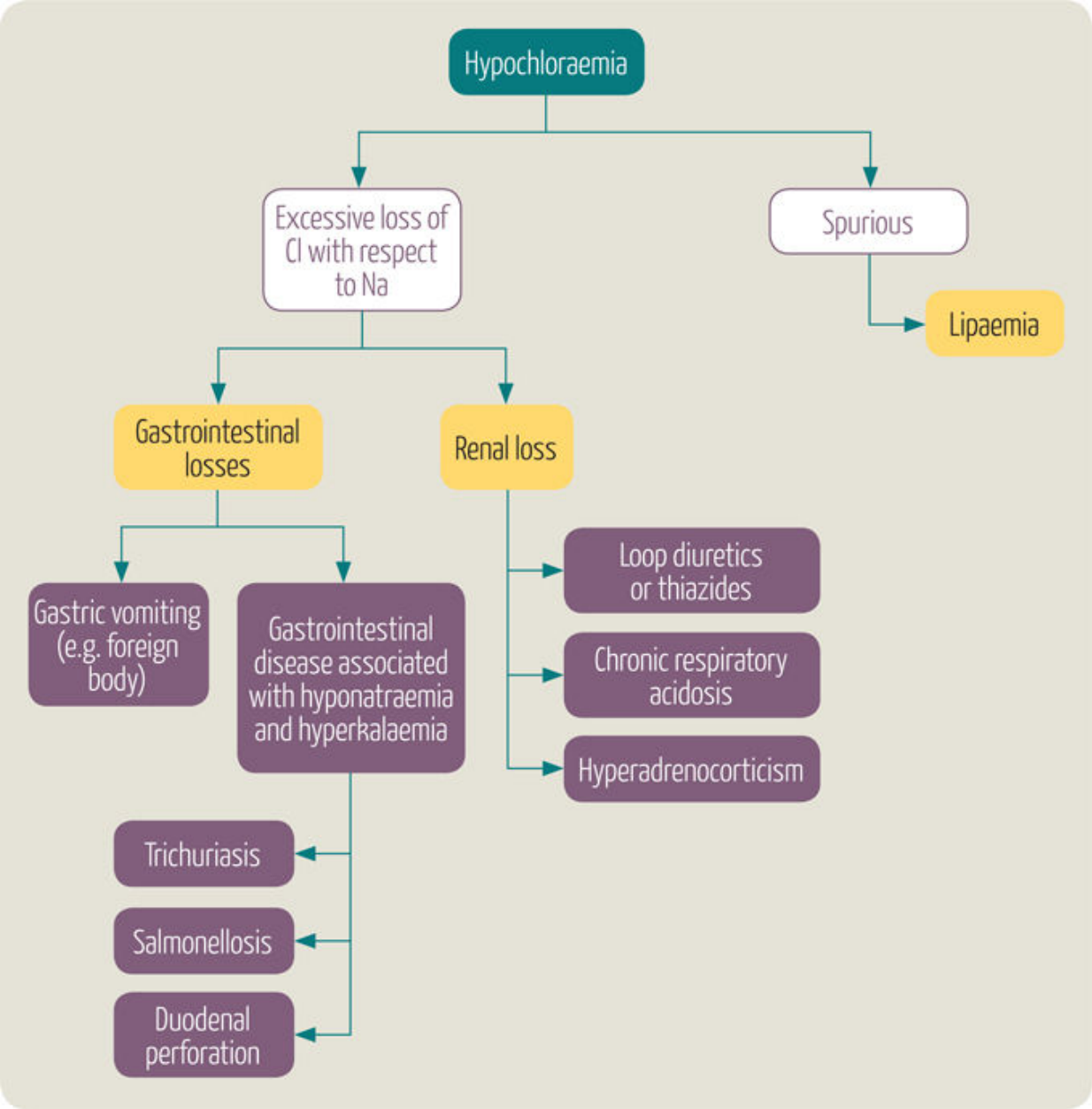


Chlorine

Hyperchloraemia

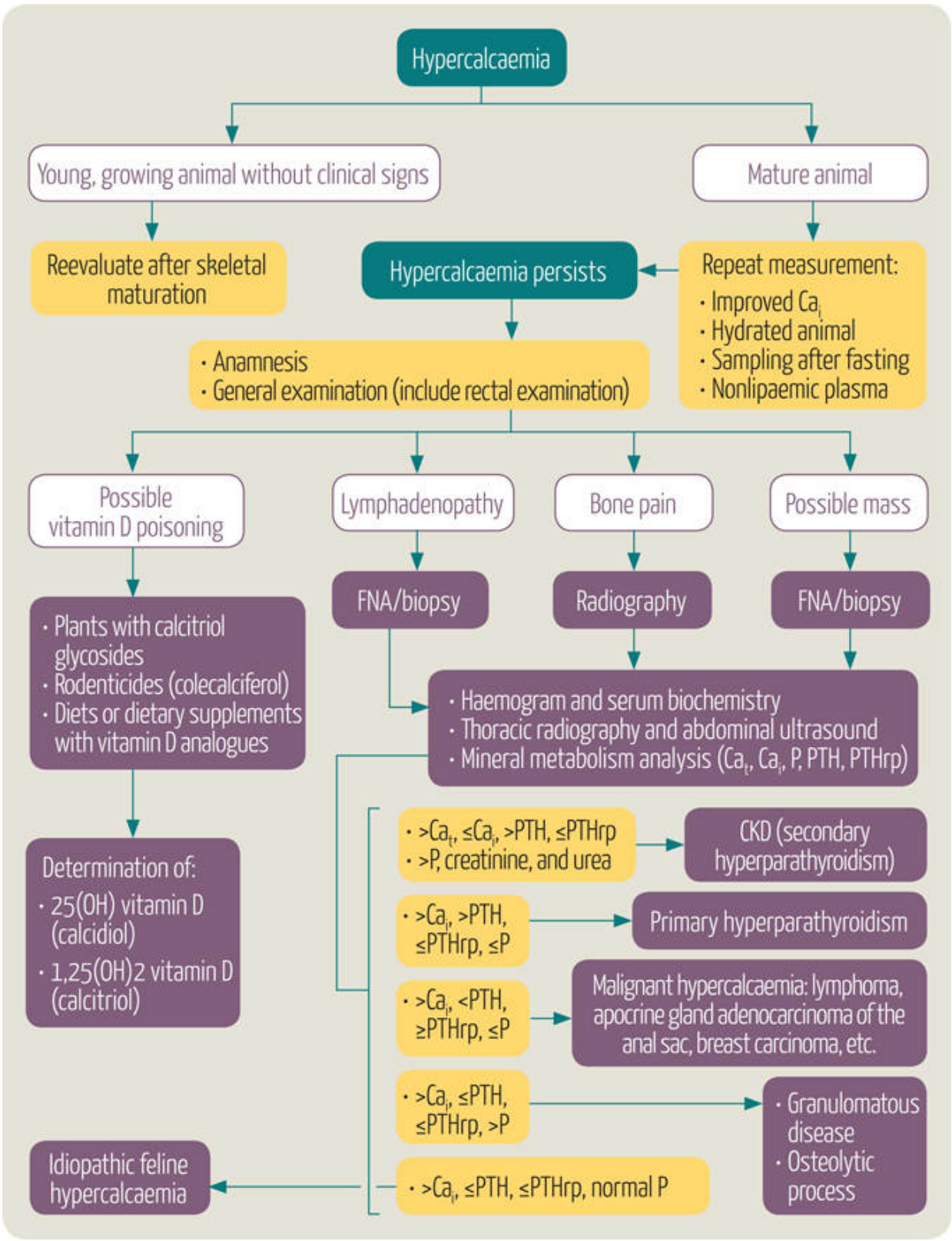


Hypochloraemia



Calcium

Hypercalcaemia


Hypercalcaemia
Young, growing animal without clinical signs
Mature animal
Reevaluate after skeletal maturation
Hypercalcaemia persists
Repeat measurement:
• Improved Ca_i
• Hydrated animal
• Sampling after fasting
• Nonlipaemic plasma
• Anamnesis
• General examination (include rectal examination)
Possible vitamin D poisoning
Lymphadenopathy
Bone pain
Possible mass
FNA/biopsy
Radiography
FNA/biopsy
• Plants with calcitriol glycosides
• Rodenticides (colecalciferol)
• Diets or dietary supplements with vitamin D analogues
• Haemogram and serum biochemistry
• Thoracic radiography and abdominal ultrasound
• Mineral metabolism analysis (Ca_t, Ca_i, P, PTH, PTHrp)
Determination of:
• 25(OH) vitamin D (calcidiol)
• 1,25(OH)2 vitamin D (calcitriol)
• >Ca_t, ≤Ca_i, >PTH, ≤PTHrp
• >P, creatinine, and urea
CKD (secondary hyperparathyroidism)
• >Ca_i, >PTH, ≤PTHrp, ≤P
Primary hyperparathyroidism
• >Ca_i, <PTH, ≥PTHrp, ≤P
Malignant hypercalcaemia: lymphoma, apocrine gland adenocarcinoma of the anal sac, breast carcinoma, etc.
• >Ca_i, ≤PTH, ≤PTHrp, >P
• Granulomatous disease
• Osteolytic process
Idiopathic feline hypercalcaemia
• >Ca_i, ≤PTH, ≤PTHrp, normal P

Differential diagnosis and diagnostic test results

Underlying causes	Ca_t	Ca_i	P	PTH	PTHrp	Calcitriol	Clinical signs
Granulomatous disease	↑ to ↑↑↑	↑ to ↑↑↑	↑ to ↑↑	↓	Low or not appreciable	↑ to ↑↑	Absent to moderate
Osteolytic alterations	↑ to ↑↑	↑ to ↑↑	Normal or ↑	↓	Low or not appreciable *	Normal or ↓	Mild to moderate
Spurious (unknown cause)	↑	Normal	Normal	Normal	Low or not appreciable	Normal	Absent
Hyperparathyroidism	↑ to ↑↑	↑ to ↑↑	Normal or ↓	Normal or ↑↑	Low or not appreciable	Normal	Absent to moderate
Hypervitaminosis D	↑↑ to ↑↑↑	↑↑ to ↑↑↑	↑ to ↑↑↑	↓	Low or not appreciable	↑ to ↑↑↑	Moderate to severe
Addison's disease	↑ to ↑↑	↑ to ↑↑	Normal	Normal or ↓	Low or not appreciable	Normal	None due to elevation of Ca
Kidney failure (secondary renal hyperparathyroidism)	↑ to ↑↑	Normal or ↓	↑ to ↑↑↑	↑ to ↑↑	Low or not appreciable	Normal or ↓	Absent to moderate
Neoplasm (malignant hypercalcaemia)	↑↑ to ↑↑↑	↑↑ to ↑↑↑	Normal or ↓↓	↓ to ↓↓	Low, not appreciable, or ↑↑**	Normal or ↓	Moderate to severe
Idiopathic (cats)	↑ to ↑↑	↑ to ↑↑	Normal	Normal to ↓	Low or not appreciable	Normal or ↓	Absent to mild

* In humans, osteolytic alterations in some carcinomas can result in regular secretion of PTHrp.

** In some cases of malignant hypercalcaemia PTHrp levels are low or negligible, although levels of other hormones and cytokines are elevated.

↑ = slight increase.

↑↑ = moderate increase.

↑↑↑ = pronounced increase.

↓ = slight decrease.

↓↓ = moderate decrease.

Diagnostic tests

Diagnostic tests*	Main findings and causes
History	Evaluation of exposure to vitamin D (rodenticides, supplements, diet).
Complete physical examination	• Palpation of the lymph nodes, the ventral cervical area, and the mammary glands. • Note lameness, if present, and palpate the spine and long bones (bone metastasis or multiple myeloma). • Chest auscultation (decreased lung sounds or heart sounds may indicate the presence of masses or fluids).
Rectal examination	Palpation of the lymph nodes and anal sacs (adenocarcinomas of the apocrine anal gland are sometimes small) and the prostate.
Fundus examination	Search for lesions suggestive of a systemic fungal infection and note haemorrhages and retinal detachment.
Haemogram	Evaluation of blood smear for the presence of abnormal cells in circulation.
Serum biochemical profile	Evaluation of Cat, P, BUN, creatinine, albumin, globulin, and electrolyte concentrations (for interpretation see table: *Differential diagnosis and diagnostic test results*).
Urinalysis	Note the presence of crystals; low urinary specific gravity is common in cases of hypercalcaemia.
Stool examination	To rule out a parasitic cause (e.g. schistosomiasis).
Repetition of serum Ca test	Repeat the test, especially in cases of borderline hypercalcaemia or if a laboratory error or spurious hypercalcaemia is suspected.
FNA and cytology	Enlarged lymph nodes and suspicious masses or lesions (including masses in the cranial

	mediastinum detected using ultrasound-guided techniques, and lesions in the bone and the anal sacs).
Chest radiography	• Identify masses in the cranial mediastinum and lymphadenopathies • Evaluation of bony structures, looking mainly for lytic lesions.
Abdominal ultrasound	• Search for lymphadenopathies (lymphoma, granulomatous diseases, adenocarcinomas of the anal apocrine glands). • Spleen and liver examination (lymphoma). • Prostate evaluation.
Stimulation with ACTH	Perform in cases of electrolyte abnormalities or suspected hyperadrenocorticism or Addison disease.
Ca_i	Measure to check for true hypercalcaemia (except in cases of secondary renal hyperparathyroidism).
PTH/PTHrp	Determine for the diagnosis of hyperparathyroidism or malignant hypercalcaemia.
• Calcitriol **• Calcidiol**	Used to identify vitamin D toxicity or granulomatous disease.
Bone examination and study	• Search for lytic lesions by puncture/biopsy (pure lytic lesions in multiple myeloma; mixed and proliferative lytic lesions in carcinomas). • Advanced bone examination with scintigraphy (areas of greater absorption will be observed: “hot spots”).
Ultrasound of the ventral cervical area	Assess the possibility that the parathyroid glands are enlarged.
Bone marrow	Evaluation of the sample to detect infiltration by

cytology	malignant lymphoblasts (lymphoma or lymphoblastic leukaemia) or plasma cells (multiple myeloma).
Protein electrophoresis	Identify monoclonal (and sometimes polyclonal) gammopathy, which occurs in myeloma and occasionally in lymphoproliferative diseases.

* It is not necessary to perform diagnostic tests in this order.

Treatment

Drug	Dose	Route of administration	Comments
Saline solution (0.9 % NaCl)	80–120 ml/kg/day	IV	• Treatment of acute hypercalcaemia. • Adjust dose depending on evolution of calcaemia.
Furosemide	1–2 mg/kg/hour	IV	• Treatment of acute hypercalcaemia • In chronic cases, the dose is reduced and can be administered orally every 8 hours.
Prednisone/ prednisolone	1–4 mg/kg/day	• IV • IM	• Adjust dose depending on evolution of calcaemia. • In chronic cases, the dose is reduced and can be administered orally.
Calcitonin	5 U/kg/8 hours	SC	Possible side effects (vomiting).
Pamidronate	0.6–2 mg/kg	IV	• Administered dissolved in 0.9 % NaCl. • Adjust dose depending on degree of hypercalcaemia.

Figure 3. Radiograph of a dog with a mediastinal mass and malignant hypercalcaemia.

Hypocalcaemia

Treatment

Phosphorus

Hyperphosphataemia

Hypophosphataemia

Magnesium

Hypomagnesaemia

Management of hypomagnesaemia

Acidaemia: aetiology and treatment

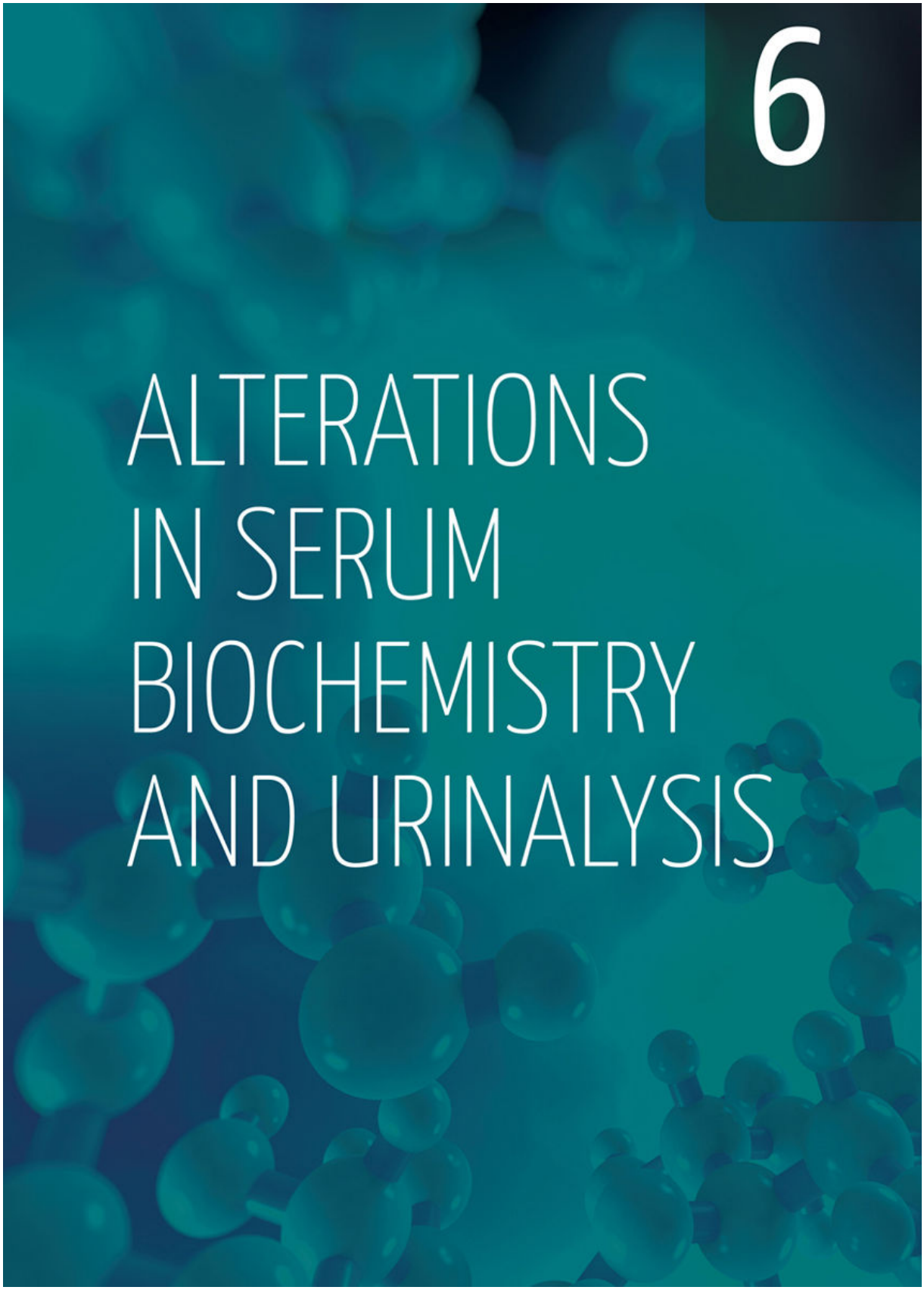
Alkalosis: aetiology and treatment

Normal blood gas values and acid-base parameters*

* Reference values will depend on the laboratory that performs the analysis.

