To my wife Sandi for 30 years of marriage.
When I was asked by Elsevier to create a second edition of Small Animal Differential Diagnosis: A Book of Lists, I envisioned an easy process of updating the lists of the first edition and adding some new material. I couldn’t have been more wrong. The goal was to duplicate the format of the first edition: a quick, concise, and practical reference to differential diagnosis, etiology, laboratory values, and classification of clinical signs and medical disorders in dogs and cats. As I reviewed each list I was surprised to see how many needed to be revised. In fact, nearly all of the lists required additions, subtractions, or sometimes complete reorganization. A project like this one is a great illustration of how much the veterinary medical literature expands in a 6-year period. Once again, this text will be a pocket-sized, rapid reference or an electronic application. Its greatest value will be to aid the clinician in making reliable on-the-scene decisions and to allow veterinary students and interns to more fully participate in clinical rounds with their instructors. It will also be used by the more seasoned practitioner to come up with those more esoteric differentials that we sometimes forget to include in our list of potential diagnoses.

The lists in this book have been compiled from comprehensive veterinary references published by Elsevier, especially:

- Ettinger and Feldman: Textbook of Veterinary Internal Medicine, seventh edition and
- Nelson and Couto: Small Animal Internal Medicine, fourth edition.

Also consulted for information were:

- Henry and Higginbotham: Cancer Management in Small Animal Practice
- Beaver: Canine Behavior: Insights and Answers, second edition
- Bonagura: Kirk’s Current Veterinary Therapy XIV
- Willard and Tvedten: Small Animal Clinical Diagnosis by Laboratory Methods, fifth edition
- Fossum: Small Animal Surgery, fourth edition

The reader is encouraged to consult these and other texts for more detailed information.
About the Book

As with the first edition, the lists are divided into three parts and serve as a concise guide to the differential diagnosis, etiology, laboratory abnormalities, and classification of clinical signs and medical disorders in dogs and cats. Part One contains lists based on clinical signs that may be identified by the clinician. Part Two approaches differential diagnosis from a systems perspective. Fifteen body systems are represented. Part Three once again is a quick reference of laboratory tests and gives typical normal ranges and differential diagnoses based on test results. Overall the book comprises 400 lists, 60 of which are new to this edition. In all lists an attempt has been made to prioritize them from least common to most common.

Acknowledgments

I wish to thank my fellow veterinarians at Brevard Animal Hospital: Dr. Christine Weaver, Dr. Clyde Brooks, Dr. Chad Lothamer, and Dr. Alana Terrell. They were a sounding board for ideas and helped me discover deficiencies in the first edition. In addition, our discussions about cases helped me determine new lists that needed to be generated.
Clinical Signs Approach to Differential Diagnosis
Abdominal Distension

Organomegaly

Hepatomegaly (infiltrative, inflammatory, lipidosis, neoplasia)
Splenomegaly (infiltrative, inflammatory, neoplasia, hematoma)
Renomegaly (neoplasia, infiltrative)
Miscellaneous neoplasia (GI tract, ovaries, uterus, pancreas, prostate, adrenal glands)
Generalized neoplasia (carcinomatosis, lymphosarcoma)
Granuloma (pythiosis, aspergillosis)
Pregnancy

Fluid

Contained in Organs
Congestion resulting from splenic torsion or volvulus, or hepatic congestion from right-sided heart failure
Cysts (paraprostatic, perinephric, hepatic)
Hydronephrosis
Distended urinary bladder
Obstruction of intestines or stomach
Ileus
Pyometra

Free Fluid in Abdomen
Transudate (portal hypertension, right-sided heart failure, hypoproteinemia secondary to protein-losing enteropathy, protein-losing nephropathy, or hepatic failure)
Modified transudate (neoplasia, postsinusoidal portal hypertension, right-sided heart failure, heartworm caval syndrome, liver disease)
Exudate (pancreatitis, feline infectious peritonitis, urine, bile, neoplasia, bowel perforation, foreign body)
Chyle (trauma, neoplasia, infection, right-sided heart failure)
Blood (coagulopathy, trauma, neoplasia)

Gas

Contained in Organs
Gastric dilatation/volvulus
Intestines secondary to obstruction
Parenchymal organs infected with gas-producing bacteria

Free in Abdomen
Iatrogenic (after laparoscopy, laparotomy)
Rupture of gastrointestinal tract or uterus
**Fat**
- Obesity/lipoma

**Weakened Abdominal Musculature**
- Hyperadrenocorticism

**Feces**
- Obstipation/megacolon

**Abdominal Effusions and Ascites**

**Transudate (<1000 Cells, <2.5 Total Solids, <1.017 Specific Gravity)**
- Portal Hypertension
  - Presinusoidal or sinusoidal liver disease
  - Right-sided heart failure
- Hypoalbuminemia (see Albumin p. 286)
  - Liver failure
  - Protein-losing enteropathy
- Glomerulopathy

**Modified Transudate (>1000 but <10000 Cells, 2.5-5.0 Total Solids, <1.025 Specific Gravity)**
- Postsinusoidal Portal Hypertension
- Right-Sided Heart Failure
  - Heartworm caval syndrome
  - Liver disease
- Neoplasia
- Increased Hydrostatic Pressure
- Vasculitis

**Exudate (>5000 Cells, >3.0 Total Solids, >1.025 Specific Gravity)**
- Nonseptic
  - Pancreatitis
  - Feline infectious peritonitis (FIP)
  - Urine
  - Bile
  - Neoplasia
- Septic
  - Bowel perforation
  - Foreign body
Chyle
- Trauma
- Neoplasia
- Infection
- Right-sided heart failure

Blood
- Coagulopathy
- Trauma
- Neoplasia (hemangiosarcoma)
- Iatrogenic (postsurgical)

Abdominal Pain, Acute

Gastrointestinal System
- Gastrointestinal ulceration
- Foreign body
- Gastric dilation-volvulus
- Gastroenteritis
- Obstipation
- Colitis
- Neoplasia
- Adhesions
- Intestinal ischemia
- Intestinal spasm

Urogenital System
- Lower urinary tract infection
- Lower urinary tract obstruction
- Nonseptic cystitis (idiopathic cystitis—cats)
- Prostatitis/prostatic neoplasia
- Uroliths/renoliths/ureterolith
- Pyelonephritis
- Neoplasm
- Metritis
- Pyometra/uterine rupture
- Uterine torsion (rare)
- Testicular torsion
- Mastitis
- Dystocia
- Ovarian cyst

Pancreatitis

Spleen
- Rupture
- Neoplasm
Infection
Torsion

**Peritoneum**
- Peritonitis
  - Septic
  - Nonseptic (e.g., uroabdomen)
- Adhesions
  - Mesenteric neoplasia, volvulus, inflammation

**Hepatobiliary**
- Hepatitis
- Hepatic abscess
- Hepatic trauma, rupture
- Hepatobiliary neoplasia
- Cholelithiasis or cholecystitis
- Cholangiohepatitis

**Musculoskeletal**
- Fractures
- Intervertebral disk disease
- Diskospondylitis
- Abscess
- Strangulated hernia

**Miscellaneous**
- Adrenalitis (associated with hypoadrenocorticism)
- Heavy metal intoxication
- Vasculopathy
  - Rocky Mountain spotted fever
  - Infarct
- Autonomic (abdominal) epilepsy
- Iatrogenic
  - Misoprostol
  - Bethanechol
  - Postoperative pain

**Aggressive Behavior**

**Cats**

**Pathophysiologic Causes of Feline Aggression**
- Rabies
- Hyperthyroidism
- Seizures (epilepsy, central nervous system inflammation)
- Paradoxical effects of therapeutic drugs
  - (e.g., benzodiazepines)
- Toxins (side effects)
Cognitive dysfunction
Brain neoplasia

**Species-Typical Patterns of Feline Aggression**
- Play
- Fear
- Petting induced
- Interspecies aggression
- Redirected
- Status/assertiveness
- Pain induced/irritable
- Maternal
- Territorial
- Predatory
- Idiopathic

**Dogs**

**Pathophysiologic Causes of Canine Aggression**
- Rabies
- Seizure activity
- Intracranial neoplasia
- Cerebral hypoxia
- Neuroendocrine disturbances

**Species-Typical Patterns of Canine Aggression**
- Fear related
- Conflict related
- Resource guarding
- Territorial/protective
- Intraspecific (intradog)
- Redirected
- Predatory
- Pain/medical/irritable
- Play
- Maternal/hormonal
- Idiopathic

**Alopecia**

**Inflammatory Alopecia**

**Traumatic**
- Allergy (flea, atopy, food)
- Parasitic dermatitis (flea, scabies, *Cheyletiella* spp., lice, chiggers, etc.)

**Infectious**
- Pyoderma
- Demodicosis
- Dermatophytosis
Viral
Leishmaniasis
*Malassezia* spp.

**Immune Mediated**
- Sebaceous adenitis
- Superficial pemphigus
- Alopecia areata
- Erythema multiforme
- Systemic lupus erythematosus (SLE), discoid lupus erythematosus (DLE)
- Epitheliotrophic lymphoma
- Vasculitis

**Atrophic**
- Dermatomyositis
- Cutaneous vasculitis
- Postvaccinal alopecia
- Lymphocytic mural folliculitis
- Paraneoplastic exfoliative dermatitis
- Pseudopelade

**Noninflammatory Alopecia**

**Hormonal**
- Hyperadrenocorticism
- Iatrogenic Cushing's syndrome
- Hypothyroidism
- Sex hormone imbalance
- Alopecia X
- Hyperthyroidism (cat)

**Canine and Feline Pinnal Alopecia**

**Canine Pattern Baldness**

**Canine Follicular Dysplasia**
- Tricorrhexis nodosa
- Pili torti
- Color mutant alopecia
- Black hair follicular dysplasia

**Feline Congenital/Hereditary**
- Alopecia universalis (Sphynx)
- Congenital hypotrichosis
- Hair shaft dysplasia (Abyssinian)
- Follicular dysplasia (Cornish rex)
- Pili torti

**Other**
- Anagen effluvium
- Telogen defluxion
Paraneoplastic alopecia
Cyclic follicular dysplasia (seasonal flank alopecia)
Postclipping alopecia
Cicatricial alopecia
Feline preauricular alopecia
Feline acquired symmetric alopecia
Psychogenic alopecia

## Anaphylaxis

### Venoms

- Insects of Hymenoptera order (bees, hornets, ants)
- Spiders (brown recluse, black widow)
- Snakes (rattlesnakes, copperheads, water moccasins)
- Lizards (Gila monster, Mexican beaded lizard)

### Drugs

- Antibiotics (penicillins, sulfonamides, lincomycin, cephalosporins, aminoglycosides, tetracyclines, chloramphenicol, polymyxin B, doxorubicin)
- Vaccines
- Allergen extracts
- Blood products
- Parasiticides (dichlorophen, levamisole, piperazine, dichlorvos, diethylcarbamazine, thiacetarsamide)
- Anesthetics/sedatives (acepromazine, ketamine, barbiturates, lidocaine, bupivacaine, narcotics, diazepam)
- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Hormones (insulin, corticotropic, vasopressin, parathyroid hormone, glucocorticoids)
- Aminophylline
- Asparaginase
- Iodinated contrast media
- Neostigmine
- Amphotericin B
- Enzymes (trypsin, chymotrypsin)
- Vitamins (vitamin K, thiamine, folic acid)
- Dextrans and gelatins
- Calcium disodium edetate

### Foods

- Milk, egg white, shellfish, legumes, citrus fruits, chocolate, grains

### Physical Factors

- Cold, heat, exercise
Anuria and Oliguria

Prerenal Azotemia

Dehydration/hypovolemia

Acute Renal Failure

One third of cases are anuric, one third are oliguric, and one third are nonoliguric; more likely to be oliguric/anuric with severe renal toxicosis

Toxic: exogenous (drugs, biologic or environmental toxins), endogenous (calcium, pigments)

Infectious: pyelonephritis, leptospirosis, infectious canine hepatitis, borreliosis, sepsis

Ischemia: progression of prerenal azotemia, NSAIDs, vascular disease (avulsion, thrombosis, stenosis), shock, decreased cardiac output, deep anesthesia, extensive surgery, hypothermia, hyperthermia, hyperviscosity (polycythemia vera, multiple myeloma, extensive cutaneous burns, transfusion reaction, disseminated intravascular coagulation (DIC)

Immune mediated: acute glomerulonephritis, systemic lupus erythematosus (SLE), transplant rejection, vasculitis

Neoplasia: lymphoma

Systemic disease with renal manifestations

• Infections (feline infectious peritonitis, borreliosis, babesiosis, leishmaniasis, bacterial endocarditis)
• Pancreatitis
• Sepsis
• Multiple organ failure
• Heart failure
• SLE
• Hepatorenal disease
• Malignant hypertension

Postrenal Azotemia

Obstruction (may appear similar to anuria/oliguria)

Anxiety and Phobias

Fears and Phobias

Fear: apprehension associated with the presence of an object, individual, or object; may be normal or abnormal, depending on context

Phobia: quickly developed, immediate, profound abnormal response to a stimulus leading to catatonia or panic
People
Babies, children, elderly
People in uniform
People who appear different than family members
• Color, height, facial hair
Disabled people
Men or women, depending on circumstance

Animals
Same species
Other species

Noise
Especially gunshots, fireworks, thunder

Places

Anxiety

Separation Anxiety

Initiators
Change in owner’s routine
Owner returning to school or work
Move to new home
Visit to new environment
After stay in kennel
New baby, new pet
Medical, cognitive

Common Features of Separation Anxiety
Hyperattached to owner
Signs of anxiety as owner leaves
Problems manifest when owner absent or when pet unable to gain access to owner
Problem behavior begins shortly after owner leaves
May even occur during short absences
Pet shows exuberant greeting behavior

Generalized Anxiety
Poorly socialized, nervous pet

Ascites
See Abdominal Effusions and Ascites.