Expected compensatory responses to primary acid-base alterations

Alteration	Primary alteration	Compensatory response
Metabolic acidosis	↓ HCO_3^-	0.7 mmHg reduction in PCO_2 for every 1 mEq/l reduction in HCO_3^-
Metabolic alkalosis	↑ HCO_3^-	0.7 mmHg increase in PCO_2 for every 1 mEq/l increase in HCO_3^-
Acute respiratory acidosis	↑ PCO_2	1.5 mmHg increase in HCO_3^- for every 10 mEq/l increase in PCO_2
Chronic respiratory acidosis	↑ PCO_2	3.5 mmHg increase in HCO_3^- for every 10 mEq/l increase in PCO_2
Acute respiratory alkalosis	↓ PCO_2	2.5 mmHg reduction in HCO_3^- for every 10 mEq/l reduction in PCO_2
Chronic respiratory alkalosis	↓ PCO_2	5.5 mmHg reduction in the HCO_3^- for every 10 mEq/l reduction in PCO_2


6
ALTERATIONS
IN SERUM
BIOCHEMISTRY
AND URINALYSIS

Kidney disease

Polyuria/polydipsia syndrome

Differential diagnosis

- **Diabetes mellitus**
- **Central diabetes insipidus**
- **Nephrogenic diabetes insipidus**
- **Drugs/diet**
- **Hyperadrenocorticism (Cushing's syndrome)**
- **Hypercalcaemia**
- **Hyperthyroidism**
- **Hypokalaemia**
- **Liver failure**
- **CKD**
- **Pyometra**
- **Primary polydipsia**
- **Addison's disease**

Verify

- **PU** (>50 ml/kg/day)
- **PS** (>100 ml/kg/day)

Clinical history and general physical examination

Clinical signs	Causes
Intact female, oestrus within last 2 last months, oestrogen administration, vaginal discharge	Pyometra
Vomiting with or without diarrhoea	Pyometra, CKD, liver failure, Addison's disease, hypercalcaemia, diabetes mellitus
Bilateral alopecia, distended abdomen, calcinosis cutis, thin skin, muscular weakness, hepatomegaly	Hyperadrenocorticism
Weight loss, polyphagia, restlessness, ↑ heart rate	Diabetes mellitus, hyperthyroidism
Lymphadenopathy, constipation, tumour	Hypercalcaemia
Diuretics, glucocorticoids, antiepileptics, salt supplementation	Drugs, acidifying diets
Behavioural alterations	Primary polydipsia
Muscle weakness, ECG abnormalities, lethargy	Hypokalaemia

Urinalysis

Urine analysis		Urine specific gravity	
Glycosuria, ketonuria	Kidney glycosuria, diabetes mellitus	**Hyposthenuria (<1.008)**	Central diabetes insipidus, nephrogenic diabetes insipidus, primary polydipsia, hyperadrenocorticism
Pyuria, cylindruria, bacteriuria	Pyelonephritis, pyometra, hyperadrenocorticism, corticosteroids	**Isosthenuria (1.008–1.016)**	Hyperadrenocorticism, CKD, pyometra
Proteinuria	Pyometra, CKD, hyperadrenocorticism	**Hypersthenuria (>1.030)**	Diabetes mellitus

Haemogram and biochemistry

Haemogram and biochemistry	
↑ Neutrophils	Pyometra, pyelonephritis, hyperadrenocorticism, corticosteroids
↑ Urea, creatinine	CKD, dehydration
↑ AP	Hyperadrenocorticism, hyperthyroidism, liver failure, pyometra, diabetes mellitus, drugs
↓ Na:K ratio	Addison's disease, diuretics
Hyperglycaemia	Diabetes mellitus
Hypercalcaemia	Paraneoplastic syndromes, primary hyperparathyroidism
↓ Urea	Liver failure
↑ ALT	Liver failure, corticoids, hyperadrenocorticism
↑ T_4	Hyperthyroidism

Specific tests

Radiography and ultrasound: pyometra, CKD, liver failure, hyperadrenocorticism
Stimulation with ACTH: hyperadrenocorticism, Addison's disease

		YES	NO
Water deprivation test	Urine concentrate	Primary polydipsia	Diabetes insipidus
Response to exogenous ADH		Central diabetes insipidus	Nephrogenic diabetes insipidus

Acute azotaemia (ARF)

Aetiology

Prerenal	Renal	Postrenal

• Dehydration
• Haemorrhage
• Congestive heart failure
↓
↓ Kidney perfusion
	• Prolonged ischaemia
	• Nephrotoxins (NSAIDs, aminoglycosides, blood pigments, etc.)
	• Infections (*Leptospira*)
	• Congenital glomerulonephropathy
	• Hypercalcaemia
	• Immune-mediated disease
		• Urinary retention
		• Urinary tract obstruction:
		  • Tumours
		  • Calculi
		  • Clots
		  • Mucous plugs

Clinical signs

Prerenal	Renal	Postrenal
• Dehydration • Concentrated urine • State of shock	• Oliguria-anuria • Digestive signs • Depressed-comatose animal	• Anuria • Dysuria, stranguria • Bladder globe • Haematuria



Figure 1. Abdominal radiograph of a cat with bladder globe caused by a urethral obstruction.

Diagnosis

		Prerenal	Renal	Postrenal
Urine	Urine specific gravity	• ≥1.035 (dog) • ≥1.040 (cat)	• 1.008–1.029 (dog) • 1.008–1.035 (cat)	• Variable • Variable
	Inactive	Sediment	Variable	• White blood cells • Red blood cells • Proteinuria
Blood	Urea	↑↑	↑↑	↑
	Creatinine	↑	↑↑	↑
	K	↑	↑	↑↑
	• pH • HCO_3^-	↓	↓	↓

Treatment

	Prerenal	Renal	Postrenal
Aetiologic	Restore renal perfusion	Depends on cause	Restore urinary flow
Symptomatic	• Fluid therapy (Ringer's lactate, 0.9 % NaCl) • Control of K (sodium bicarbonate/calcium gluconate) • Antiemetic/antacid (metoclopramide-maropitant/ranitidine-cimetidine) • Control of metabolic acidosis (pH ≥7.2, Ringer's lactate; pH ≤7.2, bicarbonate solution) • Diuretics in hydrated anuric animals (furosemide, mannitol) • Antibiotics (not nephrotoxic) • Nutrition (parenteral, enteral via feeding tube) • Renal replacement therapies (peritoneal dialysis/haemodialysis)		

Keys to treatment

- Restore renal flow/control electrolyte imbalances/control metabolic acidosis
- If there is no response to fluid therapy in 48 hours → dialysis
- Complications: anuria/oliguria, hyperkalaemia, metabolic acidosis, severe azotaemia, overhydration

Chronic azotaemia (CKD)

Aetiology

Very varied, difficult to determine in advanced stages.

Most common clinical signs

- PU/PD.
- Anorexia, vomiting.
- Loss of weight and body condition.
- Pale mucous membranes.
- Ulcers in the oral cavity.
- Halitosis.

- Acute blindness.
- Muscle weakness.

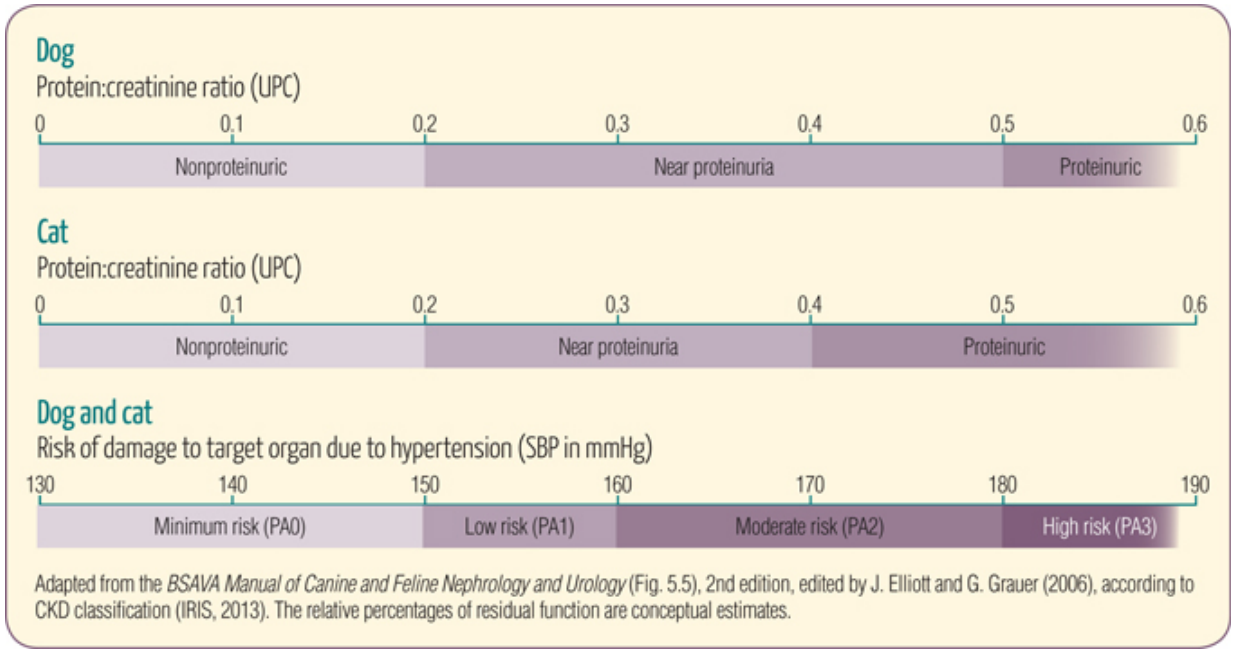
Diagnosis

Urinalysis	• Urine specific gravity: 1.008–1.030 (isosthenuria ≈1.012) • Proteinuria (in case of glomerular disease) (UPC >0.5)
Haematology	• Normocytic-normochromic nonregenerative anaemia
Biochemistry	• ↑ Urea, creatinine, and P • ↓ K (intense polyuria), ↓ albumin (intense proteinuria)
Diagnostic imaging	• Radiography • Abdominal ultrasound
Blood pressure	• SBP <160 mmHg: moderate risk • SBP <180 mmHg: high risk
Kidney biopsy	• Early stage disease/congenital disease/glomerular disease

Classification of CKD (IRIS, 2013)

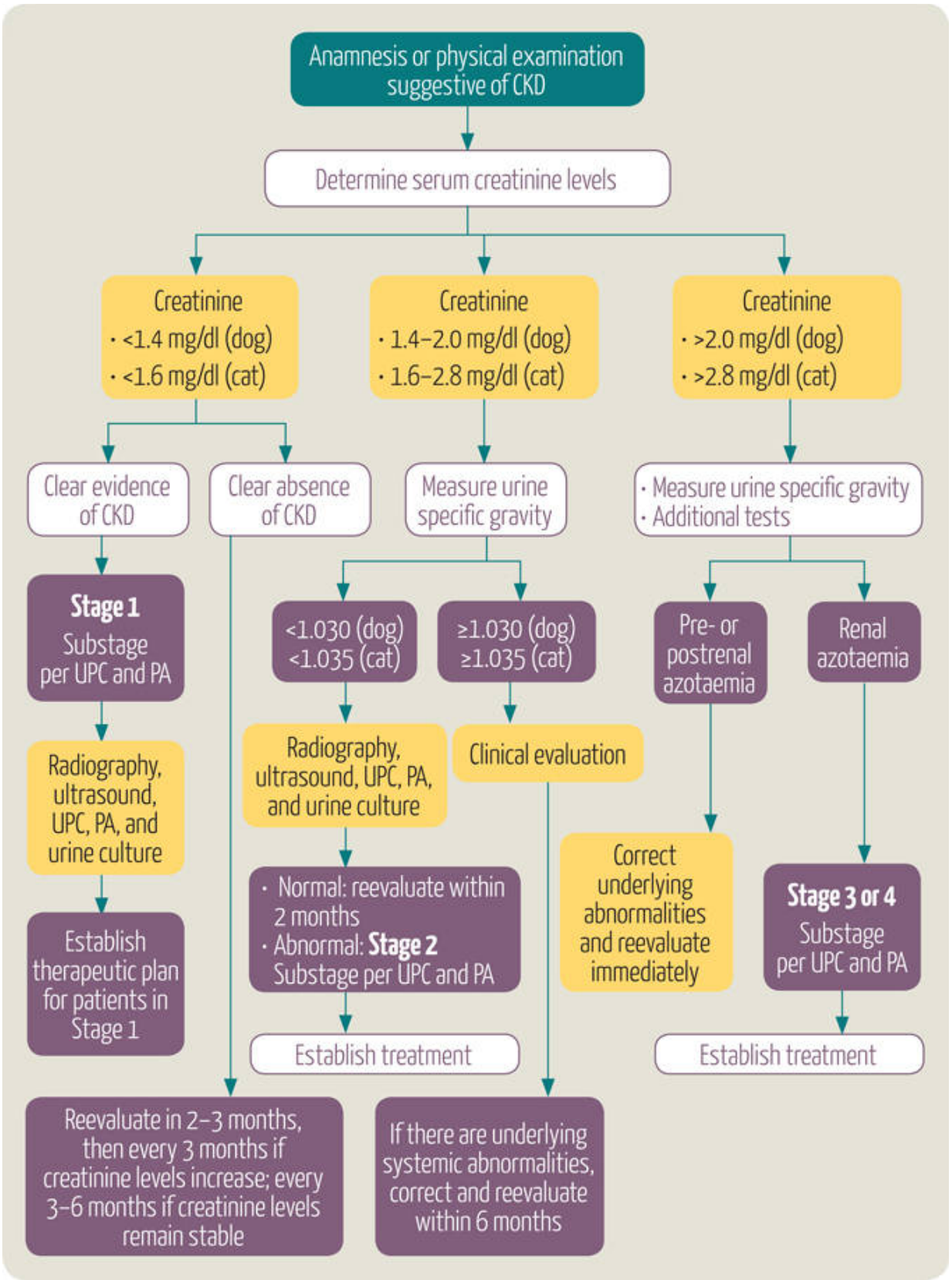
		At risk Animal at risk of developing CKD	Stage I CKD without azotaemia	Stage II Mild azotaemia	Stage III Moderate azotaemia	Stage IV Severe azotaemia
Creatinine (mg/dl)	Dog	<1.4	<1.4	1.4–2	2.1–5	>5
	Cat	<1.6	<1.6	1.6–2.8	2.9–5	
Observations		• Nephrotoxic drugs • Predisposed breed • High prevalence of infectious disease • Advanced age	• Early kidney disease • ↓ Glomerular filtrate • Does not concentrate urine well • Other renal alterations	• Mild to absent clinical signs • Poor adaptation can lead to ↑PTH, ↓K	Systemic signs present: bone pain, uraemic gastritis, anaemia, metabolic acidosis, etc.	High risk of clinical signs and uraemic crisis

In addition to plasma creatinine levels, the presence of proteinuria (UPC >0.5 [dog], UPC >0.4 [cat]) and hypertension (SBP >150 mmHg), especially in early stages, should be taken into account.



Adapted from the *BSAVA Manual of Canine and Feline Nephrology and Urology* (Fig. 5.5), 2nd edition, edited by J. Elliott and G. Grauer (2006), according to CKD classification (IRIS, 2013). The relative percentages of residual function are conceptual estimates.

Staging of CKD (IRIS, 2013)


Anamnesis or physical examination suggestive of CKD
Determine serum creatinine levels
Creatinine
· <1.4 mg/dl (dog)
· <1.6 mg/dl (cat)
Creatinine
· 1.4–2.0 mg/dl (dog)
· 1.6–2.8 mg/dl (cat)
Creatinine
· >2.0 mg/dl (dog)
· >2.8 mg/dl (cat)
Clear evidence of CKD
Clear absence of CKD
Measure urine specific gravity
· Measure urine specific gravity
· Additional tests
Stage 1
Substage per UPC and PA
<1.030 (dog)
<1.035 (cat)
≥1.030 (dog)
≥1.035 (cat)
Pre- or postrenal azotaemia
Renal azotaemia
Radiography, ultrasound, UPC, PA, and urine culture
Clinical evaluation
Radiography, ultrasound, UPC, PA, and urine culture
Correct underlying abnormalities and reevaluate immediately
Stage 3 or 4
Substage per UPC and PA
Establish therapeutic plan for patients in Stage 1
· Normal: reevaluate within 2 months
· Abnormal: Stage 2
Substage per UPC and PA
Establish treatment
Establish treatment
Reevaluate in 2–3 months, then every 3 months if creatinine levels increase; every 3–6 months if creatinine levels remain stable
If there are underlying systemic abnormalities, correct and reevaluate within 6 months

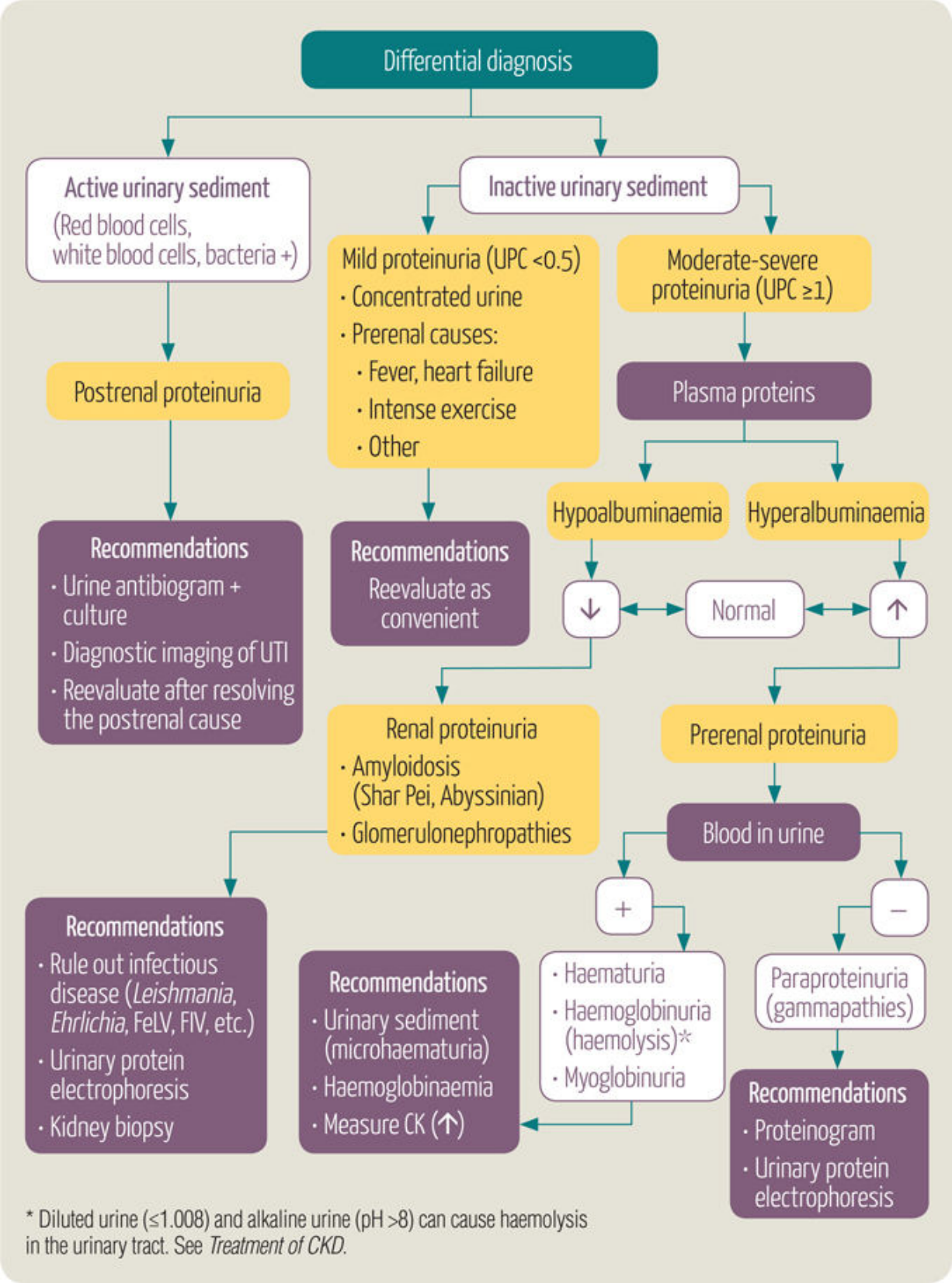
Therapeutic recommendations for CKD according to EBM

Therapeutic recommendations		Grade*
Kidney diets (reduce proteins)	Animals in stages 3 and 4 of CKD	I
	Dogs with proteinuria	II
	Dogs in stages 1 and 2 of CKD	IV
ACEIs (benazepril, enalapril, etc.)	Cats with CKD and proteinuria (UPC >0.4)	I
	Dogs with CKD and proteinuria (UPC >0.5)	II
	Animals with nonproteinuric CKD (renoprotection)	IV
ARA-II (telmisartan, losartan)	Cats with CKD and proteinuria (UPC >0.4)	I
	Dogs with CKD and proteinuria (UPC >0.5), if ACE inhibitors do not work	IV
Control of hyperphosphataemia	Restriction of P in the diet in stages 3 and 4 of CKD	III
	P chelators (aluminium salts, others)	IV
Treatment of hypertension (ACEIs, amlodipine)	Hypertensive cats with CKD (amlodipine: first choice)	III
	Hypertensive dogs with CKD (renoprotection)	IV
K supplementation (potassium gluconate or citrate)	Cats with CKD and hypokalaemia	III
	Cats with CKD	IV
Supplement with omega 3,	Dogs in stages 2–4 of CKD	III

antioxidants and water-soluble vitamins, chitosan, etc.		
Calcitriol	Dogs with CKD (control of hyperparathyroidism, if P ≤5 mg/dl)	I
EPO	Animals with advanced anaemia (Hct <20 %)	III
SC fluids (NaCl)	Animals with chronic dehydration (oral fluid administration if vomiting is absent)	IV
Alkalising agents (sodium bicarbonate)	Animals with chronic acidaemia	IV
Assisted nutrition	Animals with anorexia and malnutrition	IV
Prevention of thromboembolism: low dose aspirin/clopidogrel	Animals with intense proteinuria and albumin <1.5 g/dl (nephrotic syndrome)	IV

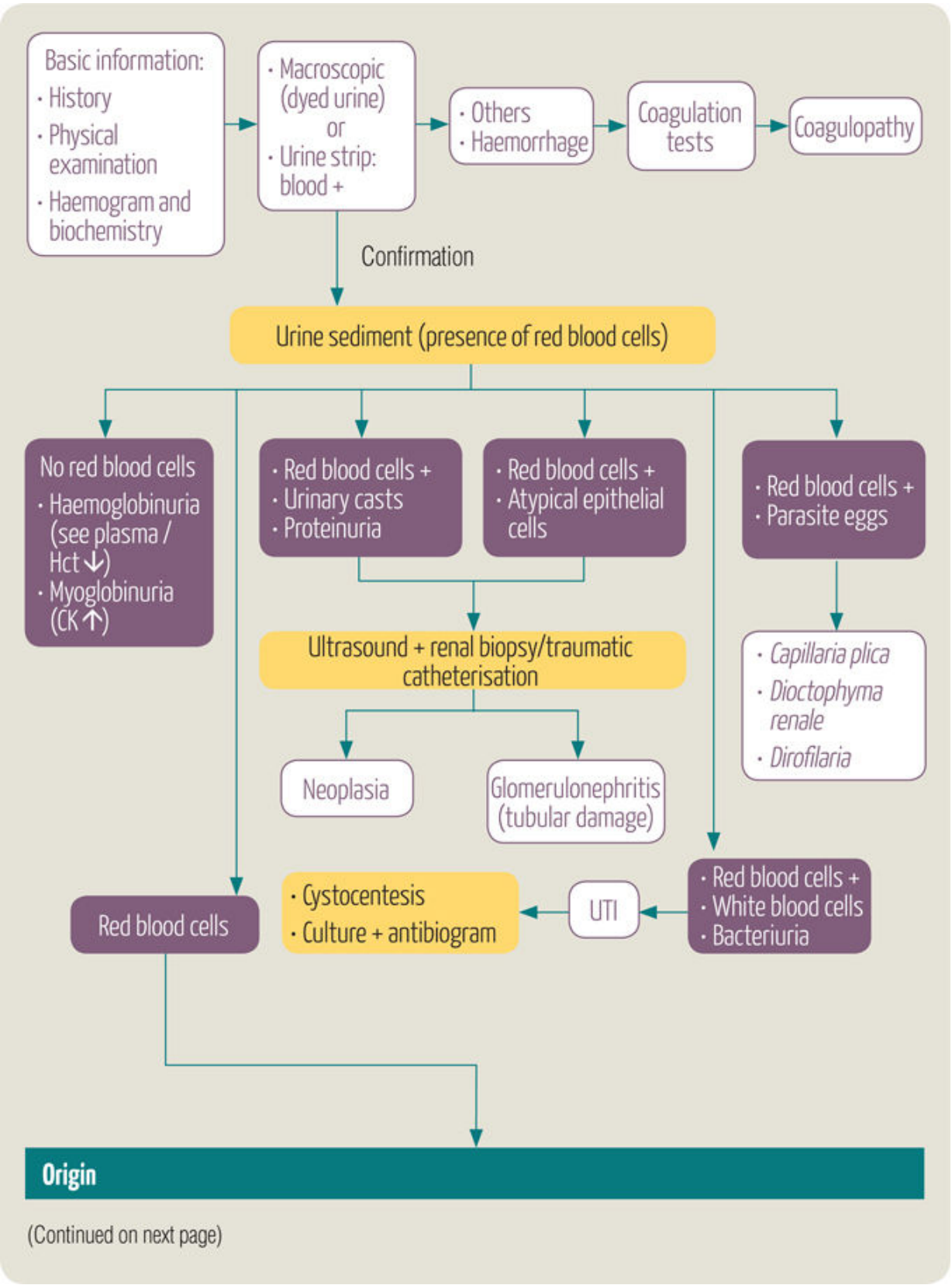
* Degrees of recommendation according to EBM:
  - I: highly recommended.
  - II: favourable recommendation.
  - III: favourable recommendation but not conclusive.
  - IV: not recommended or disapproved.

Proteinuria



* Diluted urine (≤1.008) and alkaline urine (pH >8) can cause haemolysis in the urinary tract. See *Treatment of CKD*.

Haematuria



(Continued on next page)

Origin		
Genital tract (at start of urination or independent)	• Prostatitis/neoplasia (♂) • Proestrus/pyometra/neoplasia/vaginitis (♀)	• Vaginal cytology (♀) • Ultrasound (FNA/biopsy) • Endoscopy (biopsy)
Lower urinary tract (at start of and during urination)	• Calculi • Cystitis (polypoid, FLUTD, cyclophosphamide, etc.) • Trauma • Neoplasia (TCC, etc.)	• Simple/contrast radiography • Urethral catheterisation (in case of obstruction) • Ultrasound (FNA/biopsy) • Endoscopy (biopsy)
Upper urinary tract (at end of urination)	• Renal pelvic/ureter calculi • Kidney trauma • Renal neoplasia • Infections (Leptospira, Borrelia, etc.) • Vascular alterations (benign essential haematuria)	

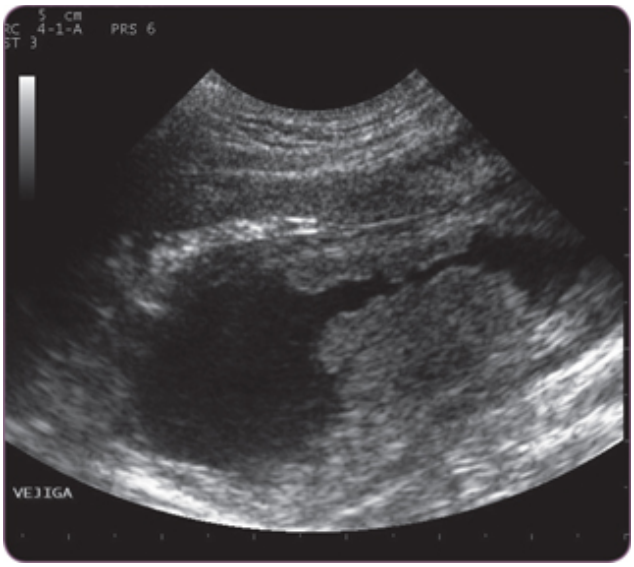


Figure 2. Ultrasound of a dog with a bladder mass (TCC).

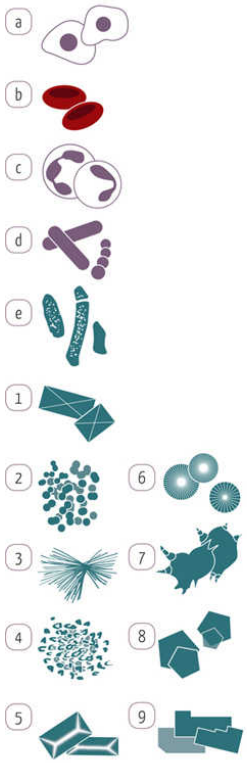


Figure 3. Kidney of a dog with macroscopic chronic intermittent haematuria due to renal haemangiosarcoma.

Interpretation of test strips

Parameter		Normal values	Differential diagnosis	Additional tests
Bilirubin		Up to 2+ (concentrated urine)	• Haemolytic anaemia • Systemic infection (*Ehrlichia*, FeLV, *Babesia*) • Hepatobiliary disease	• Blood smear + haemogram • Complete biochemistry
Glucose		Absent	• Stress/drugs (transient glycosuria) • Diabetes mellitus, hyperadrenocorticism, pancreatitis, glucagonoma, chronic liver failure • Congenital or acquired renal tubular dysfunction	• Glucose (blood) • Ketones (urine)
Blood proteins	Haematuria	Absent	• Inflammation of the urinary tract • Systemic coagulopathy (CID, rodenticide) • Iatrogenic (catheter) or genital contamination	• Urinary sediment test: presence of red blood cells
	Haemoglobinuria		• Lysis of red blood cells present in alkaline/diluted urine • Intravascular haemolysis with haemoglobinaemia (haemolytic anaemia)	• Hct + red blood cell count • Evaluate colour after centrifugation • Consider artificial lysis
	Myoglobinuria		• Muscle lesion or severe necrosis	• Biochemistry: CK and AST
Ketones		Absent	• Diabetic ketoacidosis • Endocrine tumours (insulinoma, etc.) • Anorexia or starvation, gestational toxaemia	• β-hydroxybutyrate • Serum biochemistry (glucose) • Acid-base status
pH		5.5–7.5	• Acid: hyperproteic diet, metabolic/respiratory acidosis, diabetic ketoacidosis, renal failure, pharmacotherapy • Basic: UTI with urease-producing organisms, metabolic/respiratory alkalosis, vomiting, pharmacotherapy	• Serum biochemistry • Acid-base status • Urine culture
Proteins		• Absent (normal urine) • Maximum 1+ (concentrated urine)	• See *Differential diagnosis of proteinuria*	• Specific gravity + sediment analysis + UPC • Haemogram + biochemistry (albumin)
Specific gravity (with refractometer)		• 1.030–1.045 (dog) • 1.035–1.060 (cat)	• Hyposthenuria (<1.008): diabetes insipidus, corticosteroids, primary polydipsia • Isosthenuria (1.008–1.016): CKD • Concentrated urine (>1.030): dehydration, prerenal azotaemia	• Sediment analysis • Haemogram + biochemistry • Specific tests
Urobilinogen		Absent	• Liver disease (total obstruction of bile duct) • Not very useful in veterinary medicine	• Biochemistry (liver enzymes)
White blood cells		Absent or 1+	• UTI, haematuria (2–4+) • Unreliable (cat): many false positives • Approximate (dog): false negatives	• Sediment analysis • Urine culture
Nitrites		Absent	• Presence of nitrifying bacteria in urine (UTI) • Not very sensitive or specific (dog and cat)	• Sediment analysis • Urine culture

Interpretation of urinary sediment analysis



Findings			Interpretation
Epithelial cells (a)		Squamous	Desquamation of the urethra, vagina, foreskin: of no clinical importance
		Transitional	Pyelonephritis, UTI, squamous cell carcinoma
		Tubular	Glomerulonephritis, severe tubular involvement
Red blood cells (b)			• Haematuria due to inflammation of the urinary or genital tract (>5 red blood cells/field) • Tumours
White blood cells (c)			Septic or nonseptic UTI (pyuria: >5 PMN/field)
Microorganisms (d)			• Bacteria (UTI) • Parasites (eggs of *Capillaria plica, Dioctophyma renale,* or microfilariae of *Dirofilaria immitis*) • Fungi (yeasts due to contamination)
Urinary casts (e)		Hyaline	Albuminuria, fever, intense exercise
		Granular	Tubular lesion if abundant
		Cellular	• Epithelial (acute nephritis, tubular necrosis) • Haematic (tubular/glomerular haemorrhage) • Leukocyte (acute pyelonephritis)
		Waxy	• Chronic tubular lesions • Very poor prognosis
Crystals	Predominance of acids	Calcium oxalate (1)	• Dihydrate in normal urine • Monohydrate in ethylene glycol poisoning
		Amorphous urates (2)	Noncrystalline precipitates of uric acid salts: of no clinical importance
		Tyrosine (3)	Liver disease or congenital amino acid metabolism defects
	Alkaline predominance	Amorphous phosphates (4)	Hypercalciuria/hyperphosphaturia, infections, obstructions, stasis
		Ammonium-magnesium phosphate or struvite (5)	UTI due to ureolytic bacteria (cystitis, prostatitis) together with inflammatory leukocyte reaction
		Calcium carbonate (6)	Exceptional in carnivores
		Ammonium arate (7)	• Portosystemic shunt or hyperammonaemia/liver disease • Associated with enzymatic defects (Dalmatians)
	Amphoteric (pH 6–8)	Cystine (8)	Cystinuria due to congenital amino acid metabolism defects
		Cholesterol (9)	Degradation of the cell membrane and kidney diseases (nephrotic syndrome)

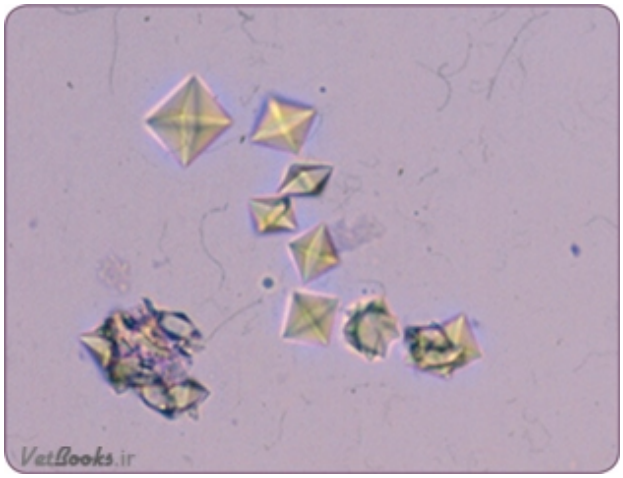


Figure 4. Calcium oxalate dihydrate crystals.