Ataxia and Incoordination

Forebrain Disease
Typically, mild ataxia and other neurologic signs predominate.
Generalized disease: generalized ataxia
Unilateral disease: contralateral conscious proprioceptive deficits, mild gait disturbance
Postictal paraparesis: transient in nature
Paraparesis may be a side effect of anticonvulsant therapy (especially potassium bromide).

**Brain Stem**

Hemiparesis or tetraparesis; lesions severe enough to cause paralysis usually result in respiratory arrest.
Vestibular nuclei may be affected, causing vestibular ataxia, head tilt, and nystagmus; distinguish central vestibular disease from peripheral vestibular disease by presence of ipsilateral conscious proprioceptive deficits.

**Peripheral Vestibular Disease**

Generalized ataxia accompanied by head tilt, rotary or horizontal nystagmus, positional strabismus, and oculovestibular eye movements
Conscious proprioceptive deficits absent

**Cerebellum**

Lesions cause dysmetria, usually hypermetria. Unilateral lesions cause ipsilateral signs.

**Cervical Spinal Cord**

May cause forelimb monoparesis (lesions affecting spinal segments C6-T2), hemiparesis, tetraparesis; may progress to paralysis

**Thoracic (T3-L3) Spinal Cord**

Mild to marked rear limb ataxia, paraparesis, paraplegia, monoparesis, or monoplegia
Rear limb reflexes exaggerated
Reduced to absent panniculus reflex caudal to lesion

**Lumbosacral (L4-S2) Spinal Cord**

Mild to marked rear limb ataxia, paraparesis, paraplegia, monoplegia
Reduced to absent rear limb reflexes
May see bladder and anal sphincter hypotonia

**Peripheral Nerve**

Mild to marked ataxia, paresis, paralysis of one or more limbs
Degenerative, inflammatory, toxic, traumatic neuropathies
Hyporeflexia usually seen
Paresis or paralysis of muscle or muscles innervated by affected nerve
Blindness

Corneal Lesions

- Edema (trauma, glaucoma, immune-mediated keratitis such as keratouveitis caused by canine adenovirus-1, endothelial dystrophy, neurotropic keratitis)
- Keratoconjunctivitis sicca
- Exposure keratitis
- Superficial keratitis (pannus)
- Corneal melanosis (entropion, ectropion, lagophthalmos, facial nerve paralysis)
- Cellular infiltrate (bacterial, viral, fungal)
- Dystrophies (lipid, genetic)
- Fibrosis (scar)

Aqueous Humor Lesions

- Fibrin (anterior uveitis: many causes)
- Hypopyon (immune-mediated, neoplastic [lymphosarcoma], infectious [blastomycosis, cryptococcus, histoplasmosis, coccidioidomycosis, toxoplasmosis, FIP, protothecosis, brucellosis, septicemia])
- Hyphema (trauma, blood-clotting deficiencies, ehrlichiosis, rickettsia, systemic hypertension, retinal detachment neoplasia)
- Lipid (hyperlipidemia with concurrent anterior uveitis to disrupt the blood-aqueous barrier)

Lens Lesions

- Cataracts (genetic, metabolic/diabetic, nutritional, traumatic, toxic, retinal degeneration, hypocalcemia, electric shock, chronic uveitis, lens luxation)

Vitreous Humor Lesions

- Hemorrhage (trauma, systemic hypertension, clotting deficiency, neoplasia, retinal detachment)
- Hyalitis (numerous infectious diseases such as feline infectious peritonitis, penetrating injury causing cellular infiltrate)

Retinal Lesions

- Glaucoma
- Sudden acquired retinal degeneration (SARD)
- Progressive retinal atrophy
- Central progressive retinal atrophy
- Toxicity (fluoroquinolone administration in cats)
- Systemic hypertension
- Retinal detachment
• Exudative/transudative (systemic hypertension, mycoses, rickettsial, toxoplasmosis, viral, bacterial, fungal)
• Neoplasia
• Retinal dysplasia
• Hereditary/congenital (e.g., Collie eye anomaly)

**Failure to Transmit Visual Message**

- Viral infections (canine distemper, feline infectious peritonitis [FIP])
- Systemic and ocular mycoses (blastomycosis, cryptococcosis, histoplasmosis, coccidioidomycosis)
- Neoplasia
- Traumatic avulsion of optic nerve (traumatic proptosis)
- Granulomatous meningoencephalitis
- Hydrocephalus
- Optic nerve hypoplasia
- Coloboma
- Immune-mediated optic neuritis

**Failure to Interpret Visual Message**

- Canine distemper virus
- Feline infectious peritonitis (FIP)
- Granulomatous meningoencephalitis
- Systemic mycoses
- Trauma
- Heat stroke
- Hypoxia
- Hydrocephalus
- Hepatoencephalopathy
- Neoplasia
- Storage diseases
- Postictal
- Meningitis

**Bradycardia, Sinus**

- Normal variation (fit animal)
- Hypothyroidism
- Hypothermia
- Drugs (tranquilizers, anesthetics, β-blockers, calcium entry blockers, digitalis)
- Increased intracranial pressure
- Brain stem lesion
- Severe metabolic disease (e.g., uremia)
- Ocular pressure
- Carotid sinus pressure
High vagal tone
Cardiac arrest (before and after)
Sinus node disease

### Cachexia and Muscle Wasting

#### Cachexia

Certain chronic disease processes stimulate the release of cytokines that suppress appetite and stimulate hypercatabolism.
- Cardiac disease
- End-stage renal disease
- Chronic infection
- Chronic fever
- Chronic inflammation
- Neoplasia

#### Muscle Wasting

**Endocrine Disease**
- Hyperadrenocorticism
- Hyperthyroidism
- Hyperparathyroidism

**Starvation**
- Underfeeding
- Poor-quality feed
- Competition for food
- Dental disease

**Impaired Ability to Use or Retain Nutrients**
- Maldigestion
- Malabsorption
- Parasitism
- Histoplasmosis
- Exocrine pancreatic insufficiency
- Diabetes mellitus
- Protein-losing nephropathy or gastroenteropathy

**Inflammatory Myopathies**
- Masticatory myositis
- Dermatomyositis
- Canine idiopathic polymyositis
- Feline idiopathic polymyositis

**Protozoal Myositis**
- Toxoplasma gondii
- Neospora caninum

**Inherited Myopathies**
- Muscular dystrophy
- Hereditary Labrador retriever myopathy
Neurologic Disorders
Spinal and peripheral neuropathies
Disuse atrophy

Compulsive Behavior Disorders

Compulsive Disorders in Dogs

Locomotor
- Spinning or tail chasing
- Stereotypic pacing/circling/jumping
- Fixation; staring/barking/freezing/scratching
- Chasing lights, reflections, shadows
- Barking; intense/rhythmic/difficult to interrupt
- Head bob/tremor/head shaking
- Attacking food bowl, attacking inanimate objects

Apparent Hallucinatory
- Air biting or fly snapping
- Staring, freezing, startled
- Star/sky gazing

Self-Injurious or Self-Directed
- Tail attacking, mutilation, growl/attack legs or rear
- Face rubbing/scratching
- Acral lick dermatitis, licking/chewing/barbering
- Nail biting
- Flank sucking
- Checking rear

Oral
- Sucking/licking
- Pica, rock chewing
- Polydipsia/polyphagia
- Licking of objects/owners

Compulsive Disorders in Cats

Locomotor
- Skin ripple/agitation/running, feline hyperesthesia
- Circling
- Freezing
- Excessive/intense chasing of imaginary objects
- Excessive vocalization/howling

Apparent Hallucinatory
- Staring at shadows/walls
- Startle
- Avoiding imaginary objects
Self-Injurious or Self-Directed
Tail attacking, mutilation, growl/attack legs or rear
Face scratching/rubbing
Chewing/licking/barbering/overgrooming
Nail biting
Hyperesthesia

Oral
Wool sucking
Pica
Polydipsia/polyphagia
Licking of objects/owners

Constipation

Dietary Causes
Excessive fiber in dehydrated patient
Ingestion of hair, bones, indigestible materials

Colonic Obstruction
Deviation of rectal canal: perineal hernia
Intraluminal or intramural disorders
• Tumor
• Granuloma
• Cicatrix
• Rectal foreign body
• Congenital stricture
Pseudocoprostasis
Perineal hernia
Extraluminal disorders
• Tumor
• Granuloma
• Abscess
• Healed pelvic fracture
• Prostatomegaly
• Prostatic or paraprostatic cyst
• Sublumbar lymphadenopathy

Behavioral or Environmental Causes
Change in routine
Soiled or absent litter box
Refusal to defecate in house
Inactivity
Drugs
- Opiates
- Anticholinergics
- Sucralfate
- Barium

Refusal to Defecate
- Pain in rectal or perineal area (perianal fistulas)
- Inability to posture to defecate
- Orthopedic or neurologic problem

Colonic Weakness

Systemic Disease
- Hypercalcemia
- Hypokalemia
- Hypothyroidism
- Chagas disease

Localized Neuromuscular Disease
- Spinal cord disease
- Pelvic nerve damage
- Dysautonomia
- Chronic dilatation of colon/irreversible stretching of colonic musculature

Miscellaneous Causes
- Severe dehydration
- Idiopathic megacolon (cats)

Coughing

Disorders of Upper Airway

Inflammatory
- Pharyngitis
- Tonsillitis
- Tracheobronchitis
- Chronic bronchitis
- Allergic bronchitis
- Bronchiectasis
- Collapsed trachea
- *Oslerus osleri* infection

Neoplastic
- Mediastinal
- Laryngeal
- Tracheal
Allergic
Bronchial asthma

Other
Bronchial compression: left atrial enlargement, hilar lymphadenopathy
Foreign body
Inhalation
Tracheal stenosis

Disorders of Lower Respiratory Tract

Inflammatory

Pneumonia
Bacterial
Viral: canine distemper virus
Fungal: blastomycosis, histoplasmosis, coccidioidomycosis
Protozoal: toxoplasmosis, pneumocystis pneumonia

Granuloma, Abscess

Chronic Pulmonary Fibrosis

Parasitic Disease
Heartworm disease (*Dirofilaria immitis*)
Lungworm disease (*Aelurostrongylus abstrusus*—cat; *Paragonimus kellicotti*—dog, cat; *Capillaria aerophilia*—dog, cat; *Filaroides hirthi*—dog; *Crenosoma vulpis*—dog; *Angiostrongylus vasorum*—dog)

Neoplasia
Primary or metastatic
Lymphoma

Cardiovascular
Left-sided heart failure: pulmonary edema
Pulmonary thromboembolism

Noncardiogenic Pulmonary Edema

Allergic
Eosinophilic pneumonitis
Eosinophilic pulmonary granulomatosis
Pulmonary infiltrate with eosinophils (PIE)

Other
Lung lobe torsion
Systemic bleeding disorder
Pleural effusion
Neoplasia of chest wall
Cyanosis

Central Cyanosis

Cardiac

*Intracardiac*
- Tetralogy of Fallot
- Atrial or ventricular septal defect with pulmonic stenosis, tricuspid valve dysplasia, or pulmonary hypertension
- Transposition complexes (double outlet right ventricle, other)

*Extracardiac*
- Pulmonary arteriovenous fistulas
- Patent ductus arteriosus (reversed)

Pulmonary

*Hypoventilation*
- Pleural effusion
- Pneumothorax
- Respiratory muscle failure (fatigue, neuromuscular disease)
- Anesthetic overdose
- Primary neurologic disease

*Obstruction*
- Laryngeal paralysis
- Foreign body in airway
- Mass lesion of large airway (neoplasia, parasitic, inflammatory)
- Low oxygen concentration of inspired air (high altitude, anesthetic complications)

*Ventilation-Perfusion Mismatch*
- Pulmonary thromboembolism
- Pulmonary infiltrate (edema, inflammation/infection, neoplasia, acute respiratory distress syndrome, chronic obstructive pulmonary disease, fibrosis, pulmonary contusions/hemorrhage)

*Methemoglobinemia*

Peripheral Cyanosis

Central cyanosis (heart failure)
- Decreased arterial supply
- Peripheral vasoconstriction (hypothermia, shock)
- Arterial thromboembolism
Low cardiac output
Obstruction of venous drainage
  • Tourniquet or foreign object (e.g., rubber band)
  • Venous thrombosis
  • Right-sided heart failure

Deafness

Congenital Sensorineural Deafness

Inherited
  Many breeds of dogs
  • Dalmatians
  • Merle or dapple coat patterns in Collies, Shetland Sheepdogs, Great Danes, Dachshunds
  • Piebald pattern in Dalmatians, Bull Terriers, Great Pyrenees, Sealyham Terriers, Greyhounds, Bulldogs, and Beagles)
  • Many other dog breeds affected
White cats with blue irides and white coloration in some breeds of dogs

Congenital Acquired Sensorineural Deafness

In utero exposure to bacteria, ototoxic drugs, low oxygen tensions, or trauma

Acquired Late-Onset Conductive Deafness

Lack of transmission of sound through tympanic membrane and auditory ossicles
  Otitis externa/media
  Otic neoplasia
  Polyps
  Trauma-induced fluid accumulation in middle ear
  Atresia of tympanum or ossicles
  Fused ossicles
  Stenosis of ear canal leading to accumulation of fluid in middle ear

Acquired Late-Onset Sensorineural Deafness

Presbycusis (age-related hearing loss)
  Ototoxicity
  Chronic exposure to loud noise
  Hypothyroidism
  Trauma
  Bony neoplasia
Diarrhea, Acute

Diet
- Intolerance/allergy
- Rapid dietary change
- Bacterial food poisoning
- Dietary indiscretion
- Poor quality food

Parasites
- Helminths
- Protozoa (*Giardia, Tritrichomonas, Coccidia spp.*)

Infections
- Viral (parvovirus, coronavirus, feline leukemia virus [FeLV], feline immunodeﬁciency virus [FIV], canine distemper virus, rotavirus)
- Bacterial (*Salmonella* spp., *Clostridium perfringens, Escherichia coli, Campylobacter jejuni, Yersinia enterocolitica*, other bacteria)
- Rickettsial
  - Salmon poisoning

Other Causes
- Hemorrhagic gastroenteritis
- Intussusception
- Irritable bowel syndrome
- Toxins (chemicals, heavy metals, toxic plants)
- Drugs (antibiotics, cancer chemotherapeutic agents, anthelmintics, NSAIDs, digitalis, lactulose)
- Pancreatitis
- Hypoadrenocorticism
- Pyometra
- Peritonitis

Diarrhea, Chronic

Small Bowel Diarrhea
- Food intolerance or allergy
- Inflammatory bowel disease
- Gastrointestinal lymphoma
- Pancreatic exocrine insufficiency
- Chronic parasitism (*hookworm, Giardia*)
- Histoplasmosis
- Intestinal lymphangiectasia
- Partial obstruction
Pancreatic carcinoma
Gastrinoma
Liver disease (hepatocellular failure, cholestasis)
Endocrine disease (hypoadrenocorticism, hypothyroidism, hyperthyroidism)
Renal disease (uremia, nephrotic syndrome)
Chronic intussusception
Small intestinal bacterial overgrowth
Pythiosis

**Large Bowel Diarrhea**

Food intolerance or allergy
Parasitism (whipworm, *Giardia, Tritrichomonas*)
Clostridial colitis
Irritable bowel syndrome
Histoplasmosis
Pythiosis
Inflammatory bowel disease
- Lymphocytic-plasmacytic colitis
- Eosinophilic colitis
- Chronic ulcerative colitis
- Histiocytic ulcerative colitis (boxers)
Neoplasia (lymphoma, adenocarcinoma)
FeLV/FIV (infections secondary to these viruses)

**Dyschezia**

*See* Tenesmus and Dyschezia.