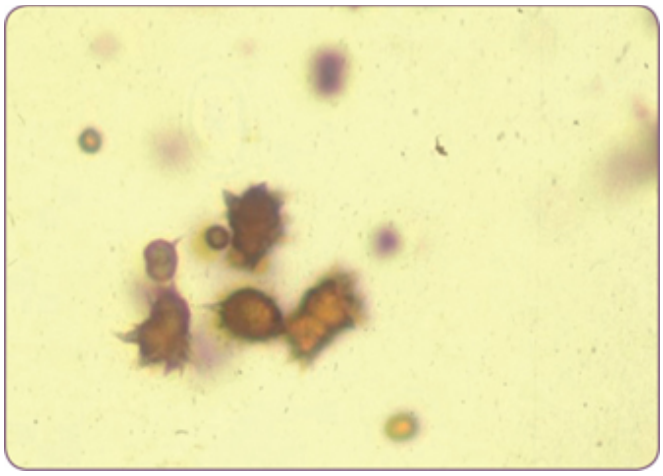


Figure 5. Ammonium urate crystals.

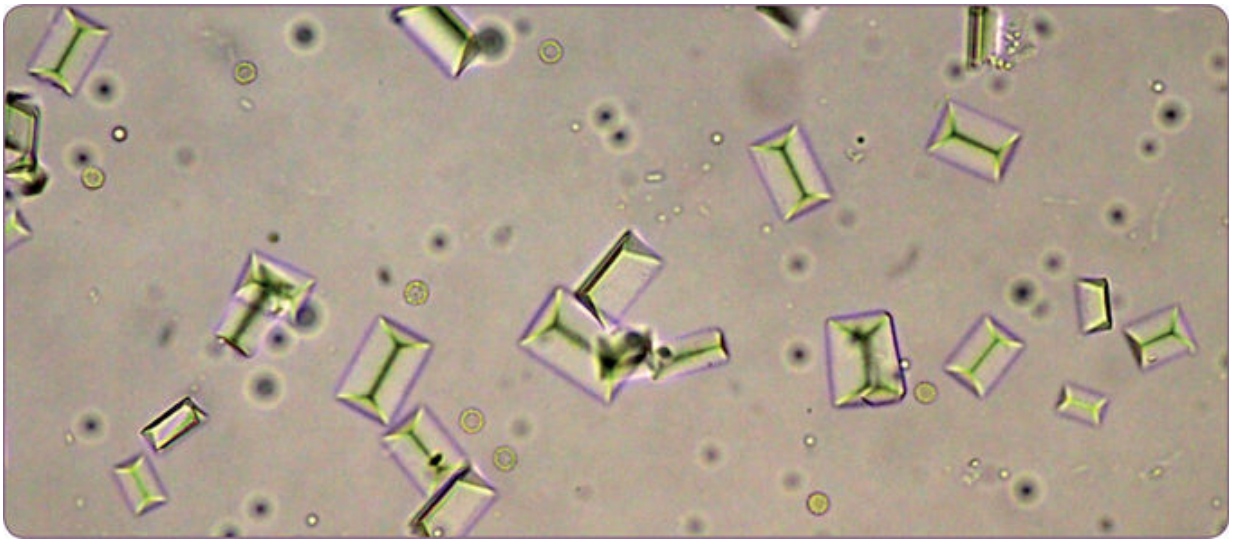


Figure 6. Struvite crystals.

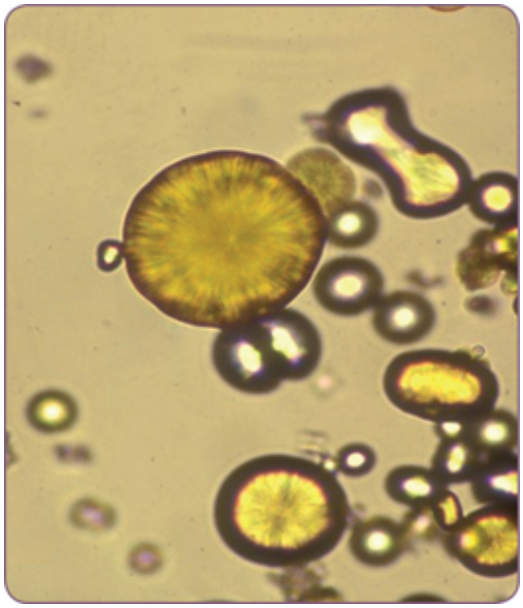


Figure 7. Calcium carbonate crystals.

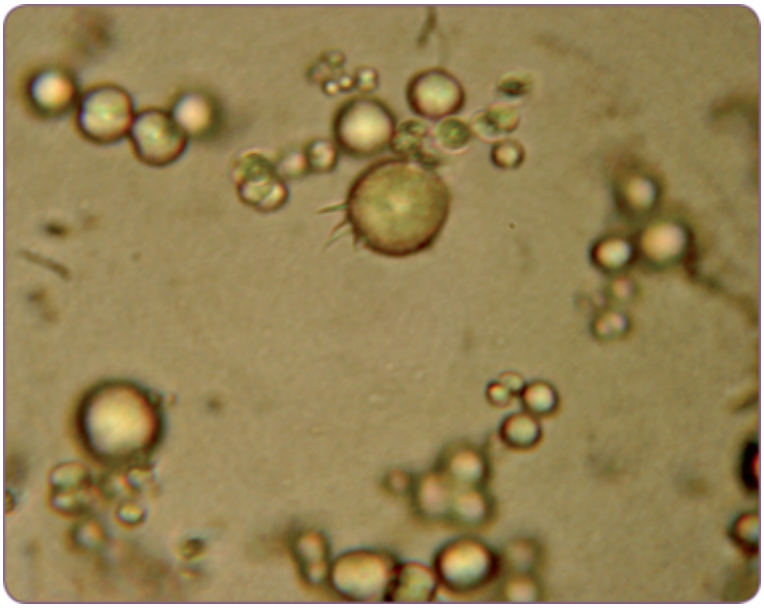
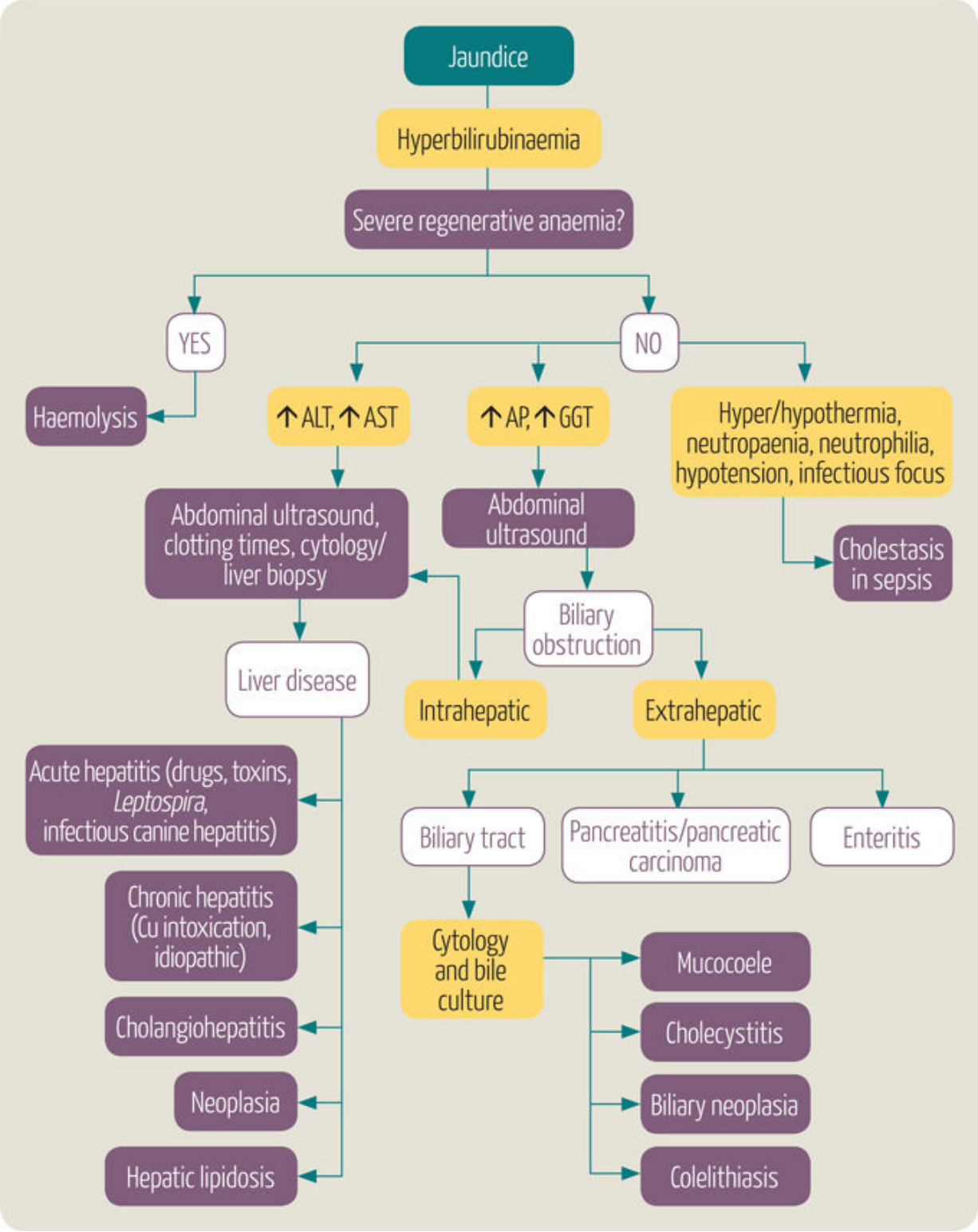


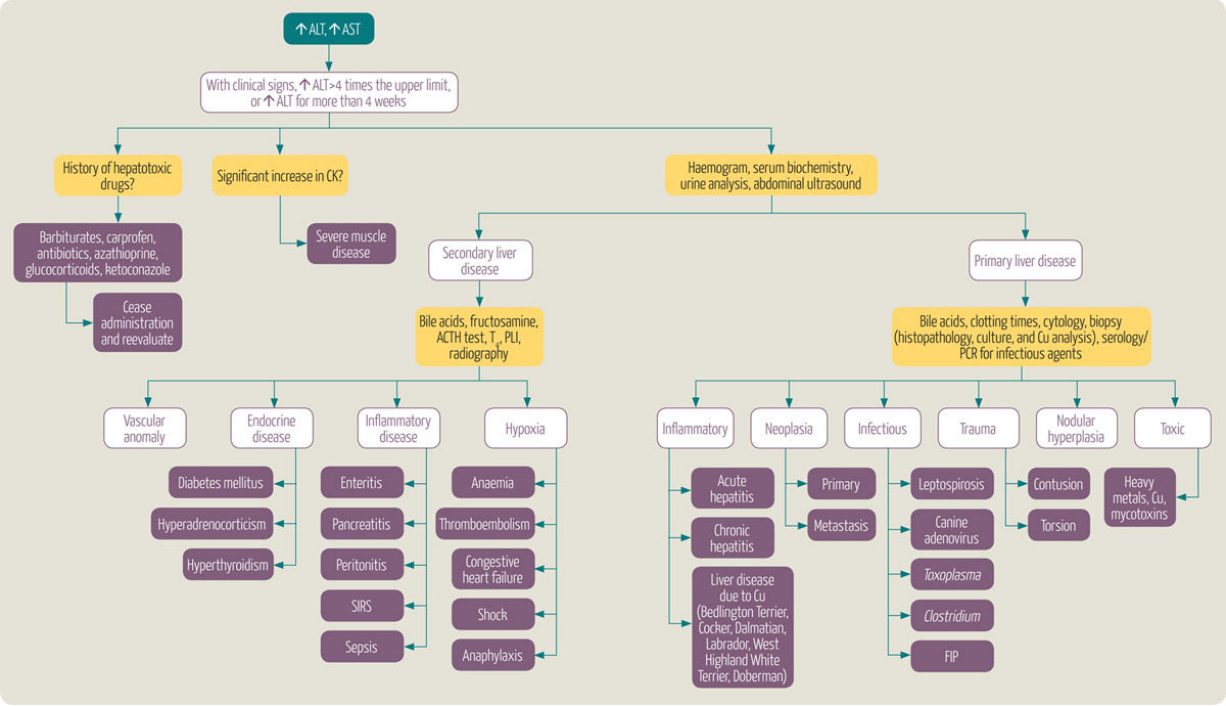
Figure 8. Xanthine crystals in a dog treated with allopurinol.