**Dysphagia**

**Oral Lesions**

Fractured bones or teeth
Periodontitis
Trauma (laceration, hematoma)
Feline resorptive lesions (caries)
Osteomyelitis
Retrobulbar abscess/inflammation
Temporal-masseter myositis
Stomatitis, glossitis, pharyngitis, gingivitis, tonsillitis, sialoadenitis
- Immune-mediated disease
- Feline herpesvirus, calicivirus, leukemia virus, immunodeficiency virus
- Lingual foreign bodies or granulomas
• Tooth root abscess
• Uremia
• Caustic chemicals
  Cleft palate
  Lingual frenulum disorder
  Cricopharyngeal achalasia/asynchrony

**Obstructive Lesion**

- Esophageal stricture/foreign object
- Esophagitis
- Electric cord burns
- Neoplasia (malignant or benign)
- Inflammatory (abscess, polyp, granuloma)
- Lymphadenopathy
- Eosinophilic granuloma
- Foreign object (oral, pharyngeal, laryngeal)
- Sialocele
- Nasopharyngeal polyp

**Neuromuscular Disease**

- Myasthenia gravis
- Acute polyradiculitis
- Masticatory myositis
- Tick paralysis
- Botulism
- Polymyositis
- Temporomandibular joint disease
- Rabies
- Trigeminal nerve paralysis or neuritis
- Neuropathies of cranial nerves V, VII, IX, X, or XII
- Brain stem disease
- Tetanus
- Hypothyroidism

**Dyspnea**

**Inspiratory Dyspnea**

**Nasal Obstruction**

Rhinitis
- Viral: feline herpesvirus, feline calicivirus, canine distemper virus
- Bacterial
- Fungal: aspergillosis, cryptococcosis, penicilliosis, rhinosporidiosis
Neoplasia: adenocarcinoma, squamous cell carcinoma, fibrosarcoma, osteosarcoma, chondrosarcoma, lymphoma, transmissible venereal tumor
Stenotic nares
Nasal foreign body
Thick nasal discharge of any etiology

**Pharyngeal or Laryngeal Disease**
- Elongated soft palate, everted laryngeal saccules
- Neoplasia/mass, abscess, granuloma, extraluminal mass
- Nasopharyngeal polyp
- Foreign body
- Laryngeal paralysis, acute/obstructive laryngitis, laryngeal collapse, laryngeal trauma

**Extrathoracic Trachea**
- Collapsing trachea
- Tracheal hypoplasia
- Tracheal trauma/stricture, foreign body, neoplasia

**Expiratory or Mixed Dyspnea**

**Intrathoracic Trachea and Bronchi**
- Collapsing trachea or main-stem bronchus
- Trauma, stricture, foreign body, neoplasia

**Small Airway Disease**
- Feline asthma
- Bronchitis
- Smoke inhalation
- Bronchopneumonia

**Pulmonary Parenchymal Disease**
- Pneumonia (viral, bacterial, fungal, protozoal, aspiration)
- Pulmonary edema
- Pulmonary thromboembolism
- Bronchial asthma
- Chronic obstructive lung disease

**Parasites/Severe Infestations/Heartworm, Lungworms**
- Pulmonary fibrosis
- Neoplasia

**Pleural Space Disease**
- Pleural effusion
- Pneumothorax
- Pleural space masses
- Diaphragmatic hernia

**Noncardiopulmonary Disease**
- Severe anemia
- Hypovolemia
Acidosis
Hyperthermia
Neurologic disease

Dysuria

See Stranguria, Dysuria, and Pollakiuria.

Ecchymoses

See Petechiae and Ecchymoses.

Edema

**Increased Hydrostatic Pressure**

*Impaired Venous Return*
- Congestive heart failure
- Constrictive pericarditis
- Ascites (cirrhosis)
- Budd-Chiari syndrome
- Venous obstruction or compression (thrombosis, external pressure, extremity inactivity)
- Iatrogenic overhydration
- Heartworm disease

*Small-Caliber Arteriolar Dilatation*
- Heat
- Neurohumoral dysregulation

**Reduced Plasma Osmotic Pressure**

*Hypoproteinemia*
- Cirrhosis (ascites)
- Malnutrition
- Protein-losing enteropathy
- Protein-losing glomerulonephropathy (nephrotic syndrome)
- Lymphangiectasia

**Lymphatic Obstruction**
- Various inflammatory causes
- Neoplasia
- Postsurgical
- After radiation therapy

**Sodium Retention**
- Excessive dietary intake with renal disease
- Renal hypoperfusion
- Increased renin-angiotension-aldosterone secretion
Inflammation

Acute and chronic
Angiogenesis

Increased Microvascular Permeability

Sepsis
Acute respiratory distress syndrome
Pancreatitis
Infection (fungal, bacterial, viral)

Mixed Mechanisms

Noncardiogenic pulmonary edema (head trauma, seizures, electrocution, upper airway obstruction)
Anaphylaxis
Organ torsion

Epistaxis

Systemic Causes

Thrombocytopenia
- Decreased production of thrombocytes (infectious, myelophthisis secondary to neoplasia, drugs, immune mediated phenomena)
- Increased destruction (immune mediated, microangiopathy)
- Increased consumption (disseminated intravascular coagulation, vasculitis, hemorrhage)
Thrombocytopathia
- Primary (von Willebrand disease)
- Secondary (uremia, ehrlichiosis, multiple myeloma, drugs such as NSAIDs)
Coagulation factor defects (e.g., hemophilia A and B)
Acquired coagulopathies (anticoagulant rodenticides, hepatic failure)
Increased capillary fragility (hypertension, hyperviscosity syndromes, hyperlipidemia, thromboembolic disease)
Polycythemia
Systemic hypertension

Local Causes

Neoplasia (nasal adenocarcinoma, lymphoma, benign polyps)
Bacterial infection (usually secondary; rarely, Bordetella, Pasteurella, or Mycoplasma can be primary cause of epistaxis)
Fungal rhinitis (Aspergillus, Cryptococcus spp.)
PART ONE  Clinical Signs Approach to Differential Diagnosis

Dental disease with oronasal fistulation
Nasal parasites: *Pneumonyssus caninum* (nasal mite), *Eucoleus boehmi* (formerly *Capillaria* spp.), *Cuterebra* spp.
Eosinophilic and lymphoplasmacytic rhinitis (uncommon)
Arteriovenous malformations

### Erosions and Ulcers of Skin and Mucous Membranes

#### Canine Diseases

**Infectious**
- Bacterial pyoderma
- Surface: Acute moist dermatitis (pyotraumatic dermatitis), intertrigo
- Deep: folliculitis/furunculosis (including pyotraumatic folliculitis), oral bacterial infections

**Fungal**
- Yeast infections (*Malassezia pachydermatis*, *Candida* spp.), systemic/subcutaneous

**Parasitic**
- Demodecosis

**Metabolic**
- Calcinosis cutis (hyperadrenocorticism)
- Uremia/renal failure
- Necrolytic migratory erythema/metabolic epidermal necrosis

**Neoplastic**
- Epitheliotropic lymphoma
- Squamous cell carcinoma

**Physical, Chemical**
- Drug reactions
- Solar injury
- Thermal injury (freeze, burn)
- Urine scald

**Immune-Mediated/Autoimmune**
- Discoid lupus erythematous
- Pemphigus group
- Uveodermatologic syndrome
- Miscellaneous autoimmune subepidermal vesiculobullous diseases: bullous pemphigoid, epidermolysis bullosa acquisita, linear IgA bullous disease, mucocutaneous pemphigoid, bullous systemic lupus-type 1
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Miscellaneous
- Arthropod bites
- Dermatomyositis
- Dystrophic epidermolysis bullosa
- Idiopathic ulceration of Collies
- Junctional epidermolysis bullosa
- Toxic epidermal necrolysis/erythema multiforme

Feline Diseases

Infectious
- Viral: calicivirus and herpesvirus
- Bacterial: atypical mycobacteriosis
- Fungal: Subcutaneous and systemic mycoses, cryptococcosis, sporotrichosis

Metabolic
- Uremia/renal disease

Neoplastic
- Fibrosarcoma
- Lymphoma
- Squamous cell carcinoma

Physical/Chemical
- Drug reactions
- Thermal

Immune-Mediated/Autoimmune
- Bullous pemphigoid
- Pemphigus foliaceous
- Toxic epidermal necrolysis/erythema multiforme

Miscellaneous/Idiopathic
- Arthropod bites
- Dystrophic epidermolysis bullosa
- Eosinophilic plaque
- Idiopathic ulceration of dorsal neck
- Indolent ulcer
- Junctional epidermolysis bullosa

Failure to Grow/Failure to Thrive

Small Stature and Poor Body Condition
- Dietary insufficiency
- Underfeeding
- Poor-quality diet
- Gastrointestinal disease
- Parasitism
- Inflammatory bowel disease
• Obstruction (foreign body, intussusception)
  • Histoplasmosis

Hepatic dysfunction
• Portovascular anomaly
• Hepatitis
• Glycogen storage disease

Cardiac disorder
• Congenital anomaly
• Endocarditis

Pulmonary disease

Esophageal disease
• Megaesophagus
• Vascular ring anomaly (persistent right aortic arch)

Exocrine pancreatic insufficiency

Renal disease
• Glomerular disease
• Pyelonephritis

Inflammatory disease

Hormonal disease
• Diabetes mellitus
• Hypoadrenocorticism
• Diabetes insipidus
• Juvenile hyperparathyroidism

Small Stature and Good Body Condition

Chondrodystrophy

Hormonal disease
• Congenital hypothyroidism
• Congenital hyposomatotropism (pituitary dwarfism)
• Hyperadrenocorticism

Fever of Unknown Origin

Infection

Bacterial
• Abscessation (inapparent subcutaneous, stump pyometra, liver, pancreas)
• Pyelonephritis
• Diskospondylitis
• Prostatitis
• Peritonitis
• Pyothorax
• Closed pyometra
• Splenic abscess
• Septic arthritis
PART ONE  Clinical Signs Approach to Differential Diagnosis

Bartonellosis
*Mycoplasma haemofilis* (formerly *Hemobartonella felis*)
Borreliosis
Bacterial endocarditis
Plague
Tuberculosis

**Fungal**
Blastomycosis
Histoplasmosis
Coccidioidomycosis

**Viral**
Feline immunodeficiency virus (FIV)
Feline leukemia virus (FeLV)
Feline infectious peritonitis (FIP; *Coronavirus*)

**Rickettsial**
Rocky Mountain spotted fever
Ehrlichiosis
Salmon poisoning

**Protozoal**
Toxoplasmosis
Babesiosis
Hepatozoonosis
Cyt luxzonosis
Trypanosomiasis (Chagas disease)
Leishmaniasis

**Neoplasia**
Lymphoma
Multiple myeloma
Leukemia
Malignant histiocytosis
Necrotic solid tumors

**Immune Mediated**
Polyarthritis
Vasculitis
Meningitis
SLE
Immune-mediated anemia
Steroid-responsive fever
Steroid-responsive neutropenia

**Other**
Hyperthyroidism
Tissue damage
Pharmacologic agents
- Tetracycline
- Penicillins
- Sulfas

Metabolic bone disease
Idiopathic

**Flatulence**

Dietary intolerance (high-fiber, high-protein, or high-fat foods; high-sulfur diets; spoiled food; food change)
Malabsorption
- Exocrine pancreatic insufficiency
- Lactose intolerance

Motility disorders (disrupt passage of gas)
Aerophagia
Behavior (aerophagia associated with competitive eating habits)
Various gastrointestinal disorders

**Gagging**

**Nutritional**
- Food texture
- Food size

**Infectious**
- Viral encephalitis (rabies, pseudorabies)
- Fungal (focal, systemic)
- Bacterial encephalitis

**Toxic**
- Chemical (caustic chemicals, smoke)
- Botulism

**Developmental**
- Cleft palate
- Hydrocephalus
- Achalasia

**Degenerative**
- Laryngeal paralysis
- Muscular dystrophy
- Myasthenia gravis
- Neuropathy of cranial nerves V, VII, IX, or XII
PART ONE  Clinical Signs Approach to Differential Diagnosis

**Mechanical**
- Foreign body
- Styloid disarticulation

**Metabolic**
- Uremia
- Hypocalcemia

**Neoplasia**
- Tonsils, pharynx, epiglottis, glottis, inner ear, nasal, central nervous system

**Trauma**
- Tracheal rupture
- Pharyngeal hematoma
- Medulla or pons ischemia or edema

**Allergic or Immune Mediated**
- Rhinitis
- Pharyngitis
- Laryngitis
- Asthma
- Granuloma complex
- Idiopathic glossopharyngitis

**Genital Dermatoses**

**Lesions of the Prepuce/Sheath**
- Bacterial folliculitis/furunculosis
- Allergic dermatitis affecting the abdomen with hyperpigmentation/lichenification/hypertrophy of the sheath
- Localized demodicosis
- Vasculitis
- Autoimmune skin diseases
- Linear dermatosis of the prepuce (estrogen-secreting tumor)
- Linear epidermal nevus
- Vascular nevus
- Various neoplasms (Stricker sarcoma, hemangiosarcoma, mast cell tumor)

**Lesions of the Scrotum**
- Contact dermatitis (most common scrotal skin disease)
- Frostbite
- Intertrigo
- Malassezia dermatitis
Protothecosis
Babesiosis
Cuterebrosis
Brucellosis
Infection with *Erysipelothrix rhusiopathiae*
Rocky Mountain spotted fever
Autoimmune diseases (bullous diseases, lupus)
Erythema multiforme
Fixed pigmented erythema
Cutaneous histiocytosis
Vascular hamartoma
Neoplasms (squamous cell carcinoma, apocrine adenocarcinoma, myxoma and fibrosarcoma, hemangioma, recurrent cystic hemangioma and hemangiosarcoma, plasmocytoma, lymphoma, histiocytoma, benign fibrous histiocytoma, mast cell tumor, melanoma)

**Female**

Intertrigo
Allergic dermatitis affecting the abdomen with hyperpigmentation/lichenification/hypertrophy of the vulva
Malassezia dermatitis
Demodicosis
Bacterial furunculosis
Contact dermatitis
Autoimmune diseases (lupus, bullous diseases)
Endocrine disorders (especially hyperestrogenism)
Neoplasms

**Halitosis**

**Oral Disease**

Periodontal disease (gingivitis, periodontitis, abscessation)
Calculus
Food traps (periodontal pockets, exposed tooth roots, oral ulcers)
Neoplasia (melanoma, fibrosarcoma, squamous cell carcinoma)
Foreign body
Trauma/fracture
Electric cord injury
Pharyngitis
Stomatitis/glossitis
**Metabolic Disease**
- Renal failure (uremia)
- Diabetic ketoacidosis

**Gastrointestinal Disease**
- Megaesophagus
- Inflammatory bowel disease
- Exocrine pancreatic insufficiency

**Respiratory Disease**
- Rhinitis/sinusitis
- Neoplasia
- Pneumonia or pulmonary abscess

**Dermatologic Disease**
- Lip fold pyoderma
- Eosinophilic granuloma
- Pemphigus complex
- Bullous pemphigoid
- Lupus erythematosus
- Drug eruption
- Cutaneous lymphoma
- Exposure to dimethyl sulfoxide (DMSO)

**Dietary**
- Aromatic foods (onions, garlic)
- Fetid food (carrion)
- Coprophagy

**Grooming Behavior**
- Anal sacculitis
- Vaginitis/balanoposthitis
- Lower urinary tract infections
- Hair retained in periodontal pockets

**Head Tilt**

**Peripheral Vestibular Disease**
- Otitis media/interna
- Feline idiopathic vestibular disease
- Geriatric canine vestibular disease
- Feline nasopharyngeal polyps
- Middle ear tumor
  - Ceruminous gland adenocarcinoma
  - Squamous cell carcinoma
- Trauma
- Aminoglycoside ototoxicity
Hypothyroidism (possibly)
Congenital (German Shepherd, Doberman Pinscher, English Cocker Spaniel, Siamese and Burmese cats)

**Central Vestibular Disease**

- Trauma/hemorrhage
- Infectious inflammatory disease
  - Rocky Mountain spotted fever
  - Feline infectious peritonitis (FIP)
  - Bacterial
  - Protozoal
  - Mycotic
  - Rickettsial
  - Others
- Granulomatous meningoencephalitis
- Neoplasia (meningioma, choroid plexus tumors)
- Vascular infarct
- Thiamine deficiency
- Metronidazole toxicity
- Viral (canine distemper virus, FIP)
- Toxic (lead, hexachlorophene)
- Degenerative diseases (storage diseases, neuronopathies, demyelinating diseases)
- Hydrocephalus

**Hematemesis**

**Alimentary Tract Lesion**

**Gastritis**
- Acute gastritis (common cause)
- Hemorrhagic gastroenteritis
- Chronic gastritis
- *Helicobacter*-associated disease

**Foreign Body**

**Gastrointestinal Tract Ulceration/Erosion**

*Introgenic*
- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Corticosteroids
- NSAIDs used in combination with corticosteroids

**Infiltrative Disease**

- Neoplasia
- Inflammatory bowel disease
- Pythiosis (young dogs, southeastern United States)
- Stress ulceration
• Hypovolemic shock
• Septic shock
• After gastric dilatation/volvulus
• Neurogenic shock
Hyperacidity
• Mast cell tumor
• Gastrinoma (rare)
Other causes
• Hepatic disease
• Renal disease
• Hypoadrenocorticism
• Inflammatory disease

**Esophageal Disease (Uncommon)**
Tumor
Severe esophagitis
Trauma

**Bleeding Oral Lesion**

**Gallbladder Disease (Rare)**

**Coagulopathy**
Thrombocytopenia/platelet dysfunction
Clotting factor deficiency
DIC

**Extraalimentary Tract Lesion**
Respiratory tract lesion
Lung lobe torsion
Pulmonary tumor
Posterior nares lesion

**Hematochezia**

**Anal Disease**
Perianal fistulas
Anal sacculitis or abscess
Stricture
Neoplasia (anal sac adenocarcinoma)
Anal trauma
Perineal hernia
Foreign body

**Rectal and Colonic Disease**
Hemorrhagic gastroenteritis
Proctitis
Colitis
• Idiopathic
• Dietary allergy
• Inflammatory bowel disease
• Stress
• Infectious (Campylobacter spp., Clostridium perfringens)
• Histoplasmosis
• Pythiosis
Parvovirus
Parasites
• Whipworms
• Hookworms
• Coccidia
Neoplasia
• Rectal polyp
• Adenocarcinoma
• Lymphoma
• Leiomyoma or leiomyosarcoma
Prolapsed rectum
Mucosal trauma
• Foreign body or foreign material
• Pelvic fractures
• Iatrogenic (thermometers, enemas, fecal loops, rectal palpation)
Iliocecal intussusception

Hematuria

Renal or Lower Urinary Tract Disease

Inflammation/infection
Urolithiasis
Obstruction
Trauma
Neoplasia
Bleeding disorder
Heat stroke
Renal infarct
Granulomatous urethritis
Feline lower urinary tract disease (FLUTD)
Parasitism
Drug induced (cyclophosphamide)
Renal pelvic hematoma
Vascular malformation
Idiopathic renal hematuria
Renal telangiectasia of Welsh Corgis
Renal hematuria of Weimaraners
Pseudohematuria (myoglobin, hemoglobin, drugs, dyes)
PART ONE  Clinical Signs Approach to Differential Diagnosis

Extraurinary Disease
- Prostatic disease (infection, tumor, cyst, abscess)
- Uterine disease (pyometra, proestrus, tumor, subinvolution of placental sites)
- Vaginal (trauma, neoplasia)
- Preputial/penile (trauma, neoplasia)

Hemoptysis

Cardiovascular
- Heartworm disease
- Cardiogenic pulmonary edema
- Arteriovenous fistula
- Bacterial endocarditis

Pulmonary
- Thromboembolism (secondary to neoplasia, endocrine, cardiac, metabolic disease)
- Bacterial pneumonia
- Pulmonary abscess
- Nocardiosis
- *Bordetella bronchiseptica* infection
- Chronic bronchitis/bronchiectasis
- Fungal pneumonia (blastomycosis, coccidiomycosis, histoplasmosis)
- Neoplasia (primary adenocarcinoma, undifferentiated carcinoma, squamous cell carcinoma, chondrosarcoma, metastatic or primary tracheal tumors)
- Lung lobe torsion
- Parasites (*Paragonimus kellicotti*, *Capillaria aerophila*, *Aelurostrongylus abstrusus*)
- Pulmonary infiltrate with eosinophils
- Systemic bleeding disorder
  - Primary (quantitative or qualitative platelet defects)
  - Secondary (factor deficiencies, anticoagulant rodenticide toxicity, disseminated intravascular coagulopathy)
- Trauma (pulmonary contusion, tracheal rupture, foreign body)
- Iatrogenic (endotracheal intubation, complication of lung biopsy/aspirate, transtracheal wash, bronchoscopy)

Hemorrhage, Prolonged

See Part Two, Section V: Differential Diagnosis for Thrombocytopenia, Platelet Dysfunction, and Coagulopathies, Inherited and Acquired.
Horner Syndrome

2.5% phenylephrine eye drops applied

No Pupillary Dilation (Assume Preganglionic Lesion)

First Order (Central)
- Intracranial disease (neoplasia, trauma, infarct)
- First cervical to third thoracic (C1-T3) spinal myelopathy (intervertebral disc disease, neoplasia, fibrocartaginous embolism, trauma)

Second Order (Preganglionic)
- Spinal cord lesion T1-T3 (trauma, neoplasia, fibrocartilaginous embolism)
- Thoracic disease (cranial mediastinal mass, thoracic spinal nerve root tumor)
- Brachial plexus avulsion
- Cervical soft-tissue neoplasia, trauma
- Skull base tumor
- Jugular furrow disease

Pupillary Dilation (Assume Postganglionic Lesion)

Third Order (Postganglionic)
- Feline leukemia virus, feline immunodeficiency virus
- Otitis media/interna
- Otic mass
- Retrobulbar injury, neoplasia
- Idiopathic

Hyperpigmentation

Increased melanin in the epidermis

Hereditary Hyperpigmentation

Lentigenes—darkly pigmented macules that develop on the ventral abdomen of healthy adult dogs and on the lips, nose, gingiva, and eyelids of orange cats. No adverse health effects.

Canine acanthosis nigricans—bilateral hyperpigmentation and lichenification of axillary skin. Primary, hereditary form seen in Dachshunds beginning before age 1. When seen in older Dachshunds or other breeds, it is likely a postinflammatory form seen with friction, intertrigo, allergies, or endocrine disease.

Acromelanism—dark areas on the points of Siamese, Himalayan-Persian, Balinese, and Burmese cats. Result of a temperature-dependent enzyme controlling melanin production in hair bulbs.
Acquired Hyperpigmentation

Postinflammatory—Mediators of inflammation (e.g., leukotrienes, thromboxanes) stimulate melanocytes to increase melanin production, which down regulates inflammation by scavenging free radicals. Examples of inflammatory conditions that lead to increased melanin production include allergies, Malassezia dermatitis, bacterial pyoderma, dermatophytosis, demodecosis, scabies, and actinic and intertrigo dermatitis. Inflammation affecting hair follicles may lead to melanotrichia (e.g., sebaceous adenitis, panniculitis, vaccine reactions).

Endocrine—hyperadrenocorticism, hypoadrenocorticism, hypothyroidism, hyperestrogenism, and other sex hormone imbalances may result in diffuse hyperpigmentation.

Papillomavirus associated—Pugs may be at risk for development of papillomavirus-associated, slightly raised, scaly, hyperpigmented macules and plaques in their groin region, abdomen, ventral thorax, and neck. Similar lesions are described in miniature Schnauzers, American Staffordshire terriers, and Pomeranians. May transform to squamous cell carcinoma.

Pigmented tumors—apocrine cysts are bluish, cutaneous hemangiomas and hemangiosarcomas appear red, dark purple, or bluish-black. Melanomas, melanocytomas, and basal cell tumors are frequently black. Squamous cell carcinomas, trichoblastomas, and fibromas also may be dark brown to black.

Hyperthermia

Fever

Exogenous pyrogens (infectious agents and their products, inflammation or necrosis of tissue, immune complexes, pharmacologic agents, bile acids)

Endogenous pyrogens (fever-producing cytokines)

Heat Stroke

High ambient temperatures
Exercise
Poor ventilation
Brachycephalic conformation
Obesity

Exercise Hyperthermia

Sustained exercise
Seizure disorders (especially prolonged or cluster seizures)
Hypocalcemic tetany (eclampsia)

Pathologic Etiologies

Lesions in or around anterior hypothalamus
Hypermimetic disorders
Hyperthyroidism
Pheochromocytoma
Malignant hyperthermia
Halothane
Succinylcholine

**Hypopigmentation**

Due to melanocyte destruction, dysfunction, or abnormal distribution of melanosomes.

**Hereditary Hypopigmentation**

Albinism—hereditary absence of pigment
Piebaldism—presence of white spots where melanocytes are absent
Waardenburg-Klein syndrome—affected animals have absence of melanocytes in areas of skin and hair, blue or heterochromatic eyes, and are also deaf. Reported in cats, bull terriers, Sealyham terriers, collies, Dalmatians
Canine cyclic hematopoiesis—lethal autosomal recessive disease of collies. Gray coat, light-colored nose, cyclic episodes of neutropenia every 12-14 days resulting in sepsis and amyloidosis
Chédiak-Higashi syndrome—rare autosomal recessive disease of blue smoke Persian cats. Partial oculocutaneous albinism with abnormal function of granulocytes and platelets resulting in hemorrhage, recurrent infections, and death at a young age.
Graying—age-associated, reduction of melanocyte replication.
Vitiligo—macular leukoderma and leukotrichia of nose, ears, buccal mucosa, and facial skin. Antimelanocyte antibodies found in serum of some affected dogs. Seen most commonly in Siamese cat, Belgian Tervuren, German Shepherd, collie, Rottweiler, Doberman Pinscher, Giant Schnauzer.
Nasal hypopigmentation—season-associated lightening of nasal planum during winter months most common in Siberian Husky, Golden Retriever, Labrador Retriever, and Bernese Mountain Dog. Seen also in many other breeds.