Liver disease

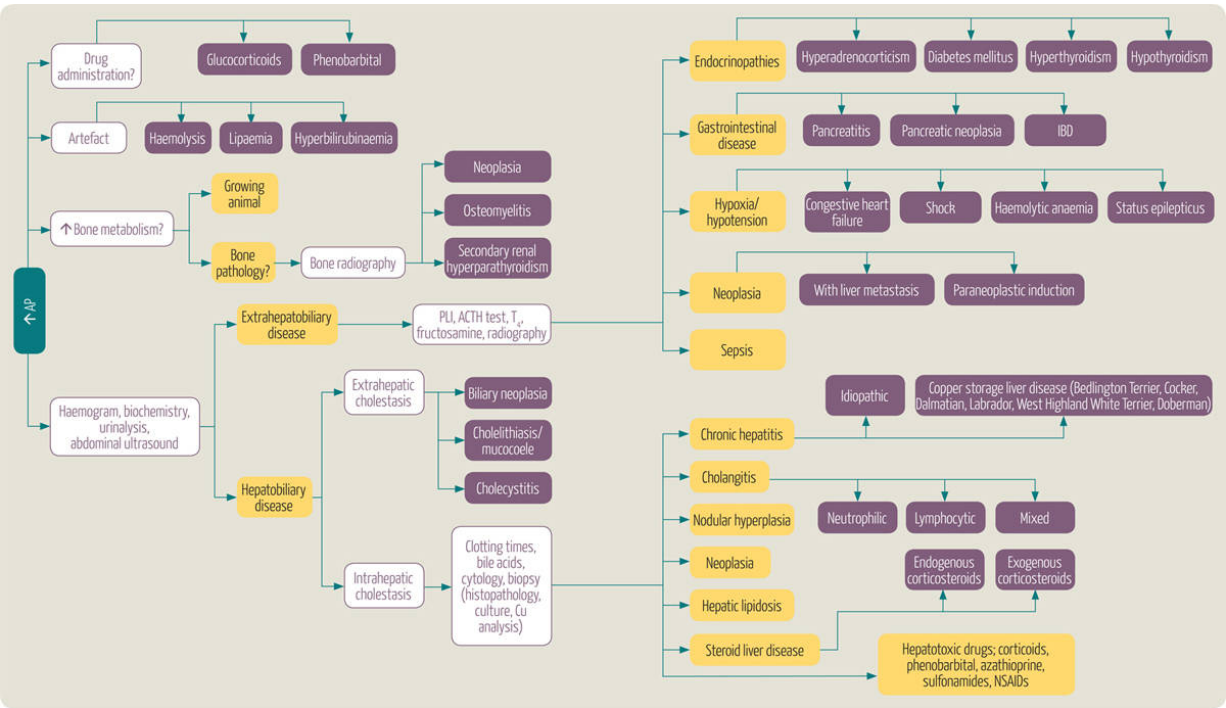
Jaundice



Increase in transaminases



Increase in alkaline phosphatase



Increase in bile acids

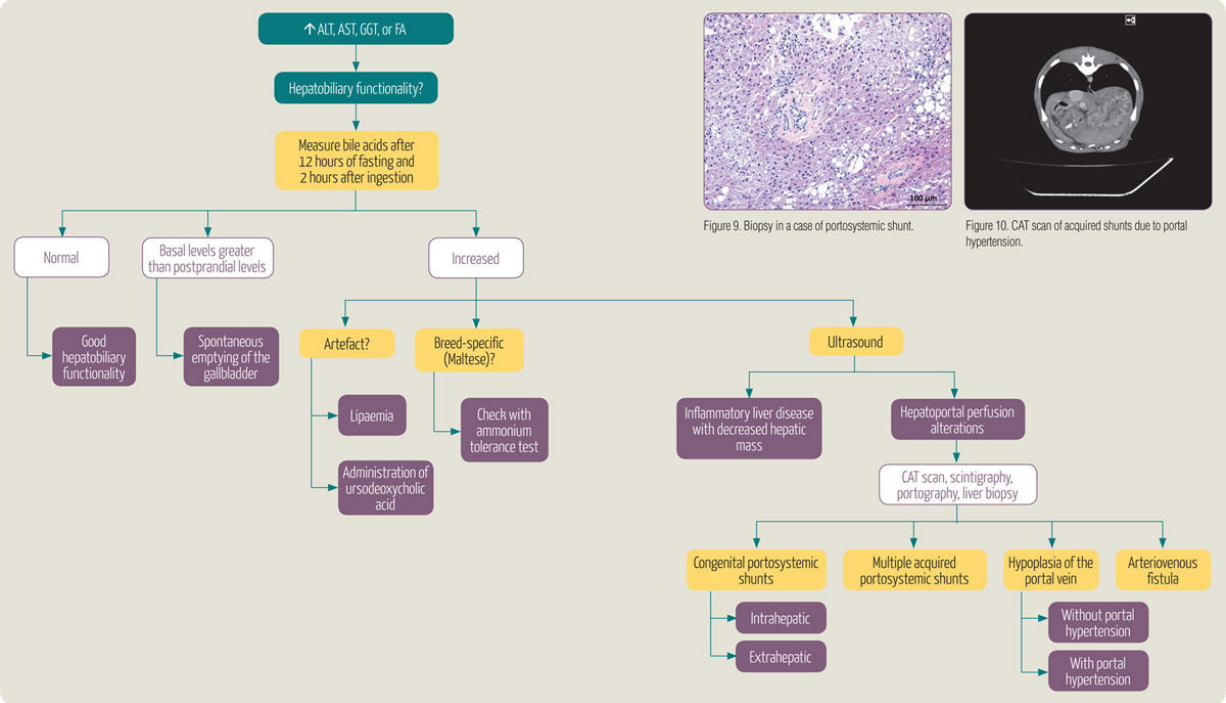
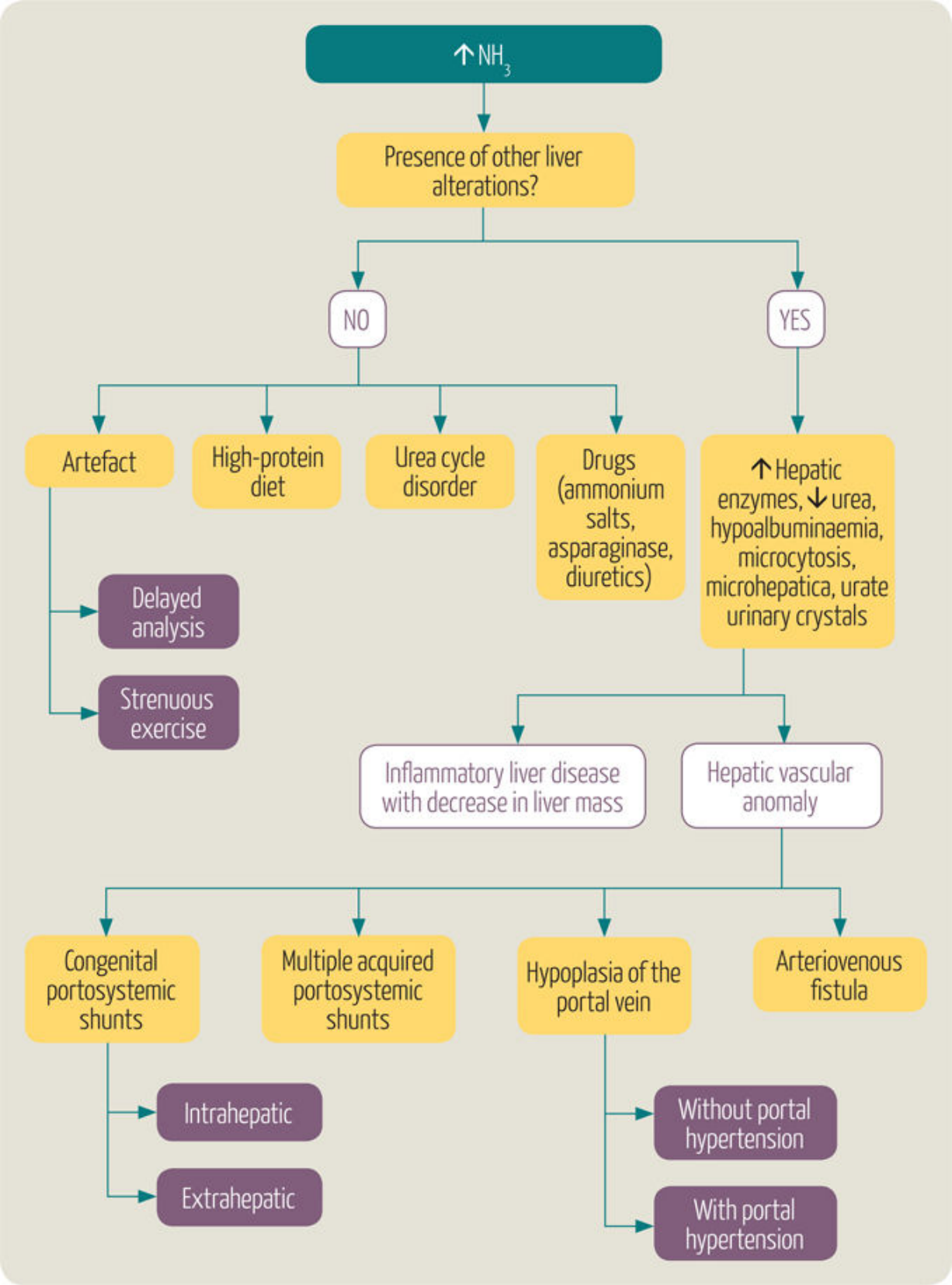


Figure 9. Biopsy in a case of portosystemic shunt.

Figure 10. CAT scan of acquired shunts due to portal hypertension.

Increase in ammonia


↑NH3
Presence of other liver alterations?
NO
YES
Artefact
High-protein diet
Urea cycle disorder
Drugs (ammonium salts, asparaginase, diuretics)
↑Hepatic enzymes, ↓urea, hypoalbuminaemia, microcytosis, microhepatica, urate urinary crystals
Delayed analysis
Strenuous exercise
Inflammatory liver disease with decrease in liver mass
Hepatic vascular anomaly
Congenital portosystemic shunts
Multiple acquired portosystemic shunts
Hypoplasia of the portal vein
Arteriovenous fistula
Intrahepatic
Extrahepatic
Without portal hypertension
With portal hypertension

Clinical and laboratory interpretation in liver disease. Summary

Diagnostic tests	Alteration	Diagnostic interpretation
History/physical examination	PU/PD	Chronic hepatitis, vascular anomaly, hyperadrenocorticism, diabetes mellitus, or hyperthyroidism
	Concomitant dermatological disease	Hyperadrenocorticism or hepatocutaneous syndrome
	Neurological disorders	Hepatic encephalopathy
	Jaundice	Haemolytic anaemia, liver disease, or posthepatic disease
	Abdominal effusion	Chronic hepatitis, neoplasia, pancreatitis, or congestive heart failure
	Hepatomegaly	Primary liver disease, steroid hepatopathy, passive congestion, hepatic neoplasia, or lipidosis
	Abdominal pain	Trauma, pancreatitis, cholecystitis, or gastric ulcer
	Intermittent chronic gastrointestinal signs	Gastric ulcer, vascular anomaly, chronic pancreatitis, IBD, or hyperthyroidism
Laboratory abnormalities	↑ AP	Intrahepatic or extrahepatic cholestasis, endocrinopathies, gastrointestinal disease, endogenous or exogenous corticosteroids, bone alterations, bone growth, renal failure, hypoxia, neoplasia, sepsis,

		anticonvulsants, lipaemia, or haemolysis
	↑ ALT	Injury or necrosis of hepatocytes, haemolysis, lipaemia, or severe muscle disease
	↑ AST	Severe lesion or necrosis of the hepatocytes or muscle (lesion at the mitochondrial level), haemolysis, or lipaemia
	↑ Bile acids	Hepatic dysfunction, congenital or acquired hepatic vascular abnormalities, or hypertriglyceridaemia
	↑ Bilirubin	Haemolysis, intrahepatic or extrahepatic cholestasis, sepsis, or lipaemia
	↓ Cholesterol	Liver failure or anorexia
	↑ Cholesterol	Cholestasis, endocrine disease, nephrotic syndrome, or primary dyslipoproteinaemia
Laboratory abnormalities	↓ Albumin	Malnutrition, malabsorption, liver disease, haemorrhage, protein-losing enteropathy, protein-losing nephropathy, or chronic disease
	↓ Glucose	Liver failure, sepsis, spurious hypoglycaemia, insulinoma, insulin-secreting tumours, fasting, or hypoadrenocorticism
	↑ NH_3	Liver failure, vascular anomaly, delay in measurement, high-protein diet, or urea cycle disorder

Radiography	Hepatomegaly	Primary liver disease, steroid hepatopathy, passive congestion, neoplasia, or hepatic lipidosis
	Microhepatica	Cirrhosis or vascular anomaly
	Radiopacity in the gallbladder	Colelithiasis
	Loss of abdominal detail	Abdominal effusion or cachexia
	Cardiomegaly +/- pulmonary oedema	Congestive heart failure
Ultrasound	Focal or multifocal lesions	Primary hepatobiliary neoplasia or metastasis, nodular hyperplasia, or abscess
	Diffuse hyperechogenicity	Hepatic lipidosis, steroid hepatopathy, or lymphosarcoma
	Diffuse hypoechogenicity	Passive congestion, lymphosarcoma, or suppurative hepatitis
	Normal	Do not rule out liver disease
	Alteration of the gallbladder/biliary tree	Mucocoele, cholestasis, cholestasis, or mineralisation
	Portal vein anomalies	Vascular anomalies, thrombosis, or passive congestion
	Hypoechoic pancreas surrounded by hyperechoic fat	Pancreatitis
	Thickening of the gastrointestinal	IBD or lymphosarcoma

	tract	
	Abdominal effusion	Chronic hepatitis, neoplasia, pancreatitis, or congestive heart failure

Extrahepatic conditions that increase liver enzyme levels. Summary

Extrahepatic condition		Altered parameter
Drugs	Corticosteroids	↑ ↑ ↑ AP, ↑ ↑ GGT, ↑ ALT
	Phenobarbital	↑ AP, ↑ ALT
Breed-specific	Scottish Terrier	↑ ↑ AP
Endocrine disease	Hyperthyroidism	↑ AP, ↑ ALT
	Hypothyroidism	↑ AP
	Diabetes mellitus	↑ AP
	Hyperadrenocorticism	↑ ↑ ↑ AP, ↑ ↑ GGT, ↑ ALT
Hypoxia	Shock, congestive heart failure, haemorrhage, epilepsy, hypotension, etc.	↑ ↑ ↑ ALT, ↑ ↑ AST, ↑ GGT, ↑ AP
Muscle damage	Necrosis, trauma, malignant hyperthermia, myopathy	↑ ALT, ↑ AST
Neoplasia	Liver metastasis	↑ ALT, ↑ AST, ↑ AP
↑ Bone metabolism	Young animals, neoplasia, osteomyelitis	↑ AP
Gastrointestinal disease		↑ ↑ AP, ↑ ALT
Pancreatitis		↑ ↑ AP, ↑ ALT
Gestation in cats		↑ AP

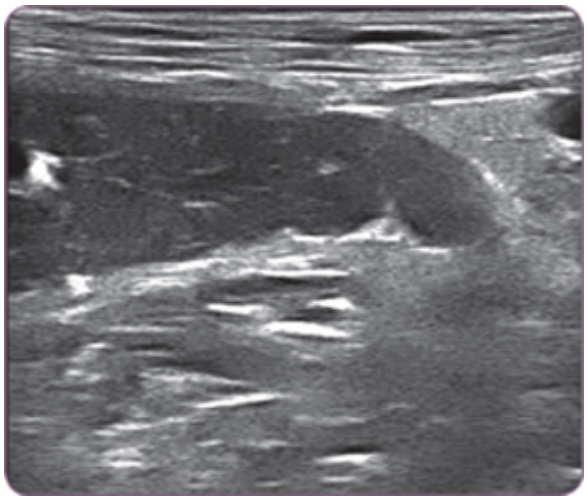


Figure 11. Ultrasound of a dog with pancreatitis.

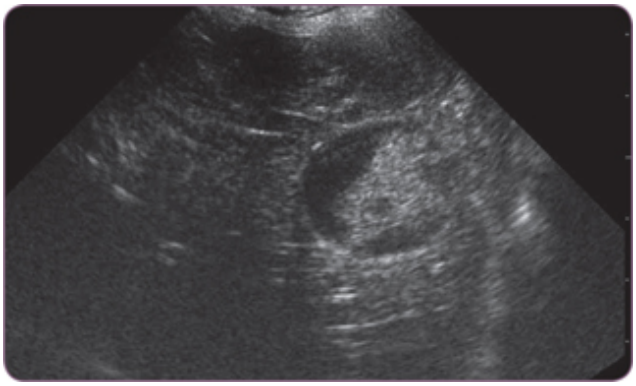
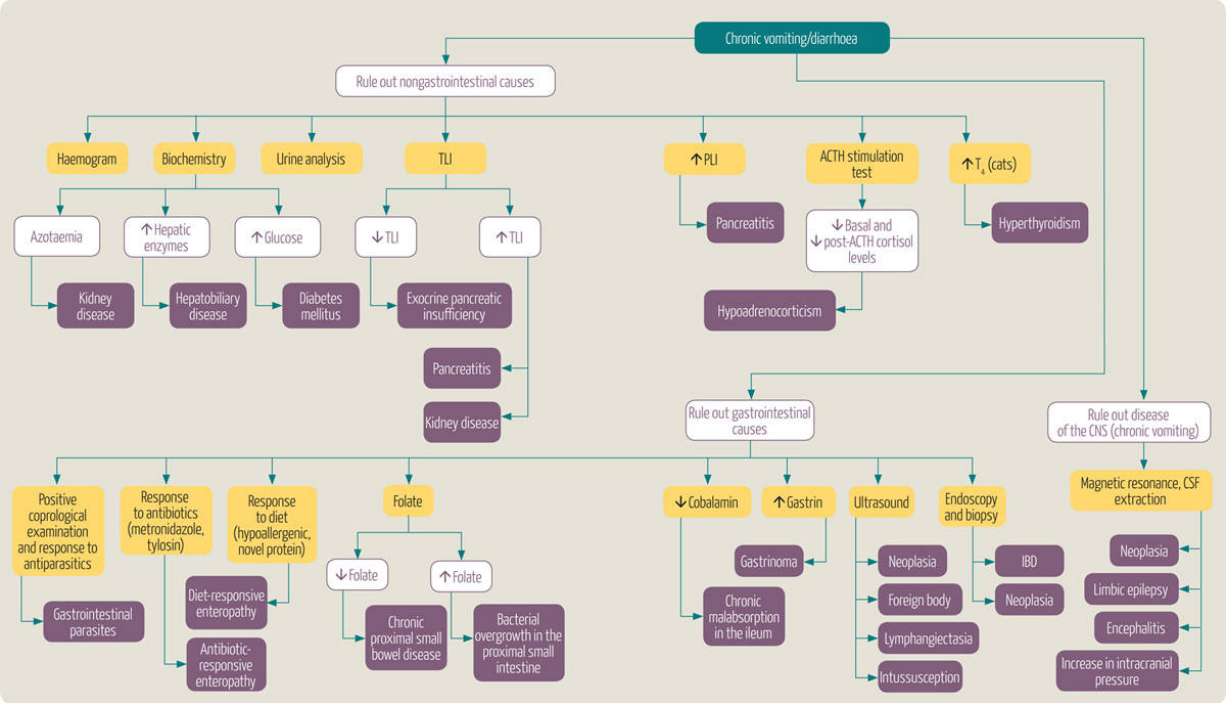


Figure 12. Liver ultrasound of a dog with liver disease secondary to hyperadrenocoticism, in which a mucocoele is observed in the gallbladder.