**Acquired Hypopigmentation**

Postinflammatory—Discoid lupus erythematosus is the most common cause of postinflammatory nasal depigmentation. Also pemphigus complex, SLE, uveodermatologic syndrome, bullous pemphigoid, mucocutaneous pyoderma, drug eruption, and contact dermatitis. Infectious causes include leishmaniasis, blastomycosis, sporotrichosis, and bacterial folliculitis.
Drug related—ketoconazole, procainamide, and vitamin E may cause diffuse coat lightening.
Nutritional/metabolic—deficiencies of zinc, pyridoxine, pantothenic acid, and lysine are associated with graying of hair. Dark hairs may become reddish in color with copper deficiency, hypothyroidism, hyperadrenocorticism, hyperestrogenism, hyperprogesteronism, chlorine exposure, and chronic exposure to ultraviolet light.

Neoplasia associated—nasal depigmentation, leukoderma, and leukotrichia sometimes seen with epitheliotropic T cell lymphoma, basal cell tumors, mammary adenocarcinoma, and gastric carcinomas.

Idiopathic—leukotrichia and patchy hypopigmentation reported as idiopathic in Labrador Retrievers, and black Newfoundlands. Siamese cats may be affected with periocular leukotrichia, which may be associated with upper respiratory tract infections, pregnancy, dietary deficiencies, or systemic illness.

### Hypothermia

**Predisposing Factors**

- Anesthesia
- Low ambient temperature
- Neonate
- Small size
- Elderly
- Sick
- Debilitated
- Near drowning
- Enema

### Icterus (Jaundice)

**Hemolysis**

- Autoimmune hemolytic anemia
- Hemolytic anemia secondary to drugs, neoplasia
- Infectious (*Ehrlichia canis, Babesia canis, Babesia felis, Mycoplasma homocanis, Mycoplasma hemofelis, Cytauxzoon felis, heartworm disease, feline leukemia virus [FELV]*)
- Toxic (onions, lead, copper, methylene blue, benzocaine, propylene glycol, acetaminophen [cats], phenazopyridine)
- Fragmentation (disseminated intravascular coagulation, hemangiosarcoma, vena cava syndrome)
- Erythrocyte membrane or enzyme defects (pyruvate kinase deficiency [Beagle, Basenji], phosphofructokinase deficiency [English Springer Spaniel], stomatocytosis of chondrodysplastic Malamutes)
Congenital porphyria
Snake, brown recluse spider, and bee venoms

**Hepatobiliary Disease**

- Cholangiohepatitis
- Chronic inflammatory hepatic disease
- Cirrhosis
- Diffuse neoplasia
- Copper toxicity
- Toxic hepatopathy (anticonvulsants, mebendazole, oxibendazole, diethylcarbamazine, inhalation anesthetics, thiacetarsamide, acetaminophen, trimethoprim-sulfa)
- Hepatic lipidosis
- Feline infectious peritonitis (FIP)
- Parasitic
- Idiosyncratic drug reaction

**Posthepatic Biliary Obstruction**

- Pancreatitis
- Enteritis/cholecystitis
- Trauma
- Neoplasia
- Calculus
- Stricture
- Mucocele
- Ruptured bile duct or gallbladder

**Inappropriate Elimination**

**Dogs**

**Medical Causes**

- **Fecal House Soiling**
  - Increased volume of feces (maldigestion, malabsorption, high-fiber diets)
  - Increased frequency of voiding (colitis, diarrhea)
  - Compromised neurologic function (peripheral nerve impairment, spinal cord disease, brain tumor, encephalitis, infection, degenerative brain disorders)
  - Joint pain
  - Sensory decline
  - Cognitive dysfunction

- **Urinary House Soiling**
  - Diseases causing polyuria (e.g., renal disease, hyperadrenocorticism, diabetes, pyometra)
  - Increased urinary frequency (urinary tract infection/inflammation, urolithiasis, bladder tumors, prostatitis, abdominal masses)
Impaired bladder control (peripheral nerve disease, spinal cord disease, brain tumor, encephalitis, infection, degenerative brain disorders)
Urethral incompetence
Anatomic problems
Urethral sphincter mechanism incompetence (estrogen-responsive incontinence)
Cognitive dysfunction

Behavioral Causes
Inadequate training
Submissive urination
Excitement urination
Marking
Separation anxiety
Management-related problems
Location or surface preference

Cats

Medical Causes

Fecal House Soiling
Increased volume of feces (maldigestion, malabsorption, high-fiber diets)
Increased frequency of voiding (colitis, diarrhea, inflammatory bowel disease)
Compromised neurologic function (peripheral nerve impairment, spinal cord disease, brain tumor, encephalitis, infection, degenerative brain disorders)
Joint pain
Anal sacculitis
Obstipation/constipation
Hyperthyroidism
Neoplasia
Cognitive dysfunction

Urinary House Soiling
Diseases causing polyuria (e.g., renal disease, hyperadrenocorticism, diabetes, pyometra)
Increased urinary frequency (feline lower urinary tract disease [FLUTD], urolithiasis, idiopathic cystitis)
Impaired bladder control (peripheral nerve disease, spinal cord disease, brain tumor, encephalitis, infection, degenerative brain disorders)
Joint pain, disk disease
Hyperthyroidism
Neoplasia
Anatomic problems
Cognitive dysfunction
Behavioral Causes

**Litterbox Aversion**
- Aversive disorder (deodorant, ammonia)
- Inadequate cleaning
- Discomfort during elimination (FLUTD, constipation, diarrhea, arthritis)
- Unacceptable litter (texture, depth, odor, plastic liner)
- Unacceptable box (too small, sides too high, covered)
- Disciplined, medicated, or frightened in box

**Location Aversion**
- Too much traffic
- Traumatic/fearful experience in area

**Other**
- Location preference
- Surface preference
- Anxiety (owner absence, high cat density, moving, new furniture, inappropriate punishment, teasing, household changes, remodeling in home)
- Need for privacy (other pets, anything that makes box less accessible to cat)

**Urine Marking**
- Hormones
- Temperament
- Feline population density
- Indirect signaling from other cats (scent on visitor’s clothing)
- Changes in environment (new roommate, remodeling home, new furniture, and other novel items in home)
- Owner absence from home
- Lack of owner attention
- Inappropriate punishment

**Incontinence, Fecal**

**Nonneurologic Disease**

**Colorectal Disease**
- Inflammatory bowel disease
- Neoplasia
- Constipation

**Anorectal Disease**
- Perianal fistula
- Neoplasia
- Surgery (anal sacculectomy, perianal herniorrhaphy, rectal resection and anastomosis)
Miscellaneous
Decreased mentation
Old age
Severe diarrhea
Irritable bowel disease

Neurologic Disease

Sacral Spinal Cord Disease
Diskospondylitis
Neoplasia
Degenerative myelopathy
Congenital vertebral malformation
Sacrococcygeal hypoplasia of Manx cats
Sacral fracture
Sacrococcygeal subluxation
Lumbosacral instability
Meningomyelocele
Viral meningomyelitis

Peripheral Neuropathy
Trauma
Penetrating wounds
Repair of perineal hernia
Perineal urethrostomy
Hypothyroidism
Diabetes mellitus
Dysautonomia

Incontinence, Urinary

Bladder Distended

Neurogenic
Lower motor neuron disease (sacral [S1-S3] segments or peripheral nerves)
Bladder easily expressed, dribbles urine
Detrusor areflexia with sphincter areflexia
Upper motor neuron disease
Bladder difficult to express; may be associated with paresis, paralysis
Detrusor areflexia with sphincter hypertonia
Dysautonomia

Obstructive
Reflex dyssynergia (functional obstruction)
Mechanical obstruction (uroliths, tumors, strictures, granulomatous urethritis, urethral inflammation, prostatic disease, mucoid or crystalline plug [feline])
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Bladder Not Distended

Dysuria/Pollakiuria Absent
Urethral sphincter mechanism incompetence  
(middle-aged to older spayed or neutered dogs)  
Congenital (ectopic ureters, patent urachus)

Dysuria/Pollakiuria Present
Detrusor hyperreflexia/instability (uroliths, urinary tract infection, urethral mass)

Infertility, Female

Normal Cycles

Improper breeding management
Infertile male
Elevated diestrual progesterone
- Early embryonic death
- Lesions in tubular system (vagina, uterus, uterine tubes)
- Placental lesions (brucellosis, herpes infection)
Normal diestrual progesterone
- Cystic follicles (ovulation failure)

Abnormal Cycles

Abnormal Estrus

Will Not Copulate
Not in estrus
Inexperience
Partner preference
Vaginal anomaly
Hypothyroidism?

Prolonged Estrus
Cystic follicles
Ovarian neoplasia
Exogenous estrogens
Prolonged proestrus

Short Estrus
Observation error
Geriatric
Split estrus

Abnormal Interestrual Interval

Prolonged Interval
Photoperiod (queen)
Pseudopregnant/pregnant (queen)
Normal breed variation
Glucocorticoids (bitch)
Geriatric
Luteal cysts

**Short Intervals**
Normal (especially queen)
Ovulation failure (especially queen)
Corpus luteum failure
“Split heat” (bitch)
Exogenous drugs

**Not Cycling**
Prepubertal
Ovariohysterectomy
Estrus suppressants
Silent heat
Unobserved heat
Photoperiod (queen)
Intersex (bitch)
Ovarian dysgenesis
Hypothyroidism (possibly)
Glucocorticoid excess
Hypothalamic-pituitary disorder
Geriatric
Ovarian neoplasia
Premature ovarian failure

**Infertility, Male**

**Inflammatory Ejaculate**
Prostatitis
Orchitis
Epididymitis

**Azoospermia**
Sperm-rich fraction not collected
Sperm not ejaculated
• Incomplete ejaculation
• Obstruction
• Prostate swelling
Sperm not produced
• Endocrine
• Testicular
• Metabolic
Abnormal Motility/Morphology

Iatrogenic
Prepubertal
Poor ejaculation
Long abstinence

Abnormal Libido

Female not in estrus
Behavioral
Pain
Geriatric

Normal Libido

Improper stud management
Infertile female

Normal Libido/Abnormal Mating Ability

Orthopedic
Neurologic
Prostatic disease
Penile problem
Prepuce problem

Joint Swelling

Trauma
Degenerative joint disease
Neoplasia
Inflammatory joint disease—infectious
  • Septic (bacterial)
  • Fungal arthritis
    • Blastomycosis
    • Coccidioidomycosis
    • Cryptococcosis
  • Lyme borreliosis
  • Rickettsial arthritis
  • Mycoplasma
  • Bacterial L-form–associated arthritis (cats)
  • Viral arthritis (calicivirus infection—kittens)
Inflammatory joint disease—noninfectious
  • Nonerosive
    • Immune-mediated polyarthritis (idiopathic)
    • SLE
    • Breed-specific polyarthritis syndromes
    • Akita, Boxer, Weimaraners, Bernese Mountain Dog,
      German Shorthaired Pointer, Beagle, Shar-Pei
• Lymphocytic/plasmacytic synovitis
• Drug reaction (e.g., trimethoprim-sulfadiazine in Doberman Pinschers)
• Chronic infection causing secondary immune-mediated polyarthritis (bacterial, ehrlichiosis, Anaplasmosis, Rocky Mountain spotted fever, Lyme borreliosis, heartworm disease)
• Erosive
• Rheumatoid arthritis
• Erosive polyarthritis of greyhounds
• Feline chronic progressive polyarthritis

Lameness

Orthopedic

Trauma
Fracture
Luxation, subluxation
Toenail trauma
Bone contusion

Infectious
Osteomyelitis (bacterial, fungal)

Developmental
Patellar luxation
Osteochondrosis
Panosteitis
Hypertrophic osteodystrophy
Avascular necrosis of femoral head
Nonunited anconeal process
Bone cysts

Nutritional
Vitamin D deficiency (rickets)

Neoplasia
Osteosarcoma
Multiple myeloma
Metastatic to bone

Joint Disease

See Joint Swelling.