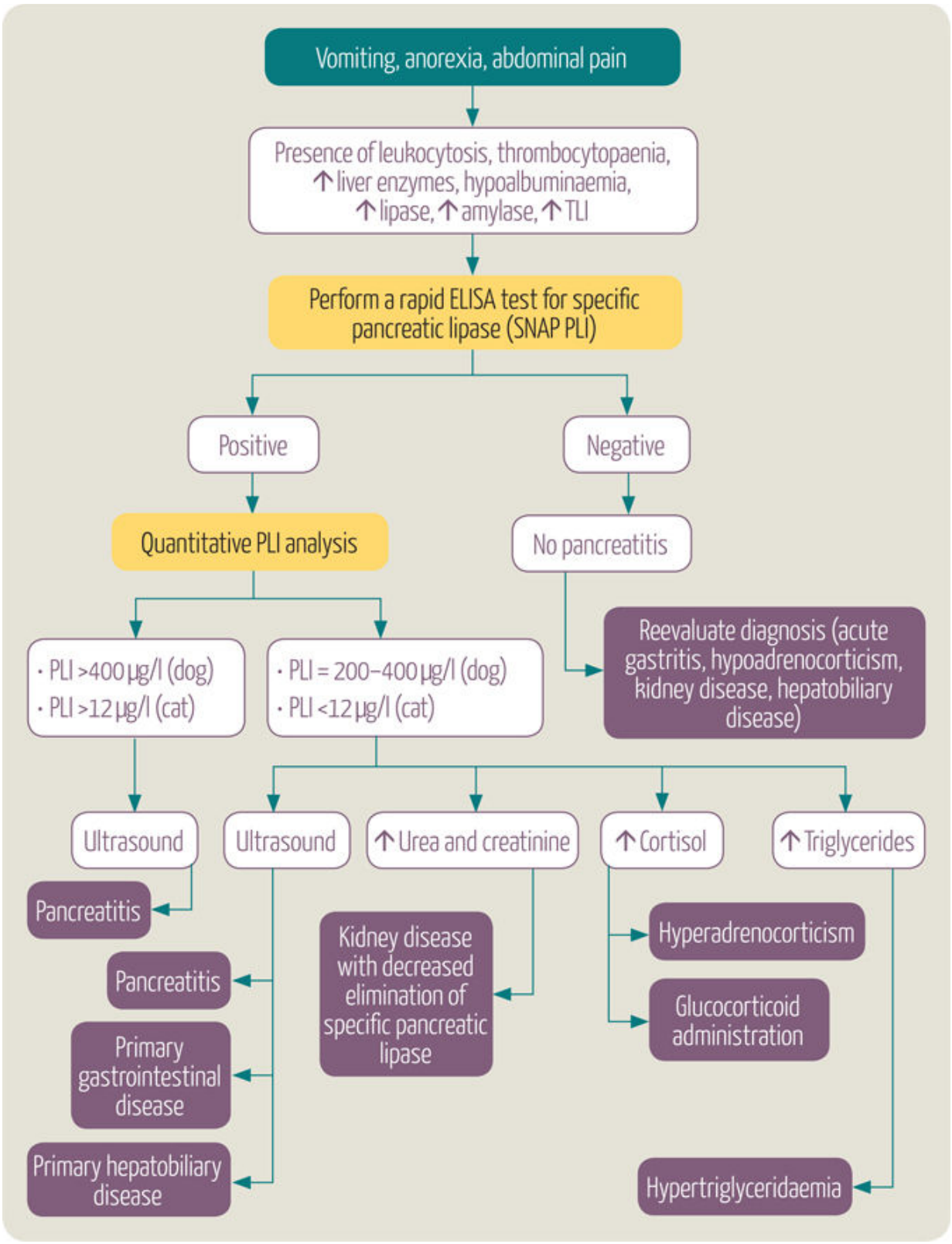
Gastrointestinal disease

Clinical and laboratory approach to gastrointestinal signs



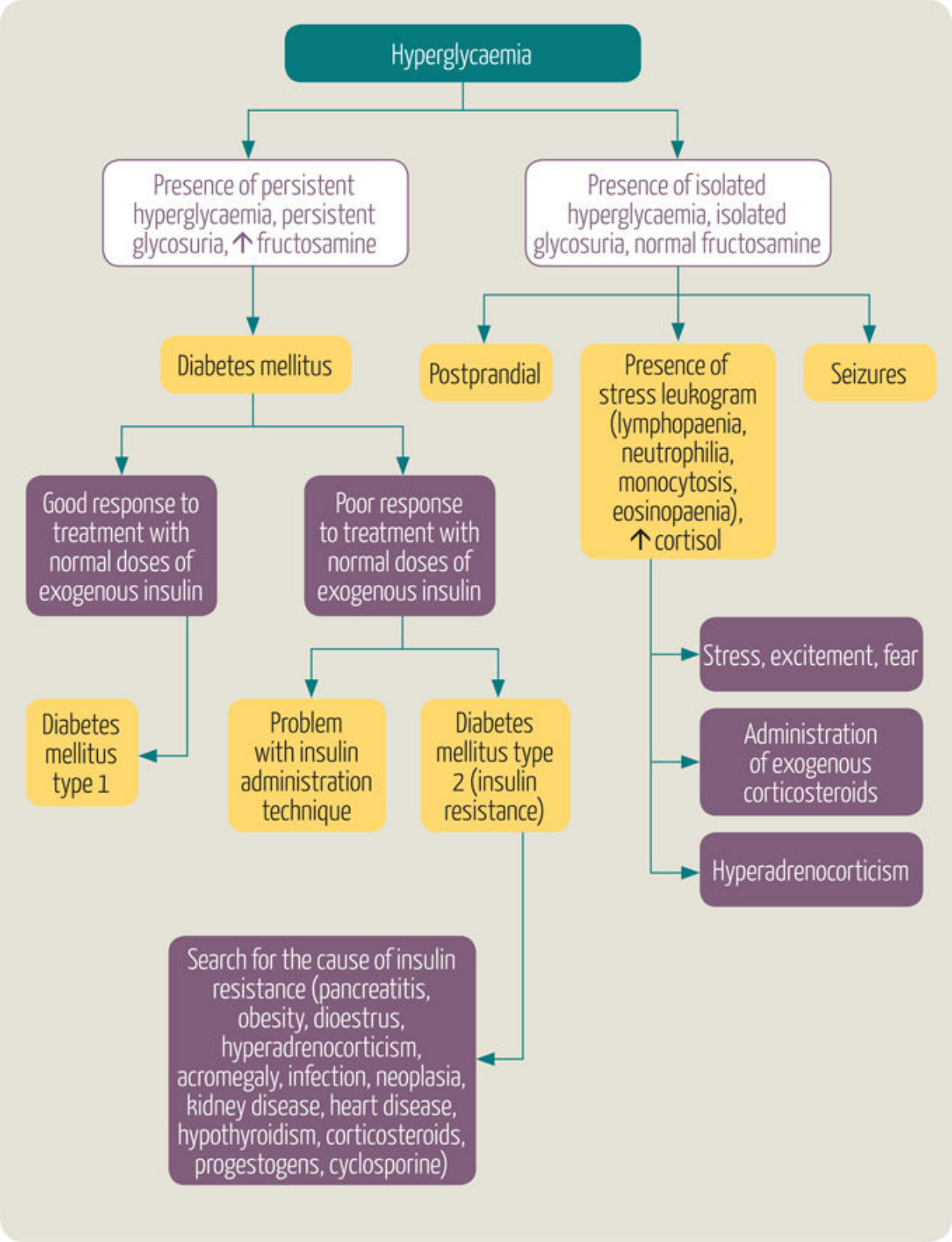
Pancreatic disease

Laboratory approach in case of suspected pancreatitis

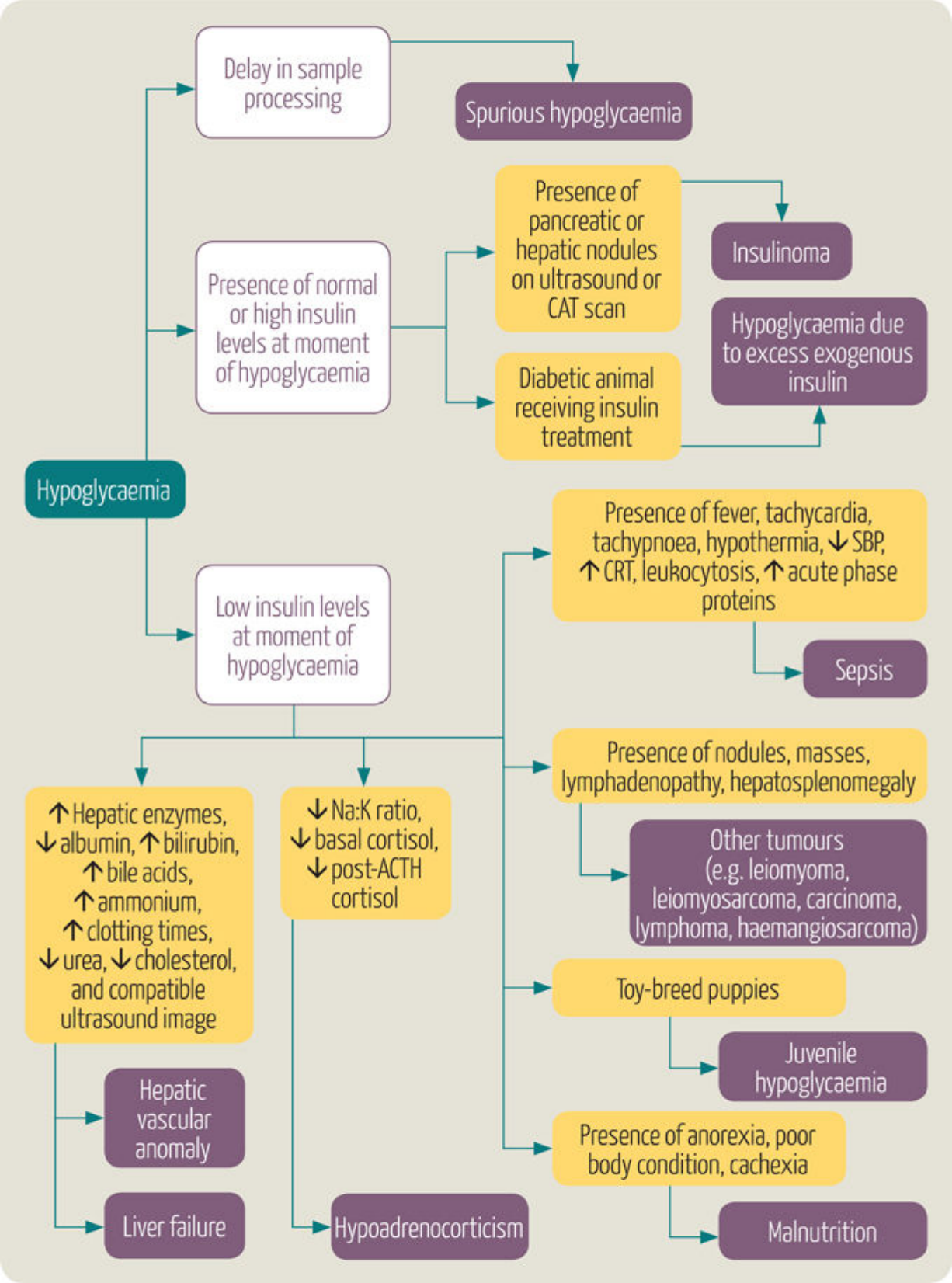

Vomiting, anorexia, abdominal pain
Presence of leukocytosis, thrombocytopaenia, ↑liver enzymes, hypoalbuminaemia, ↑lipase, ↑amylase, ↑TLI
Perform a rapid ELISA test for specific pancreatic lipase (SNAP PLI)
Positive
Negative
Quantitative PLI analysis
No pancreatitis
• PLI >400 µg/l (dog)
• PLI >12 µg/l (cat)
• PLI = 200–400 µg/l (dog)
• PLI <12 µg/l (cat)
Reevaluate diagnosis (acute gastritis, hypoadrenocorticism, kidney disease, hepatobiliary disease)
Ultrasound
Ultrasound
↑Urea and creatinine
↑Cortisol
↑Triglycerides
Pancreatitis
Pancreatitis
Primary gastrointestinal disease
Primary hepatobiliary disease
Kidney disease with decreased elimination of specific pancreatic lipase
Hyperadrenocorticism
Glucocorticoid administration
Hypertriglyceridaemia

Glucose alterations

Hyperglycaemia

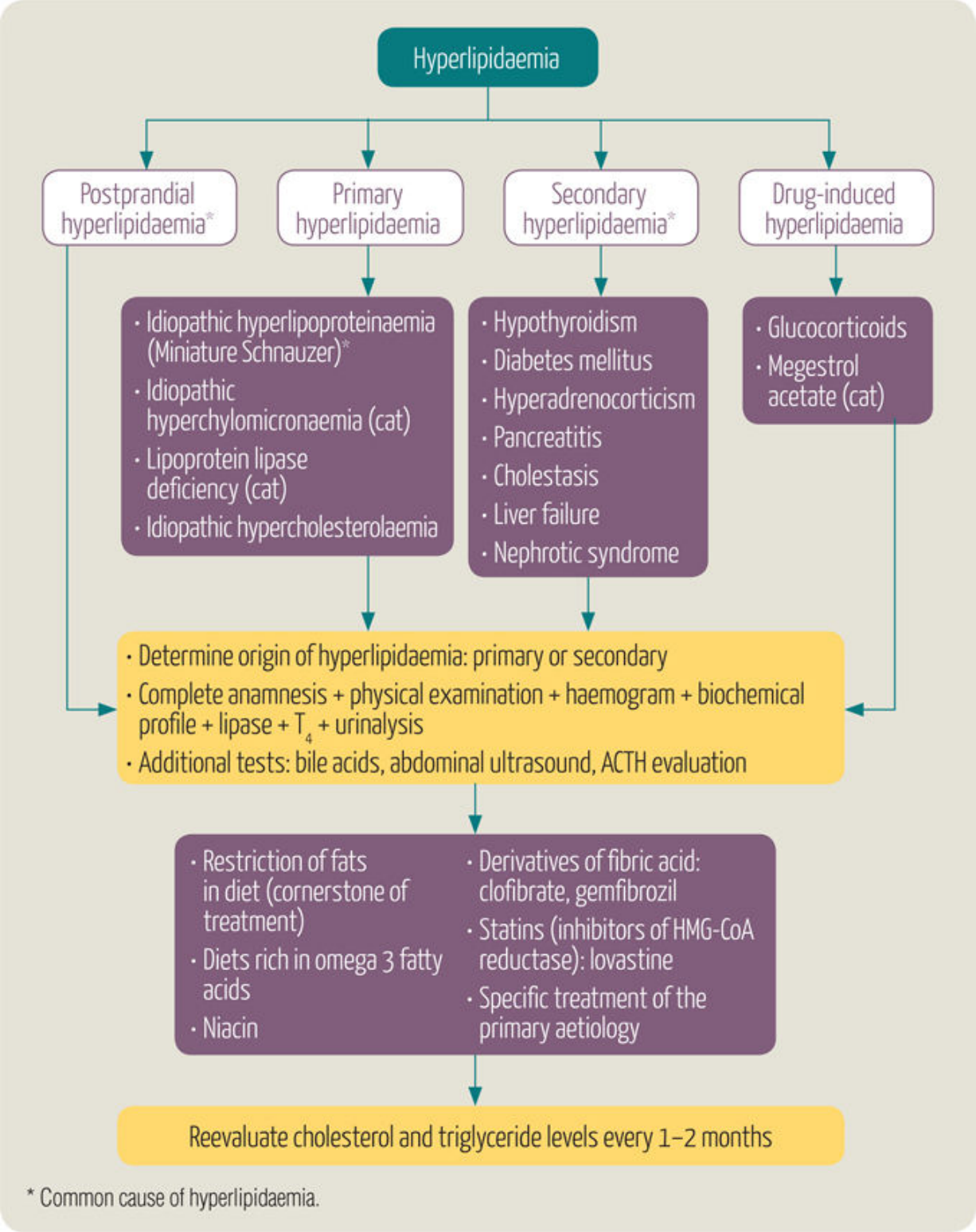


Hypoglycaemia

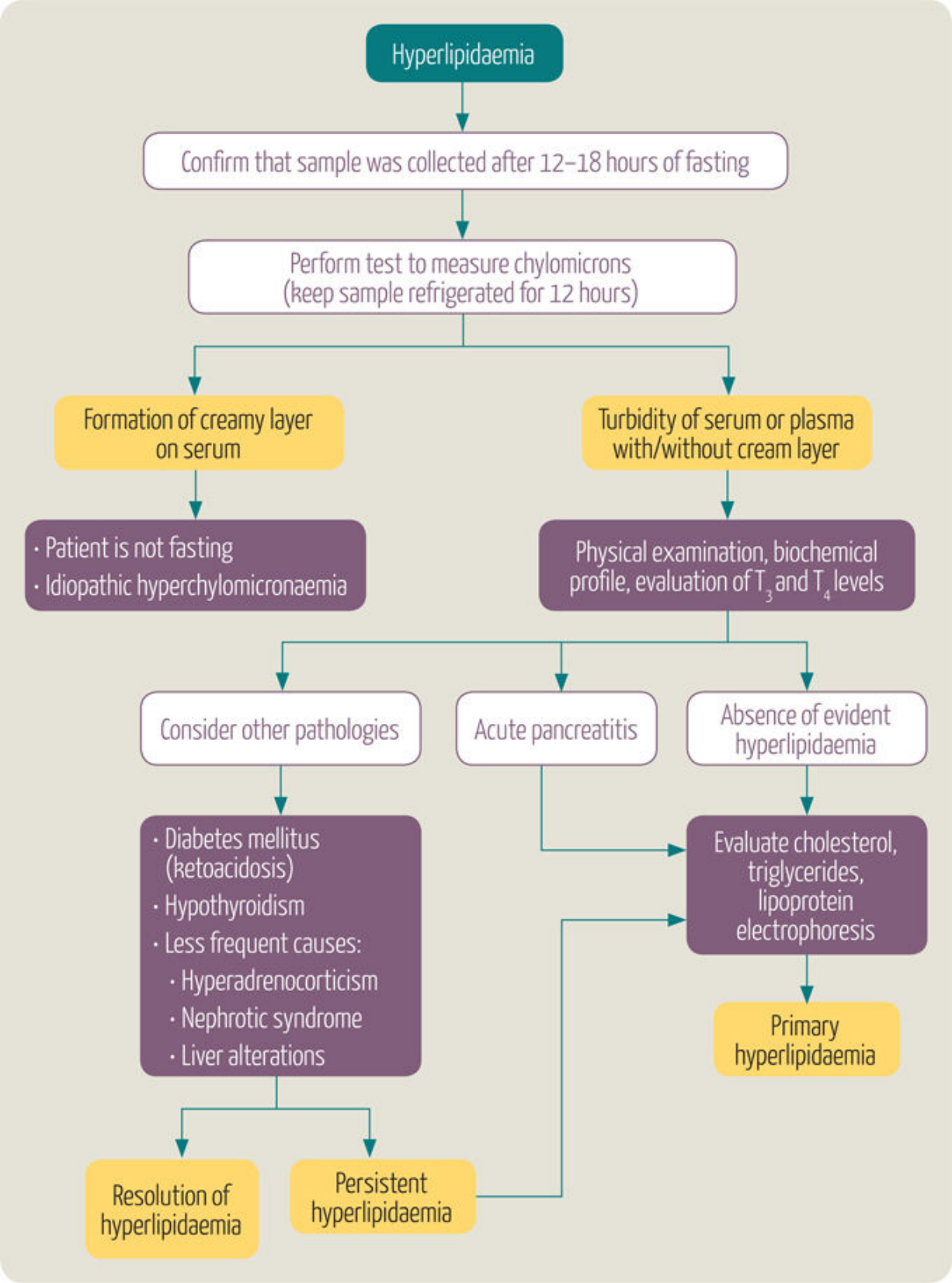

Hypoglycaemia
Delay in sample processing
Spurious hypoglycaemia
Presence of normal or high insulin levels at moment of hypoglycaemia
Presence of pancreatic or hepatic nodules on ultrasound or CAT scan
Insulinoma
Diabetic animal receiving insulin treatment
Hypoglycaemia due to excess exogenous insulin
Low insulin levels at moment of hypoglycaemia
Presence of fever, tachycardia, tachypnoea, hypothermia, ↓SBP, ↑CRT, leukocytosis, ↑acute phase proteins
Sepsis
Presence of nodules, masses, lymphadenopathy, hepatosplenomegaly
Other tumours (e.g. leiomyoma, leiomyosarcoma, carcinoma, lymphoma, haemangiosarcoma)
↑Hepatic enzymes, ↓albumin, ↑bilirubin, ↑bile acids, ↑ammonium, ↑clotting times, ↓urea, ↓cholesterol, and compatible ultrasound image
↓Na:K ratio, ↓basal cortisol, ↓post-ACTH cortisol
Toy-breed puppies
Juvenile hypoglycaemia
Hepatic vascular anomaly
Presence of anorexia, poor body condition, cachexia
Liver failure
Hypoadrenocorticism
Malnutrition

Lipid alterations

Hyperlipidaemia

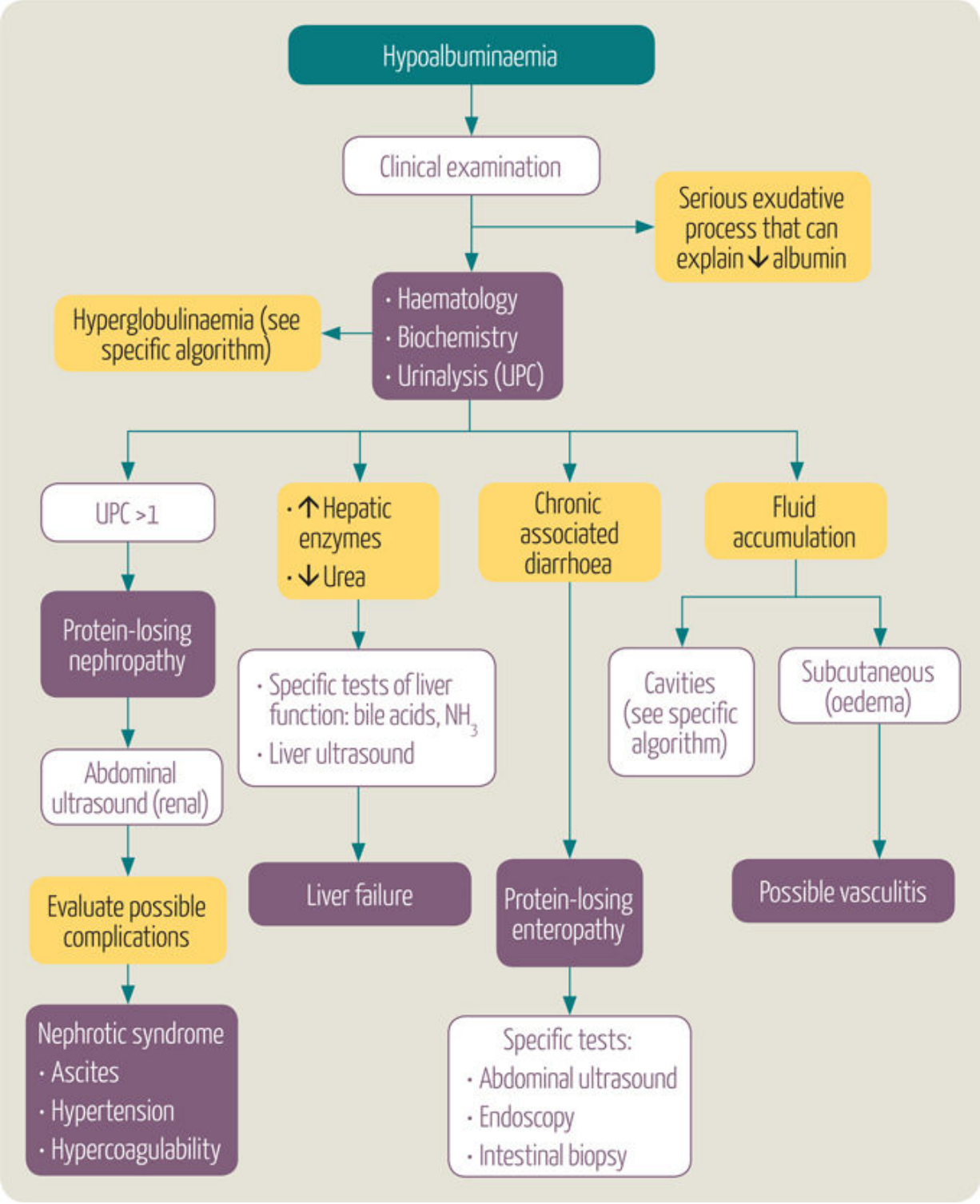


* Common cause of hyperlipidaemia.

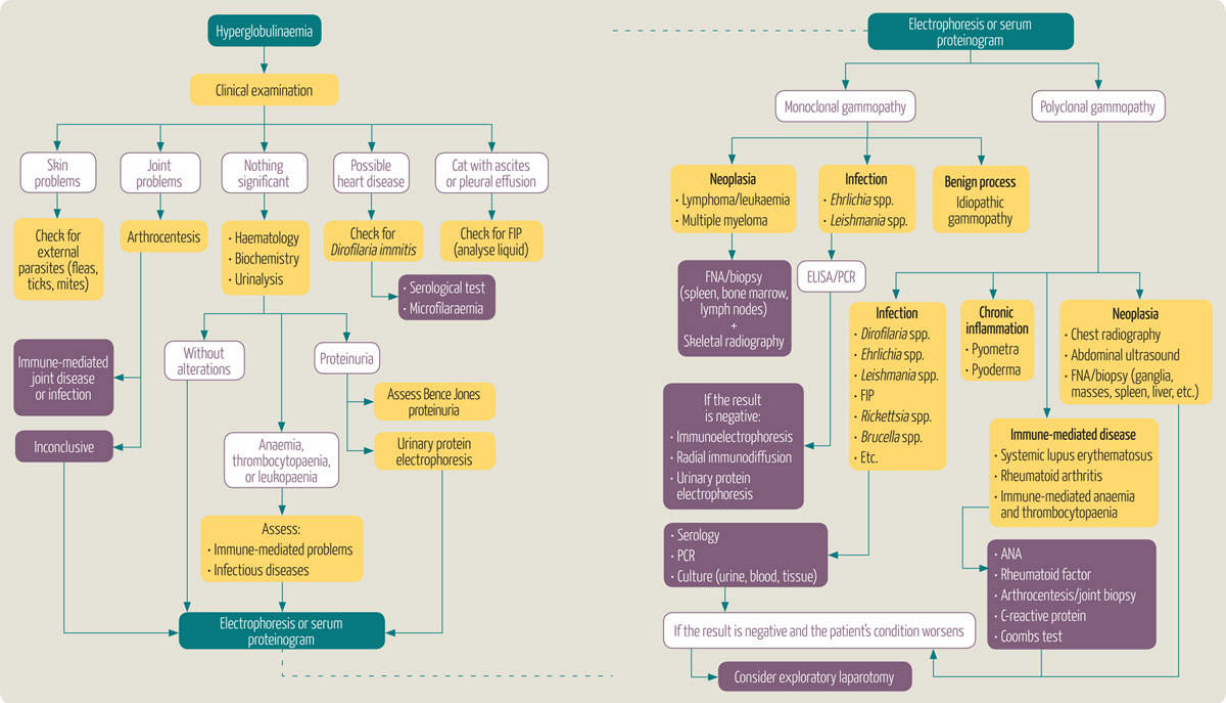

Hyperlipidaemia
Confirm that sample was collected after 12–18 hours of fasting
Perform test to measure chylomicrons (keep sample refrigerated for 12 hours)
Formation of creamy layer on serum
Turbidity of serum or plasma with/without cream layer
· Patient is not fasting
· Idiopathic hyperchylomicronaemia
Physical examination, biochemical profile, evaluation of T_3 and T_4 levels
Consider other pathologies
Acute pancreatitis
Absence of evident hyperlipidaemia
· Diabetes mellitus (ketoacidosis)
· Hypothyroidism
· Less frequent causes:
· Hyperadrenocorticism
· Nephrotic syndrome
· Liver alterations
Evaluate cholesterol, triglycerides, lipoprotein electrophoresis
Primary hyperlipidaemia
Resolution of hyperlipidaemia
Persistent hyperlipidaemia

Alterations in plasma proteins

Hypoalbuminaemia

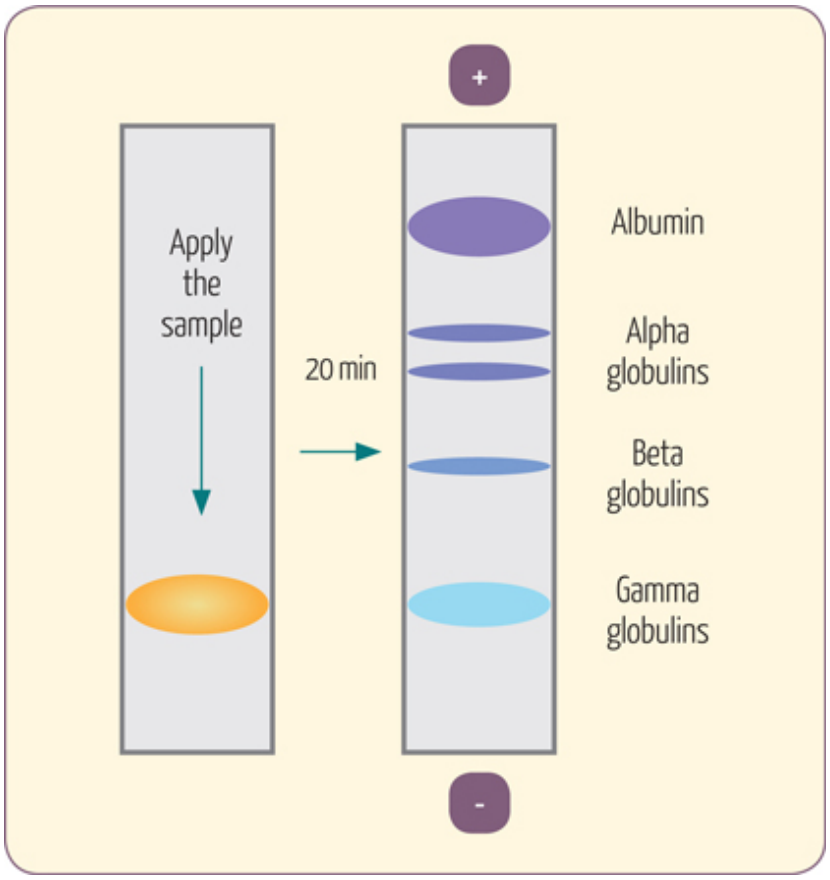


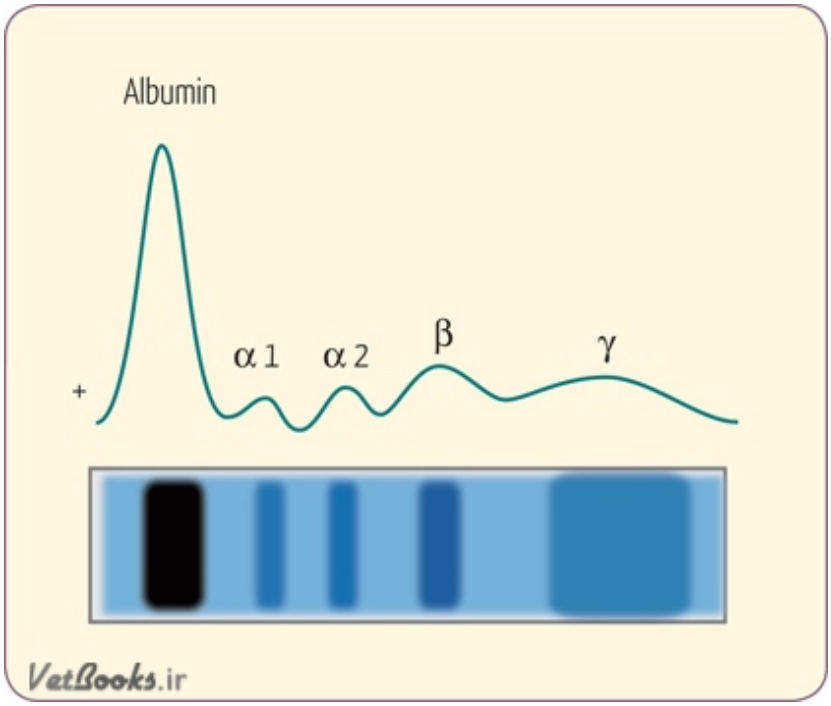
Hyperglobulinaemia



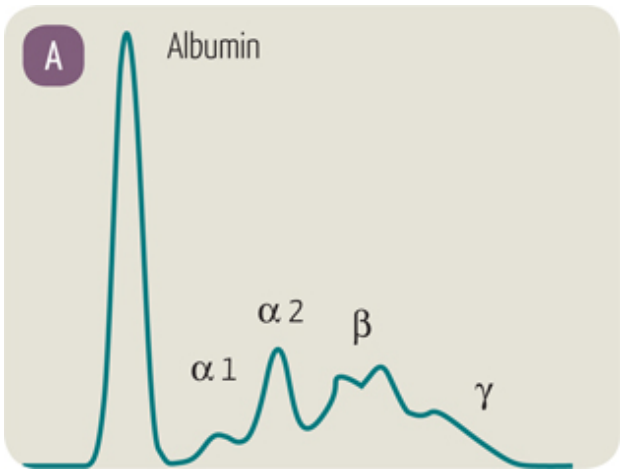
Proteinogram

Separation of serum proteins by electrophoresis (serum proteinogram)

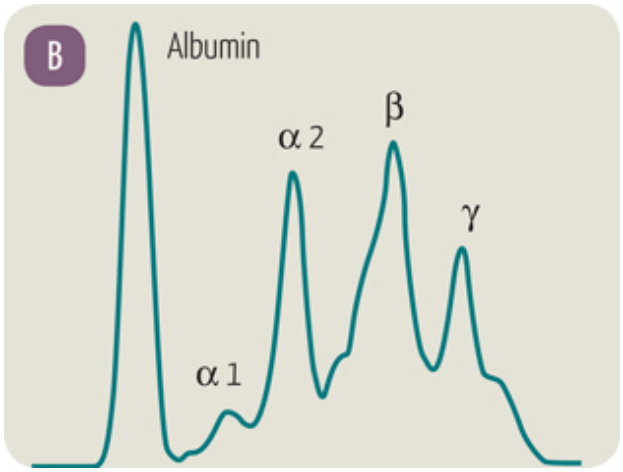




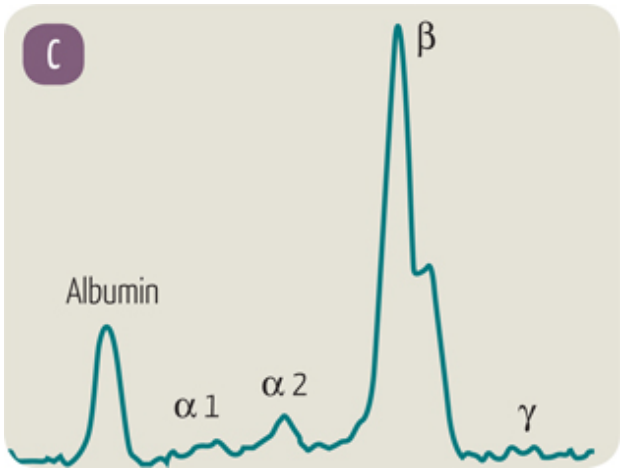
Normal proteinogram (dog).



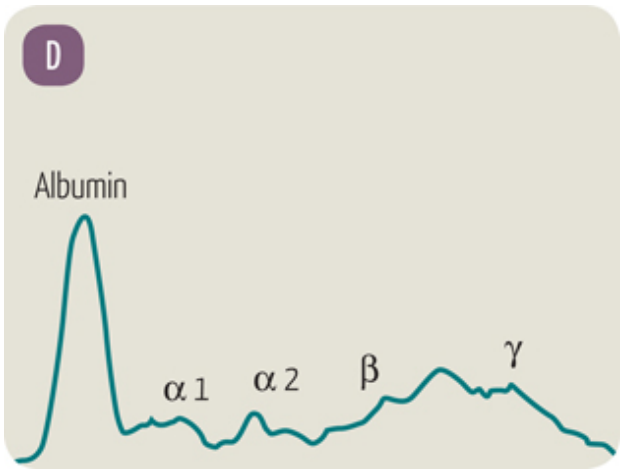
Proteinogram of a normal dog.



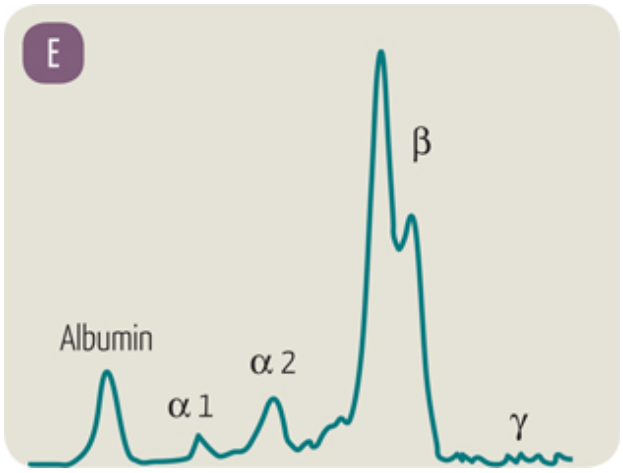
Proteinogram of a dog with *Leishmania* : polyclonal gammopathy.



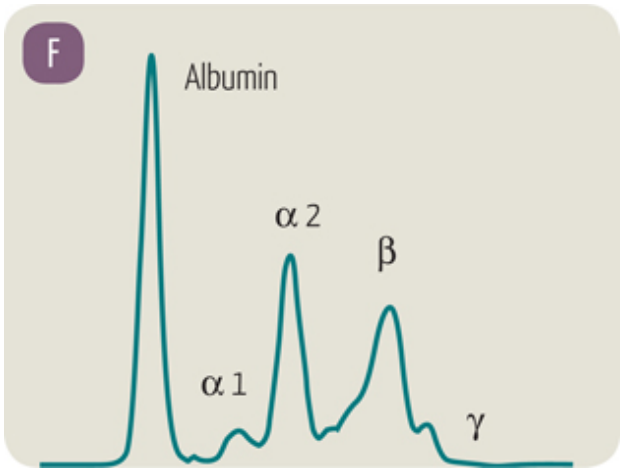
Proteinogram of a dog with multiple myeloma: biclonal gammopathy in the beta region.



Proteinogram of a dog with discospondylitis: decrease in albumin and increase in globulins.



Proteinogram of a dog with multiple myeloma: monoclonal gammopathy in the beta region.