Muscles

Trauma
Contusion
Strain
Laceration  
Rupture  

**Inflammatory**  
- Canine idiopathic polymyositis  
- Feline idiopathic polymyositis  
- Dermatomyositis  

**Infectious**  
- Protozoal myositis  

**Tendons**  

**Trauma**  
- Laceration  
- Severance  
- Avulsion  

**Ligaments**  

**Trauma**  
- Rupture  
- Tear  
- Hyperextension  

**Lymphadenopathy (Lymph Node Enlargement)**  

**Infiltrative Lymphadenopathies**  

**Neoplastic**  
- Primary hemolymphatic (lymphoma, multiple myeloma, systemic mast cell disease, leukemias, malignant histiocytosis, lymphomatoid granulomatosis)  
- Metastatic neoplasia (carcinomas, sarcomas, malignant melanoma, mast cell tumors)  

**Nonneoplastic**  
- Eosinophilic granuloma complex  
- Nonneoplastic mast cell infiltration  

**Proliferative and Inflammatory Lymphadenopathies**  

**Infectious**  
- Bacterial  
  - Localized bacterial infection  
  - Septicemia  
  - Systemic infection (e.g., *Borrelia burgdorferi, Brucella canis, Yersinia pestis, Corynebacterium, Mycobacterium, Nocardia, Streptococcus, Actinomyces, Bartonella spp.*)  
  - Contagious streptococcal lymphadenopathy
Parasitic (toxoplasmosis, demodicosis, babesiosis, 
cytauxzoonosis, hepatozoonosis, leishmaniasis, 
trypanosomiasis, *Neospora caninum*)
Rickettsial (ehrlichiosis, Rocky Mountain spotted fever, 
anaplasmosis, salmon poisoning)
Viral (feline immunodeficiency virus, feline leukemia 
 virus, feline infectious peritonitis, canine viral enteritis, 
infectious canine hepatitis)
Fungal (blastomyosis, cryptococcosis, histoplasmosis, 
aspergillosis, coccidioidomycosis, phaeohyphomycosis, 
phycomycosis, sporotrichosis, others)
Algal (protothecosis) *Pneumocystis carinii*

**Noninfectious**
- Immune-mediated disorders
  - SLE
  - Rheumatoid arthritis
  - Immune-mediated polyarthritis
  - Juvenile cellulitis
- Drug reactions
- Localized inflammation
- Postvaccinal
- Dermatopathic lymphadenopathy
- Idiopathic
  - Distinctive peripheral lymph node hyperplasia
  - Plexiform vascularization of lymph nodes

### Melena

#### Ingested Blood
- Oral lesions
- Nasopharyngeal lesions
- Pulmonary lesions
- Diet

### Parasitism
- Hookworms

### Neoplasia
- Adenocarcinoma
- Lymphoma
- Leiomyoma or leiomyosarcoma
- Mast cell tumor
- Gastrinoma

### Upper Gastrointestinal Inflammation
- Acute gastritis
- Gastroduodenal ulceration/erosion
Hemorrhagic gastroenteritis
Inflammatory bowel disease
Foreign body
Esophagitis

**Infection**

- *Campylobacter*
- *Clostridium perfringens*
- *Salmonella*
- *Parvovirus*
- *Neorickettsia helminthoeca* (salmon poisoning)
- *Histoplasma*
- *Pythium*

**Drugs**

- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Glucocorticoids

**Miscellaneous**

- Pancreatitis
- Liver failure
- Renal failure
- Hypoadrenocorticism
- Gastrointestinal ischemia (shock, volvulus, intussusception)
- Arteriovenous fistula
- Polyps
- Coagulopathies (thrombocytopenia, factor deficiencies, rodenticide toxicity, DIC)

**Muscle Wasting**

*See Cachexia and Muscle Wasting.*

**Nasal Discharge**

*See Sneezing and Nasal Discharge.*

**Nystagmus**

**Peripheral Vestibular Disease**

Horizontal nystagmus; fast phase toward normal side; no change with varying head position
- Otitis media/interna
- Feline idiopathic vestibular disease
- Canine geriatric vestibular disease
- Neoplasia
- Granuloma
- Trauma (iatrogenic secondary to ear cleaning)
Ototoxic drugs
Neuropathy (hypothyroid, cranial nerve VIII disease)
Congenital (German Shepherd, English Cocker Spaniel, Doberman Pinscher, smooth-haired Fox Terrier, Siamese, Burmese, Tonkinese)

**Central Vestibular Disease**
Horizontal, vertical, or rotary nystagmus; direction may change with varying head position
- Trauma/hemorrhage
- Infectious inflammatory disease
- Viral (canine distemper virus, feline infectious peritonitis)
- Rickettsial (RMSE, ehrlichiosis)
- Fungal (cryptococcosis)
- Toxoplasmosis
- Neosporosis
- Granulomatous meningoencephalitis
- Neoplasia
- Vascular infarct
- Thiamine deficiency
- Metronidazole toxicity
- Toxic (lead, hexachlorophene)
- Degenerative diseases (storage diseases, neuronopathies, demyelinating diseases)
- Hydrocephalus
- Anomaly (caudal occipital malformation syndrome in Cavalier King Charles Spaniels)
- Head trauma

**Obesity**

**Causes**
- Excessive feeding
- Malnutrition
- High-carbohydrate diet (especially cats)
- Lack of exercise
- Inactivity (indoor life style, middle age)
- Neutering?
- Genetic predisposition
- Hypothyroidism
- Hyperadrenocorticism
- Hyperinsulinism
- Acromegaly
- Hypopituitarism
- Hypothalamic dysfunction
- Drugs (glucocorticoids, progestagens, phenobarbital, primidone)
Health Risks

Degenerative joint disease
Cruciate ligament disease
Hip dysplasia
Traumatic joint disease
Intervertebral disk disease
Dyspnea: (Pickwickian syndrome)
Heat intolerance
Exercise intolerance
Diabetes mellitus (insulin resistance)
Hepatic lipidosis (cats)
Pancreatitis
Dystocia
Urinary tract disease
Skin fold dermatoses
Increased anesthetic risk

Oliguria

See Anuria and Oliguria.

Pallor

Anemia

Regenerative Anemia

 Immune-mediated hemolytic anemia (extravascular, intravascular)
 Erythrocytic parasites (Bartonella, Babesia, Cytazuaxoon spp.)
 Fragmentation (disseminated intravascular coagulation, heartworm disease, hemangiosarcoma, vasculitis, hemolytic uremic syndrome, diabetes mellitus)
 Pyruvate kinase deficiency
 Phosphofructokinase deficiency
 Feline porphyria
 Copper toxicity
 Neonatal isoerythrolysis
 Oxidative injury (onions, acetaminophen, zinc, benzocaine, mothballs, phenazopyridine)
 Blood loss (external blood loss, blood loss to a body cavity, coagulopathies, endoparasites, gastrointestinal blood loss)

Nonregenerative Anemia

 Anemia of chronic disease
 Anemia from renal failure
Feline leukemia virus (FeLV)
Endocrine (mild anemia associated with hypoadrenocorticism, hypothyroidism)
Myeloaplasia/aplastic anemia (FeLV infection, ehrlichiosis, trimethoprim-sulfa, estrogen toxicity, phenylbutazone, chemotherapy, chloramphenicol)
Myelodysplasia
Myeloproliferative and lymphoproliferative disorders
Myelofibrosis

**Shock**

**Cardiogenic**
Decreased ventricular function
- Dilated cardiomyopathy
- Myocarditis
- Myocardial infarction
Compromised ventricular filling
- Hypertrophic cardiomyopathy
- Cardiac tamponade
Severe endocardiosis
Outflow obstruction
- Intracardiac tumors
- Aortic stenosis
- Hypertrophic obstructive cardiomyopathy
- Heartworm disease
- Thrombosis
- Severe arrhythmia

**Noncardiogenic**
Trauma
Hypovolemia
- Severe blood loss
- Dehydration
- Hypoadrenocorticism
Disruptions in blood flow
- Sepsis and endotoxemia
- Hypotension

**Papules and Pustules**
- Bacterial pyoderma (papules and pustules)
- Demodicosis (papules and pustules)
- Dermatophytosis (rare papules, uncommon pustules)
- Sarcoptes mange (papules, no pustules)
- Cheyletiellosis (rare papules, no pustules)
- Otacariosis (rare papules, no pustules)
• Trombiculosis (papules, rare pustules)
• Hypersensitivity (papules, rare pustules)
• Pemphigus (papules and pustules)
• Early-stage neoplasia (papules, no pustules)

**Paresis and Paralysis**

**Upper Motor Neuron**

Tetraparesis or hemiparesis
- Severe forebrain lesion
- Brain stem lesion
- First to fifth cervical (C1-C5) spinal lesion

Paraparesis or rear limb monoparesis
- Third thoracic to third lumbar (T3-L3) spinal lesion

**Lower Motor Neuron**

Tetraparesis
Generalized lower motor neuron disease
- Flaccid paresis/paralysis
  - Acute polyradiculoneuritis/“coonhound paralysis”
  - Tick paralysis
  - Botulism
  - Myasthenia gravis
- Toxicants
  - Coral snake
  - Black widow spider
  - Herbicides (2,4 D)
  - Macadamia nuts

Paraparesis
- Fourth lumbar to second sacral (L4-S2) spinal lesion

Hemiparesis with lower motor neuron forelimb
- Sixth cervical to second thoracic (C6-T2) spinal lesion
Aortic thromboembolism
Degenerative myelopathy
Monoparesis
Peripheral nerve lesion

**Petechiae and Ecchymoses**

**Thrombocytopenia**

**Increased Platelet Destruction**
- Immune-mediated thrombocytopenia
- Systemic lupus erythematosus (SLE)
- Heartworm disease
Decreased Platelet Production

**Bone Marrow Suppression**
- Infectious disease (ehrlichiosis, babesiosis, Rocky Mountain spotted fever, leishmaniasis, feline leukemia virus, feline immunodeficiency virus)
- Neoplasia
- Drug reactions
- Myeloproliferative disease
- Virus-associated myelodysplasia
- Estrogen toxicity

**Consumption of Platelets**
- Disseminated intravascular coagulation (DIC)
- Vasculitis

**Sequestration of Platelets (Unlikely to Cause Clinical Signs)**
- Splenomegaly
- Hepatomegaly
- Endotoxemia

**Thrombopathia**

**Inherited**
- Cocker Spaniel, Otterhound, Great Pyrenees, Bassett Hound, American Cocker Spaniel, cats

**Acquired**
- Drugs (aspirin, cephalothin, carprofen, hydroxyethyl starch)
- Uremia
- Liver disease
- Dysproteinemias

**Von Willebrand Disease**
- Lack of von Willebrand factor leads to impaired platelet adhesion.

**Vascular Purpura**
- Vasculitis secondary to infectious, inflammatory, immune-mediated, neoplasia, drug reaction, hyperadrenocorticism

**Pollakiuria**
- See Stranguria, Dysuria, and Pollakiuria.

**Polyuria and Polydipsia**
- Renal insufficiency or failure
- Diabetes mellitus
Hyperadrenocorticism (Cushing syndrome)
Lower urinary tract disease
- Infection
- Urolithiasis
- Neoplasia
- Anatomic problem
- Neurologic problem
Pyometra
Hypercalcemia
Hypoadrenocorticism (Addison disease)
Pyelonephritis
Hypokalemia
Iatrogenic (corticosteroids, diuretics, anticonvulsants)
Hyperthyroidism
Hepatic insufficiency
Postobstructive
Diabetes insipidus
- Central
- Renal
Psychogenic drinking
Renal glycosuria

Pruritus

Allergy
- Flea allergy
- Atopic dermatitis
- Food allergy/intolerance
- Contact dermatitis
- Mosquito-bite hypersensitivity
- Eosinophilic plaque (cats)

Parasites
- Flea infestation
- Scabies
- Pediculosis (lice)
- Cheyletiellosis
- Chiggers
- Cutaneous larval migrans
- Demodicosis (often not pruritic)
- Otodectic acariasis

Infectious Agents
- Pyoderma
- Malassezia dermatitis
- Dermatophytosis
**Behavioral**
- Acral lick dermatosis
- Psychogenic alopecia

**Immune-Mediated**
- Pemphigus foliaceus

**Drug Eruption**

**Miscellaneous**
- Cornification defects
- Superficial necrolytic dermatitis
- Tail dock neuroma
- Rhabditic dermatitis

**Ptyalism (Excessive Salivation)**

**Oral Cavity Disease**
- Oral trauma (tooth fractures, mandibular fractures, maxillary fractures, TMJ luxation)
- Severe periodontal disease
- Oral masses (neoplasia, granuloma, eosinophilic granuloma)
- Stomatitis (toxins, infections, immune-mediated disease, immunologic or nutritional deficiency)
- Glossitis (chemical or environmental irritants, viral infections, uremia, immune-mediated disease, tumors)
- Faucitis (cats)
- Mucocutaneous junction lesions
- Foreign body
- Developmental (severe brachygnathism, lip fold pyoderma)

**Oral Cavity Normal**
- Drugs and toxins (bitter taste; insecticides such as organophosphates, pyrethrins, and d-limonene; caustic chemicals; poison toads and salamanders)
- Nausea
- Hepatic encephalopathy/portosystemic shunt
- Seizures
- Space-occupying lesions in pharynx
- Cranial nerve (CN) deficits (CN V: inability to close mouth; CN VII: inability to move lip; CNs X, XI, and XII: loss of gag lesion and inability to swallow)
- Rabies virus
- Dysphagia
- Behavior (associated with food [Pavlovian], contentment/mood in cats when purring, pain)
- Salivary gland hypersecretion
Regurgitation

Esophageal Disease
- Megaesophagus (primary or secondary)
- Esophagitis
- Mechanical obstruction (foreign body, vascular ring anomaly, stricture)

Alimentary Disorders
- Pyloric outflow obstruction
- Gastric dilatation/volvulus
- Hiatal hernia

Neuropathies
- Peripheral neuropathy (polyradiculitis, polyneuritis, lead poisoning, giant cell axonal neuropathy)
- Central nervous system (brain stem lesion, neoplastic, traumatic, distemper)
- Dysautonomia

Neuromuscular Junction Abnormalities
- Myasthenia gravis (focal or generalized)
- Tetanus
- Botulism
- Acetylcholinesterase toxicity

Immune-Mediated Disorders
- Systemic lupus erythematosus (SLE)
- Polymyositis
- Dermatomyositis

Endocrine Disease
- Hypothyroidism
- Hypoadrenocorticism

Infectious
- Spirocercosis
- Pythium insidiosum

Reverse Sneezing
- Loud inspiratory noise, occurs in paroxysms; initiated by nasopharyngeal irritation
- Purpose is to move secretions and foreign material into the oropharynx to be swallowed
- Causes include excitement, foreign bodies, nasal mites (*Pneumonyssus caninum*), viral infections, and epiglottic entrapment of the soft palate
- Often idiopathic, nonprogressive, and common in small dogs and cats