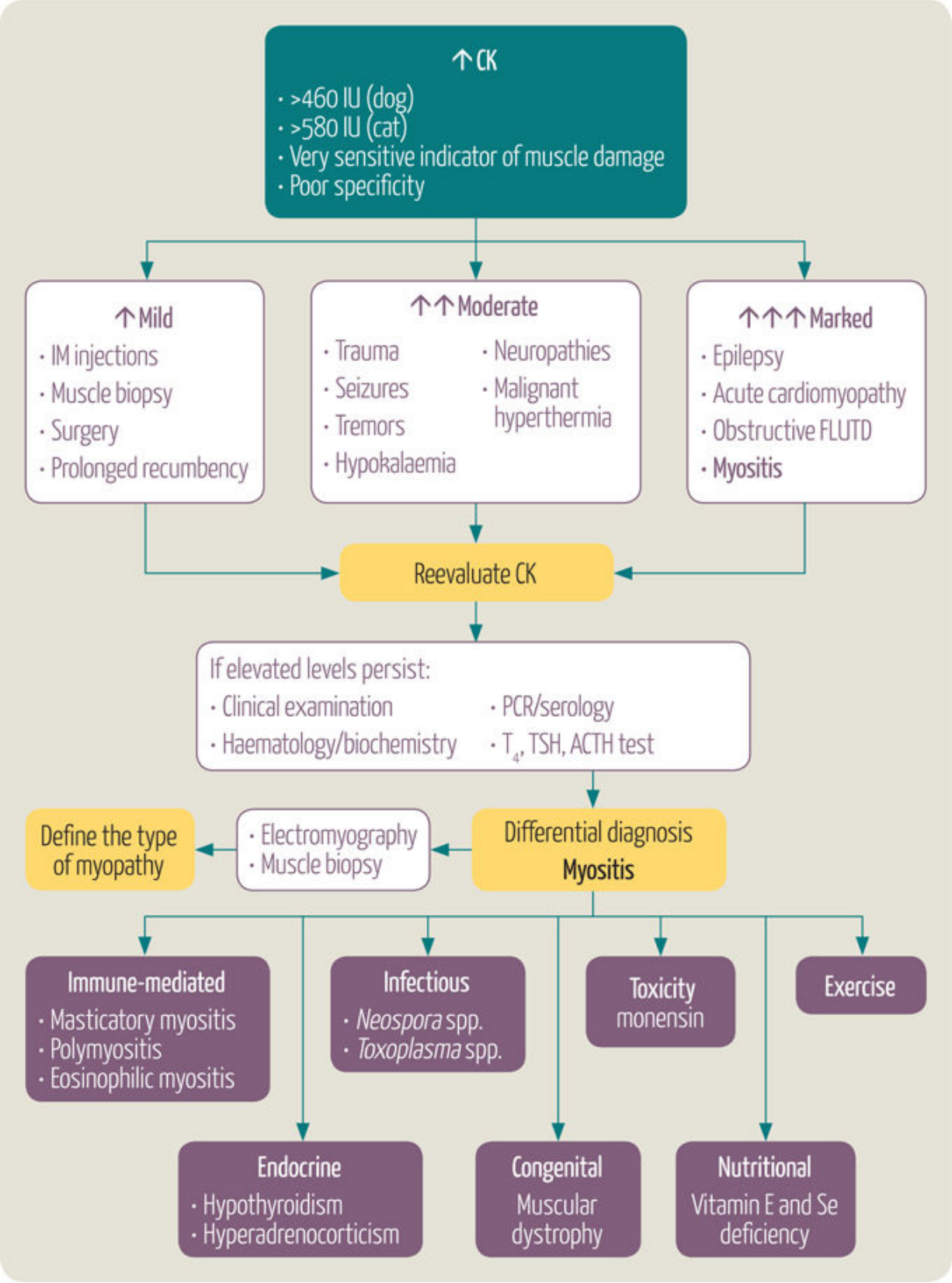
Proteinogram of the same dog with multiple myeloma after several months of treatment with melphalan: marked decrease in globulins and increase in albumin.

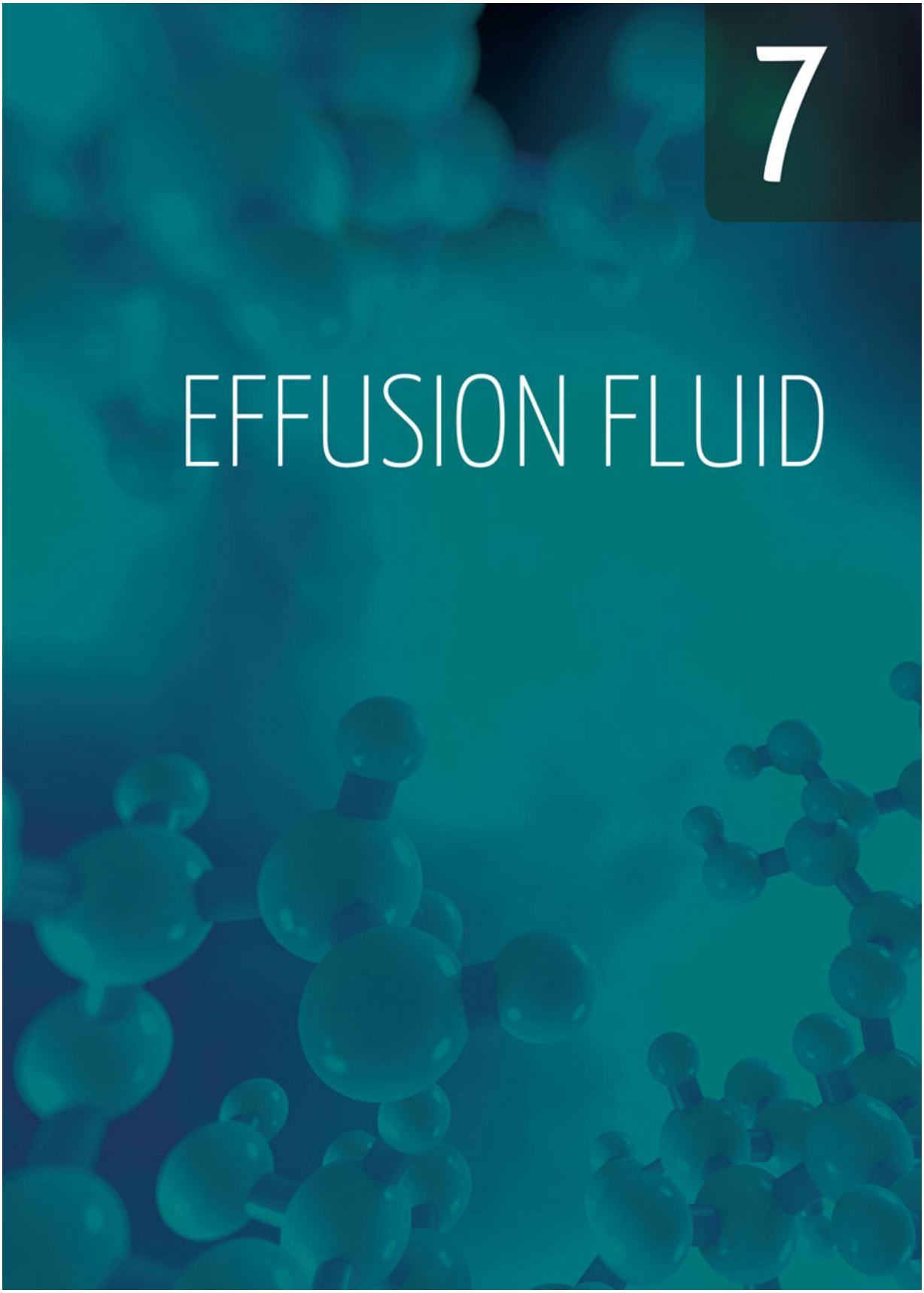
Summary of the main proteins detected by serum electrophoresis

Fraction (g/dl)	Proteins	Function	Increase	Decrease
Albumin • 5.4–7.1 (dog) • 5.4–7.8 (cat)	• Albumin	• Regulates oncotic pressure • Transporter	• Dehydration	• Malnutrition • Liver failure • Renal failure (> glomerular permeability) • Burns • Haemorrhage • Fever • Parasites
Alpha 1 globulins • 2.0–5.0 (dog) • 2.0–11.09 (cat)	• α_1-lipoprotein (HDL) • α_1-acid glycoprotein • T_4-binding globulin • α_1-antitrypsin and α_1-antichymotrypsin	• Cholesterol transport • Acute-phase inflammatory protein • Thyroid hormone transport • Both with inhibitory enzymatic character • Anti-inflammatory	• Gestation • Hepatoma • Acute inflammation	
Alpha 2 globulins • 3.0–11.09 (dog) • 4.0–9.0 (cat)	• α_2-prothrombin • Haptoglobins • α_2-macroglobulin • Ceruloplasmin	• Coagulation factor • Binding and transport of Hb • Inhibition of proteases: anti-inflammatory • Cu transporter	• Acute inflammation • Nephrotic syndrome • Diabetes mellitus • Hypothyroidism • Steroid therapy	
Beta globulins • Beta 1 • 7.0–13.0 (dog) • 3.0–9.0 (cat) • Beta 2 • 6.0–14.0 (dog) • 6.0–10.0 (cat)	• Transferrin • Lipoproteins • Complement fractions • Plasminogen and plasmin	• Fe transporter • β-lipoprotein (LDL) transport • Proinflammatory: chemotactic • Role in fibrinolysis	• Acute inflammation • Dermatopathies • Acute and chronic hepatitis • Hypothyroidism • Nephrotic syndrome	
Gamma globulins • Gamma 1 • 5.0–13.0 (dog) • 3.0–25.0 (cat) • Gamma 2 • 4.0–9.0 (dog) • 14.0–19.0 (cat)	• Igs A and M • Ig G • C-reactive protein	• Binding to Ags: humoral immune response • Binding to Ags: humoral immune response • Acute-phase inflammatory protein	• Infectious diseases • Chronic hepatitis • Abscesses • Autoimmune diseases • Tumours	• Neonates • Immunodeficiencies • Aglobulinaemias

Concentrations are for guidance only. It is important to note the reference range of the laboratory in question.

Creatine kinase

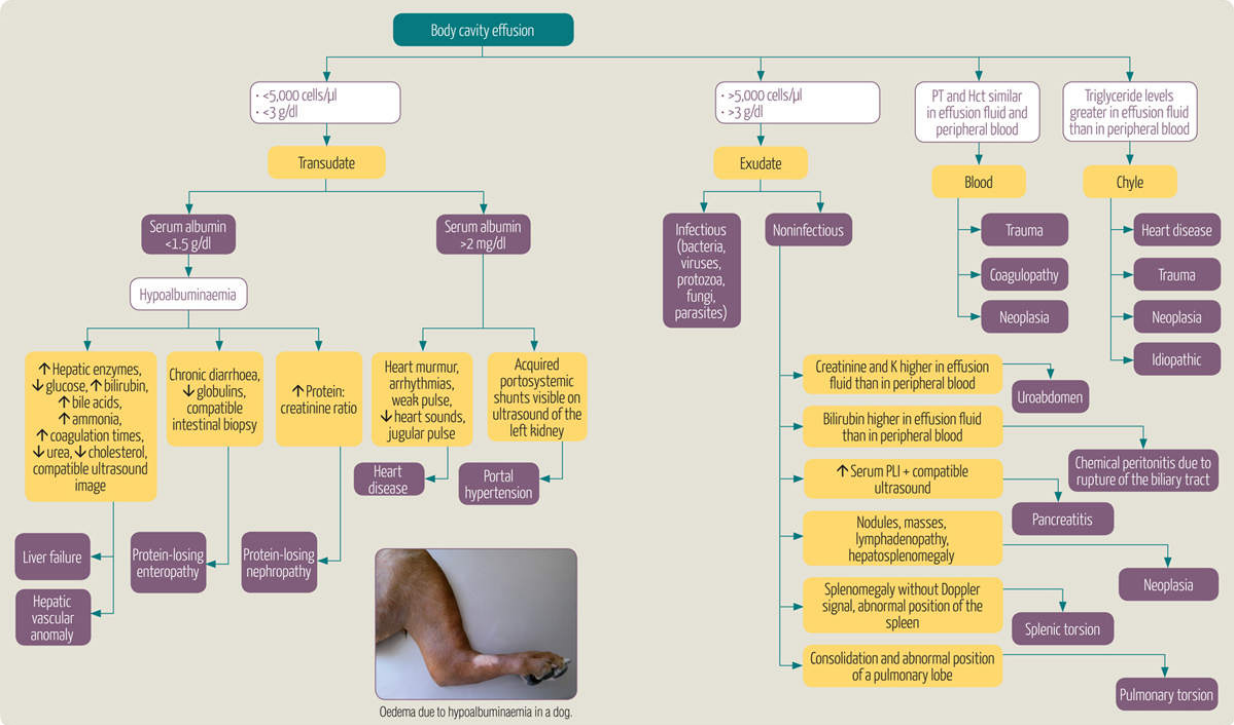

↑CK
• >460 IU (dog)
• >580 IU (cat)
• Very sensitive indicator of muscle damage
• Poor specificity
↑Mild
• IM injections
• Muscle biopsy
• Surgery
• Prolonged recumbency
↑↑Moderate
• Trauma
• Seizures
• Tremors
• Hypokalaemia
• Neuropathies
• Malignant hyperthermia
↑↑↑Marked
• Epilepsy
• Acute cardiomyopathy
• Obstructive FLUTD
• Myositis
Reevaluate CK
If elevated levels persist:
• Clinical examination
• Haematology/biochemistry
• PCR/serology
• T_4, TSH, ACTH test
Differential diagnosis
Myositis
• Electromyography
• Muscle biopsy
Define the type of myopathy
Immune-mediated
• Masticatory myositis
• Polymyositis
• Eosinophilic myositis
Infectious
• *Neospora* spp.
• *Toxoplasma* spp.
Toxicity
monensin
Exercise
Endocrine
• Hypothyroidism
• Hyperadrenocorticism
Congenital
Muscular dystrophy
Nutritional
Vitamin E and Se deficiency



7

EFFUSION FLUID

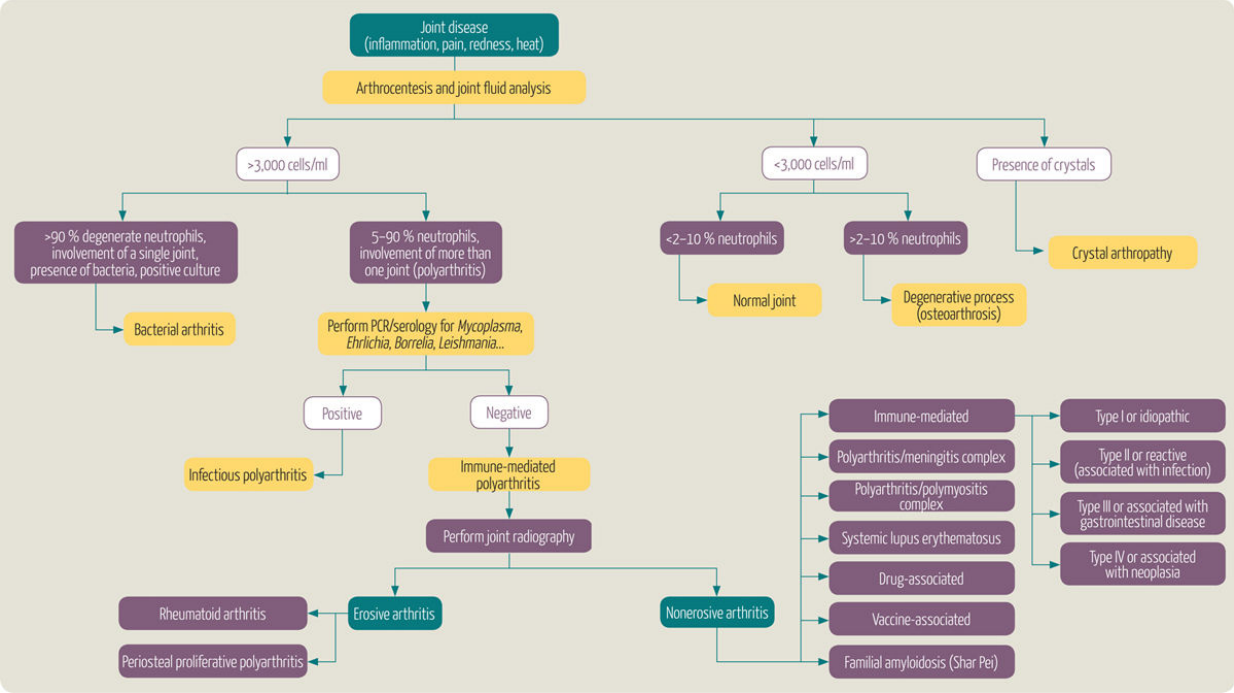
Body fluid analysis



Oedema due to hypoalbuminaemia in a dog.

Joint disease

Joint fluid analysis


Joint disease (inflammation, pain, redness, heat)
Arthrocentesis and joint fluid analysis
>3,000 cells/ml
<3,000 cells/ml
Presence of crystals
>90 % degenerate neutrophils, involvement of a single joint, presence of bacteria, positive culture
5–90 % neutrophils, involvement of more than one joint (polyarthritis)
<2–10 % neutrophils
>2–10 % neutrophils
Crystal arthropathy
Bacterial arthritis
Normal joint
Degenerative process (osteoarthrosis)
Perform PCR/serology for Mycoplasma, Ehrlichia, Borrelia, Leishmania...
Positive
Negative
Infectious polyarthritis
Immune-mediated polyarthritis
Perform joint radiography
Rheumatoid arthritis
Erosive arthritis
Periosteal proliferative polyarthritis
Nonerosive arthritis
Immune-mediated
Polyarthritis/meningitis complex
Polyarthritis/polymyositis complex
Systemic lupus erythematosus
Drug-associated
Vaccine-associated
Familial amyloidosis (Shar Pei)
Type I or idiopathic
Type II or reactive (associated with infection)
Type III or associated with gastrointestinal disease
Type IV or associated with neoplasia

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