**Scaling and Crusting**

**Bacterial**
- Superficial folliculitis
- Deep pyoderma
- Mucocutaneous pyoderma
- Pyotraumatic dermatitis

**Fungal**
- Dermatophytosis
- *Malassezia* dermatitis
- Deep fungal infection (e.g., blastomycosis, cryptococcosis)

**Parasitic**
- Fleas
- Scabies
- Demodecosis
- Cheyletiellosis
- Notoedric mange
- Pediculosis

**Protozoal**
- Leishmaniasis

**Viral**
- Feline leukemia virus

**Allergic**
- Atopic dermatitis
- Food hypersensitivity
- Flea bite hypersensitivity
- Military dermatitis

**Endocrine and Metabolic**
- Hyperadrenocorticism
- Hypothyroidism
- Necrolytic migratory erythema

**Immune-Mediated**
- Pemphigus foliaceus
- Discoid lupus erythematosus
- Erythema multiforme
Congenital and Hereditary
- Primary seborrhea
- Ichthyosis
- Schnauzer comedo syndrome
- Familial canine dermatomyositis

Keratinization Defects
- Secondary seborrhea
- Vitamin-A responsive dermatosis
- Ear margin dermatosis

Environmental
- Solar dermatitis

Nutritional
- Zinc-responsive dermatosis
- Fatty acid deficiency

Other
- Cutaneous lymphoma
- Sebaceous adenitis
- Otitis externa

Seizure

Extracranial Causes
- Toxins (e.g., strychnine, chlorinated hydrocarbons, organophosphates, carbamates, lead, ethylene glycol, metaldehyde)
- Metabolic disease (e.g., hepatic encephalopathy, hypoglycemia, hypocalcemia)
- Hepatic disease
- Electrolyte disturbances (e.g., hypernatremia)
- Severe uremia
- Hyperlipoproteinemia
- Hyperviscosity (multiple myeloma, polycythemia)
- Hyperosmolality (diabetes mellitus)
- Heat stroke

Intracranial Causes

See Part Two, Section XI: Differential Diagnosis for Inflammatory Disease of the Nervous System.
- Infectious disease
- Neoplasia (primary brain tumor, lymphoma, metastatic tumors)
- Granulomatous meningoencephalitis
Hemorrhage/infarct (renal failure, hypothyroidism, hyperthyroidism, hypertension, septic emboli, neoplasia, coagulopathies, heartworm disease, vasculitis)  
Congenital malformations (lissencephaly, hydrocephalus)  
Necrotizing encephalitis  
Degenerative diseases (metabolic storage diseases, leukodystrophies, hypomyelination disorders, spongy disorders)  

**Idiopathic Epilepsy**  

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**Sneezing and Nasal Discharge**

**Nasal and Upper Respiratory Disease**

**Infectious**  
Viral: herpesvirus, calicivirus, canine distemper virus  
Bacterial: *Mycoplasma* spp., *Bordatella bronchiseptica*  
Fungal: *Aspergillus*, *Cryptococcus*, *Rhinosporidium*, *Penicillium* spp.  
Parasitic: *Pneumonyssus caninum* (nasal mite), *Eucoleus boehmi* (formerly *Capillaria* spp.), *Cuterebra* spp.

**Inflammatory**  
Allergic rhinitis  
Lymphocytic-plasmacytic rhinitis  
Acquired nasopharyngeal stenosis  
Nasopharyngeal polyps  
Polypoid rhinitis

**Neoplasia**  
Adenocarcinoma, squamous cell carcinoma  
Fibrosarcoma, osteosarcoma, chondrosarcoma  
Lymphoma, transmissible venereal tumor, neuroendocrine carcinoma

**Foreign Body**

**Congenital**  
Cleft palate  
Ciliary dyskinesia  
Nasopharyngeal stenosis  
Choanal atresia

**Dental Disease**  
Tooth root abscess  
Oronasal fistula
Trauma

Vascular Malformation

Systemic Disease

Infectious
- Canine distemper virus
- Canine infectious tracheobronchitis
- Pneumonia

Hypertension
- Hyperthyroidism
- Hyperadrenocorticism
- Renal disease
- Pheochromocytoma
- Hypothyroidism
- Acromegaly
- Polycythemia
- Diabetes mellitus
- Overhydration

Coagulopathies
- Thrombocytopenia
- Rocky Mountain spotted fever
- Thrombocytopenia
- von Willebrand disease
- Factor deficiencies
- Congenital (hemophilia A, B, others)
- Acquired (vitamin K rodenticide toxicity, DIC, hepatic failure)

Vasculitis
- Toxic
- Inflammatory
- Immune mediated (SLE)
- Neoplastic
- Infectious (ehrlichiosis, FIP, Rocky Mountain spotted fever, leishmaniasis)

Hyperviscosity
- Multiple myeloma
- Lymphoma
- IgM (Waldenstrom) macroglobulinemia
- Chronic lymphocytic leukemia
- Ehrlichiosis
- Amyloidosis
- Plasma cell leukemia
- FIP (rare)
**Sтертор и Cтридor**

### Sтерtor

Snoring or snorting associated with partial nasal or nasopharyngeal obstruction.

**Intranasal Disorders**
- Congenital deformities
- Masses
- Exudates
- Clotted blood

**Pharyngeal Disease**
- Brachycephalic airway syndrome
- Elongated soft palate
- Nasopharyngeal polyp
- Foreign body
- Neoplasia
- Abscess
- Granuloma
- Extraluminal mass

### Cтридor

High-pitched wheeze caused by air turbulence in upper airway associated with laryngeal disease or narrowing of extrathoracic trachea.

**Laryngeal Disease**
- Neoplasia
- Polyps
- Laryngeal paralysis
- Laryngeal trauma
- Foreign body
- Acute laryngitis/obstructive laryngitis

**Extrathoracic Tracheal Disease**
- Neoplasia
- Foreign body
- Extrathoracic collapsing trachea
- Extraluminal mass

### Stranguria, Dysuria, and Pollakiuria

**Stranguria/Pollakiuria**

**Small Bladder**
- Cystitis
  - Infectious agents
  - Idiopathic cystitis (cats)
Detrusor hyperspasticity
Urethritis
Urethral mass

**Large Bladder**
Lower urinary tract obstruction
- Functional
- Mechanical

**Urinary Retention**

**Easy Catheterization**

*Normal Neurologic Examination*
- Cystic calculi or mass
- Detrusor areflexia from overdistension
- Reflex dyssynergia

*Abnormal Neurologic Examination*
- Detrusor areflexia with sphincter areflexia (lower motor neuron)
- Detrusor areflexia with sphincter hypertonia (upper motor neuron)
- Dysautonomia

**Difficult Catheterization**
- Urethral spasm
- Urethral calculi
- Urethral neoplasia
- Transitional cell carcinoma
- Granulomatous urethritis
- Urethral inflammation
- Prostatic disease
- Mucoid or crystalline plug (cats)

**Stomatitis**

Infectious disease
- Feline immunodeficiency virus (FIV)
- Feline leukemia virus (FeLV)
- Feline syncytium-forming virus
- Feline calicivirus
- Feline herpesvirus
- Feline infectious peritonitis (FIP)
- Bartonellosis
- Canine distemper virus
- Feline panleukopenia virus
- Candidiasis

Immunosuppressive disease
- Feline eosinophilic granuloma complex
Idiopathic feline chronic gingivitis/stomatitis
Immune-mediated disease
• Systemic lupus erythematosus (SLE)
• Bullous (pemphigus) disease
• Idiopathic vasculitis
• Toxic epidermal necrolysis
• Ulcerative gingivitis/stomatitis of Maltese Terriers
Uremic stomatitis
Radiation-induced

Stupor and Coma

Increased Intracranial Pressure
Encephalitis
Meningitis
Neoplasia
Granulomas
Abscess
Vascular events
Trauma
Underlying metabolic injury (e.g., hypertension)

Cerebral Edema
Vasogenic (brain masses that lead to breakdown of blood-brain barrier)
Cytotoxic (hypoxia, neuroglycopenia)
Interstitial (hydrocephalus)

Herniation of Brain Tissue
Caudal transtentorial herniation
Foramen magnum herniation

Extracranial Causes
Hypoglycemia
Severe hypothyroidism
Toxins
Hepatic disease
Hyperadrenocorticism

Syncope
Normal Cerebral Perfusion
Severe hypoxemia
Hypoglycemia
Cerebral Hypoperfusion

**Normotension**
- Cerebrovascular disease
- Cerebral vasoconstriction

**Systemic Hypotension**

*Decreased Cardiac Output*

**Loss of Preload**
- Cardiac tamponade, atrial ball thrombi, atrial myxoma, atrioventricular (AV) valve stenosis, hypovolemia, diuretics

**Obstruction to Flow**
- Aortic and subaortic stenosis, pulmonic stenosis, pulmonary hypertension, pulmonary thromboembolism, outflow tract tumors, myocardial infarction, hypertropic and restrictive cardiomyopathy, systolic anterior motion of mitral valve, infundibular stenosis, heartworm disease

**Arrhythmias**
- Bradyarrhythmias: sick sinus syndrome, third-degree AV block, persistent atrial standstill, β-blockers, calcium channel blockers
- Tachyarrhythmias: atrial fibrillation, atrial tachycardia, AV reentrant tachycardia, ventricular tachycardia, drug-induced proarrhythmia, torsades de pointes

**Loss of Vascular Resistance**
- Drug therapy: angiotensin-converting enzyme (ACE) inhibitors, β-blockers, calcium channel blockers, hydralazine, nitrates, β-blockers, phenothiazines
- Reflex syncope (neurally mediated): orthostatic, postexertion, micturition, defecation, cough, emotional distress, pain, carotid sinus hypersensitivity
- Autonomic nervous system disease: primary or secondary (diabetes mellitus, paraneoplastic, chronic renal failure, autoimmune disease, amyloidosis)
- Cyanotic heart disease (tetralogy of Fallot, reversed shunt)
Tachycardia, Sinus
Anxiety/fear
Excitement
Exercise
Pain
Hyperthyroidism
Heart failure
Hyperthermia/fever
Anemia
Hypoxia
Shock
Hypotension
Sepsis
Drugs (anticholinergics, sympathomimetics)
Toxicity (e.g., chocolate, amphetamines, theophylline)
Electric shock
Any cause of high sympathetic tone

Tenesmus and Dyschezia

Colonic or Rectal Obstruction
Constipation
Pelvic fracture
Rectal neoplasia
Extraluminal neoplasia
Prostatomegaly
Perineal hernia
Pelvic canal mass
Rectal granuloma
Rectal foreign body
Rectal stricture

Perineal Inflammation or Pain
Anal sacculitis
Perianal fistula
Perianal abscess/abscessed anal sac

Rectal Inflammation or Pain
Rectal tumor/polyp
Proctitis
Histoplasmosis
Pythiosis

Colonic Inflammation
Idiopathic colitis
Bacteria
Fungal
Parasites
Dietary indiscretion
Inflammatory bowel disease
Neoplasia

**Tremor**

**Physiologic Tremor**
- Hypothermia
- Heavy exercise/exhaustion

**Pathologic Tremor**
- Metabolic disorders (renal disease, hypoglycemia, hypocalcemia, hypoadrenocorticism)
- Intracranial infectious disease (*Neospora caninum*, cerebellar hypoplasia secondary to intrauterine panleukopenia infection)
- Intracranial disease (fibrinoid leukodystrophy, neuraxonal dystrophy, Labrador Retriever axonopathy, spongiform encephalopathy, neuronal abiotrophies, subacute necrotizing encephalopathy, lysosomal storage diseases)
- Hind end tremor (intervertebral disk herniation, tumors, diskospondylitis, nerve root compression, peripheral neuropathies)
- Corticoid-responsive tremor syndrome (formerly “white shaker disease”)
- Myasthenia gravis
- Cerebellar malformation
- Hypomyelination
- Spong degeneration
- Tremorgenic toxins (mycotoxins penitrem A and roquefortine produced by *Penicillium* spp. growing on spoiled foods; metaldehyde, hexachlorophene, bromethalin, organophosphates, carbamates, pyrethroids, xanthines, macadamia nuts, strychnine)
- Idiopathic head tremor in Doberman Pinschers and Bulldogs
- Idiopathic tremor of hind legs of geriatric dogs

**Urine, Discolored**

**Red, Pink, Red-Brown, Red-Orange, or Orange**
- Hematuria
- Hemoglobinuria
- Myoglobinuria
- Porphyrinuria
- Pyuria
### Orange-Yellow
- Highly concentrated urine
- Urobilin
- Bilirubin

### Yellow-Brown or Green-Brown
- Bile pigments

### Brown to Black
- Melanin
- Methemoglobin
- Myoglobin
- Bile pigments

### Brown
- Methemoglobin
- Melanin

### Colorless
- Dilute urine

### Milky White
- Lipid
- Pyuria
- Crystals

### Pale Yellow
- Normal
- Dilute urine

### Urticaria/Angioedema

#### Immediate Hypersensitivity Reaction
- Insect bites/stings
- Food
- Drugs/vaccines
- Airborne allergens (atopy)

#### Nonimmunologic Stimulus by Irritant
- Weeds
- Insects
- Physical stimuli (cold, heat, sunlight)
- Psychogenic stimuli

### Vision Loss, Sudden
*See Blindness.*
Vomiting

**Gastric Disease**

- Gastritis
- Parasites
- Foreign body
- Obstruction
- Ulceration
- Neoplasia
- Dilatation/volvulus
- *Helicobacter* infection
- Gastric ulcer
- Hiatal hernia
- Motility disorders
- Pyloric stenosis
- Gastric antral mucosal hypertrophy

**Small Intestinal Disease**

- Parasites
- Inflammatory bowel disease
- Foreign body
- Bacterial overgrowth/enteritis
- Hemorrhagic gastroenteritis
- Neoplasia
- Viral enteritis (parvovirus, canine distemper virus)
- Intussusception
- Nonneoplastic infiltrative disease (e.g., pythiosis)

**Large Intestinal Disease**

- Colitis
- Obstruction
- Parasites

**Dietary**

- Indiscretion
- Intolerance
- Allergy

**Drugs**

- Cancer chemotherapeutic agents
- Antibiotics (especially erythromycin, tetracycline)
- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Cardiac glycosides
- Apomorphine
- Xylazine
- Penicillamine
Extraalimentary Tract Disease

- Peritonitis
- Pancreatitis
- Hepatobiliary disease
- Neoplasia
- Uremia
- Diabetes mellitus/ketoacidosis
- Hyperthyroidism
- Hypoadrenocorticism
- Hepatic disease
- Hepatic encephalopathy
- Septicemia/endotoxemia
- Pyometra
- Acid-base disorders
- Electrolyte disorders
- Hypertriglyceridemia
- Gastrinoma (Zollinger-Ellison syndrome)
- Mastocytosis

Intoxicants

Numerous inorganic, organic, and plant toxins can cause gastrointestinal irritation and vomiting.

Neurologic Disease

- Epilepsy, tumor, meningitis, increased intracranial pressure, dysautonomia

Weakness

Very nonspecific clinical sign of disease
Metabolic disease
Inflammation
- Infectious disease (bacterial, viral, fungal, rickettsial, protozoal, parasitic)
- Immune-mediated disease
Fever
Electrolyte disorders
- Hypokalemia, hyperkalemia, hyponatremia, hypernatremia, hypocalcemia, hypomagnesemia
Acid-base disorders
Anemia
Poor oxygen delivery
Endocrine disease
- Diabetes mellitus, hypothyroidism, hypoadrenocorticism, hyperadrenocorticism, hypoglycemia, hyperparathyroidism, hypoparathyroidism, pheochromocytoma

Cardiovascular disease
Hypotension, hypertension

Respiratory disease

Neuromuscular disease
- Brain disease (encephalitis, cerebrovascular accidents, space-occupying lesions, vestibular disease, idiopathic epilepsy)
- Spinal cord diseases
- Neuropathies (e.g., polyradiculoneuritis, myasthenia gravis, developmental disorders, toxoplasmosis, neosporosis)

Neoplasia
Cachexia

Physical and psychologic stress
Malnutrition
Drugs
- Anticonvulsants, antihistamines, glucocorticoids, tranquilizers, narcotics, cardiac drugs

Toxins
Pain

**Weight Gain**

*See Obesity.*

**Weight Loss**

*See Cachexia and Muscle Wasting.*
Systemic Approach to Differential Diagnosis

Section I  Cardiopulmonary Disorders
Section II  Dermatologic Disorders
Section III  Endocrinologic and Metabolic Disorders
Section IV  Gastroenterologic Disorders
Section V  Hematologic Disorders
Section VI  Immunologic and Immune-Mediated Disorders
Section VII  Infectious Disease
Section VIII  Joint and Bone Disorders
Section IX  Liver and Exocrine Pancreatic Disorders
Section X  Neoplasia
Section XI  Neurologic and Neuromuscular Disorders
Section XII  Ocular Disorders
Section XIII  Toxicology
Section XIV  Urogenital Disorders
Section XV  Pain Diagnosis
SECTION I

Cardiopulmonary Disorders

Arrhythmias
Arterial Thromboembolism
Aspiration Pneumonia
Atrioventricular Valve Disease, Chronic (Mitral or Tricuspid Valve)
Cardiomegaly
Chylothorax
Congenital Heart Disease
Heart Failure
Heartworm Disease
Hypertension
Laryngeal and Pharyngeal Disease
Lower Respiratory Tract Disease
Mediastinal Disease
Myocardial Diseases
Murmurs
Pericardial Effusion
Pleural Effusion
Pulmonary Disease
Pulmonary Edema
Pulmonary Thromboembolism
Tachycardia, Sinus

Arrhythmias

Differential Diagnosis

Slow, Irregular Rhythms
  Sinus bradyarrhythmias
  Sinus arrest
  Sick sinus syndrome
  High-grade second-degree atrioventricular (AV) block

Slow, Regular Rhythms
  Sinus bradycardia
  Complete AV block with ventricular escape rhythm
  Atrial standstill with ventricular escape rhythm

Fast, Irregular Rhythms
  Atrial or supraventricular premature contractions
  Paroxysmal atrial or supraventricular tachycardia
  Atrial flutter
SECTION I  Cardiopulmonary Disorders

Atrial fibrillation
Ventricular premature contractions
Paroxysmal ventricular tachycardia

Fast, Regular Rhythms
Sinus tachycardia
Sustained supraventricular tachycardia
Sustained ventricular tachycardia

Normal, Irregular Rhythms (require no treatment)
Respiratory sinus arrhythmia
Wandering pacemaker

Arterial Thromboembolism

Clinical Findings

Acute Limb Paresis
Posterior paresis (“saddle” thrombus: most common presentation)
Monoparesis (right subclavian artery thrombus; second most common presentation in cats)
Intermittent claudication
Severe limb pain
Cool distal limbs
Cyanotic nail beds
Arterial pulse absent
Contracture of affected muscles
Vocalization (pain, distress)

Renal Infarction
Renal pain
Acute renal failure

Splanic Infarction
Lethargy
Anorexia
Vomiting
Diarrhea

Mesenteric Infarction
Abdominal pain
Vomiting
Diarrhea

Cerebral Infarction
Neurologic deficits
Seizures
Sudden death
Signs of Heart Failure
- Systolic murmur
- Gallop rhythm
- Tachypnea/dyspnea
- Weakness/lethargy
- Anorexia
- Arrhythmias
- Hypothermia
- Cardiomegaly
- Effusions
- Pulmonary edema

Hematologic and Biochemical Abnormalities
- Azotemia
- Increased alanine aminotransferase activity
- Increased aspartate aminotransferase activity
- Increased lactate dehydrogenase activity
- Increased creatine kinase activity
- Hyperglycemia
- Lymphopenia
- Disseminated intravascular coagulation

Aspiration Pneumonia

Etiology of Aspiration Pneumonia

Esophageal Disorders
- Megaeosophagus
- Reflux esophagitis
- Esophageal obstruction
- Myasthenia gravis (localized)
- Bronchoesophageal fistulae

Localized Oropharyngeal Disorders
- Cleft palate
- Cricopharyngeal motor dysfunction
- Laryngoplasty
- Brachycephalic airway syndrome

Systemic Neuromuscular Disorders
- Myasthenia gravis
- Polyneuropathy
- Polymyopathy

Decreased Mentation
- General anesthesia
- Sedation
- Post ictus
Head trauma
Severe metabolic disease

**Iatrogenic**
- Force-feeding
- Stomach tubes

**Vomiting (in combination with other predisposing factors)**

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### Atrioventricular Valve Disease, Chronic (Mitral or Tricuspid Valve)

**Potential Complications**

#### Acute Worsening of Pulmonary Edema

- Arrhythmias
  - Frequent atrial premature contractions
  - Paroxysmal atrial/supraventricular contractions
  - Atrial fibrillation
  - Ventricular tachyarrhythmias
- Ruptured chordae tendineae
- Iatrogenic volume overload
  - Excessive fluid or blood administration
  - High-sodium fluids
- High sodium intake
- Increased cardiac workload
  - Physical exertion
  - Anemia
  - Infection/sepsis
  - Hypertension
  - Disease of other organ systems (pulmonary, hepatic, renal, endocrine)
  - Environmental stress (heat, humidity, cold, etc.)
- Inadequate medication for stage of disease
- Erratic or improper drug administration
- Myocardial degeneration and poor contractility

#### Causes of Reduced Cardiac Output

- Arrhythmias
- Ruptured chordae tendineae
- Cough-related syncope
- Left atrial tear, intrapericardial bleeding, cardiac tamponade
- Secondary right-sided heart failure
- Myocardial degeneration, poor contractility
## Cardiomegaly

### Differential Diagnosis

**Generalized Cardiomegaly**
- Dilated cardiomyopathy
- Pericardial effusion
- Mitral and tricuspid valve insufficiency
- Tricuspid dysplasia
- Pericardioperitoneal diaphragmatic hernia
- Ventricular septal defect
- Patent ductus arteriosus

**Left Atrial Enlargement**
- Mitral valve insufficiency
- Hypertrophic cardiomyopathy
- Early dilated cardiomyopathy (especially in Doberman Pinschers)
- Subaortic or aortic stenosis

**Left Atrial and Ventricular Enlargement**
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Mitral valve insufficiency
- Aortic valve insufficiency
- Ventricular septal defect
- Patent ductus arteriosus
- Subaortic or aortic stenosis
- Systemic hypertension
- Hyperthyroidism

**Right Atrial and Ventricular Enlargement**
- Advanced heartworm disease
- Chronic severe pulmonary disease
- Tricuspid valve insufficiency
- Atrial septal defect
- Pulmonic stenosis
- Tetralogy of Fallot
- Reversed-shunting congenital defects
- Pulmonary hypertension
- Mass lesion within right heart

## Chylothorax

### Diagnostic Criteria

Protein concentration is greater than 2.5 g/dL
Nucleated cell count ranges from 400 to 10,000/μL
Predominant cell type on cytology is the small lymphocyte (also see neutrophils, macrophages, plasma cells, and mesothelial cells)
Triglyceride concentration of pleural fluid is greater than that of serum (definitive test)

**Causes of Chylothorax**

**Traumatic**
- Blunt force trauma (e.g., vehicular trauma)
- Postthoracotomy

**Nontraumatic**
- Neoplasia (especially mediastinal lymphoma in cats)
- Cardiomyopathy
- Dirofilariasis
- Pericardial disease
- Other causes of right heart failure
- Lung lobe torsion
- Diaphragmatic hernia
- Systemic lymphangiectasia

**Idiopathic** (most commonly diagnosed)

**Diagnostic Tests to Identify Underlying Cause of Chylothorax in Dogs and Cats**

**CBC, Serum Chemistry, Urinalysis**
- Evaluation of systemic status

**Cytologic Examination of Pleural Fluid**
- Infectious agents
- Neoplastic cells

**Thoracic Radiographs (after fluid removal)**
- Cranial mediastinal masses
- Other neoplasia
- Cardiac disease
- Heartworm disease
- Pericardial disease

**Ultrasonography (before fluid removal)**
- Cranial mediastinum (masses)
- Echocardiography (cardiomyopathy, heartworm disease, pericardial disease, congenital heart disease)
- Ultrasound of body wall and pleural space (neoplasia, lung lobe torsion)

**Heartworm Antibody and Antigen Tests**
- Heartworm disease
Lymphangiography
  • Preoperative and postoperative assessment of thoracic duct

**Congenital Heart Disease**

**Breed Predispositions**

**Patent Ductus Arteriosus**
Maltese, Pomeranian, Shetland Sheepdog, English Cocker Spaniel, English Springer Spaniel, Keeshond, Bichon Frise, toy and miniature Poodle, Yorkshire Terrier, Collie, Cocker Spaniel, German Shepherd, Chihuahua, Kerry Blue Terrier, Labrador Retriever, Newfoundland; female affected more than male

**Subaortic Stenosis**
Newfoundland, Golden Retriever, Rottweiler, Boxer, German Shepherd, English Bulldog, Great Dane, German Shorthaired Pointer, Bouvier des Flandres, Samoyed

**Aortic Stenosis**
Bull Terrier

**Pulmonic Stenosis**
English Bulldog (male affected more than female), Mastiff, Samoyed, Miniature Schnauzer, Newfoundland, West Highland White Terrier, Cocker Spaniel, Beagle, Basset Hound, Airedale Terrier, Boykin Spaniel, Chihuahua, Scottish Terrier, Boxer, Fox Terrier, Chow Chow, Labrador Retriever, Schnauzer

**Atrial Septal Defect**
Samoyed, Doberman Pinscher, Boxer

**Ventricular Septal Defect**
English Bulldog, English Springer Spaniel, Keeshond, West Highland White Terrier, cats

**Tricuspid Dysplasia**
Labrador Retriever, German Shepherd, Boxer, Weimaraner, Great Dane, Old English Sheepdog, Golden Retriever, various other large breeds

**Mitral Dysplasia**
Bull Terrier, German Shepherd, Great Dane, Golden Retriever, Newfoundland, Mastiff, Rottweiler, cats

**Tetralogy of Fallot**
Keeshond, English Bulldog

**Persistent Right Aortic Arch**
German Shepherd, Great Dane, Irish Setter
Cor Triatriatum
Medium- to large-breed dogs (Chow Chow), rarely small-breed dogs or cats

Peritoneopericardial Diaphragmatic Hernia
Weimaraner

Heart Failure

Causes of Chronic Heart Failure

Left-Sided Heart Failure

Volume-Flow Overload
Mitral valve regurgitation (degenerative, congenital, infective)
Aortic regurgitation (infective endocardiosis, congenital)
Ventricular septal defect
Patent ductus arteriosus

Myocardial Failure
Myocardial ischemia/infarction
Drug toxicity (e.g., doxorubicin)

Pressure Overload
Aortic/subaortic stenosis
Systemic hypertension

Restriction of Ventricular Filling
Hypertrophic cardiomyopathy
Restrictive cardiomyopathy

Left- or Right-Sided Heart Failure

Myocardial Failure
Idiopathic dilated cardiomyopathy
Infective myocarditis

Volume-Flow Overload
Chronic anemia
Thyrotoxicosis

Right-Sided Heart Failure

Volume-Flow Overload
Tricuspid endocarditis
Tricuspid endocardiosis
Tricuspid dysplasia

Pressure Overload
Pulmonic stenosis
Heartworm disease
Pulmonary hypertension
Restriction to Ventricular Filling
Cardiac tamponade
Constrictive pericardial disease

Severity

Classification Systems

New York Heart Association Functional Classification

Class I: Heart disease present, but no evidence of heart failure or exercise intolerance; cardiomegaly minimal to absent

Class II: Signs of heart disease with evidence of exercise intolerance; radiographic cardiomegaly present

Class III: Signs of heart failure with normal activity or signs at night (e.g., cough, orthopnea); radiographic signs of significant cardiomegaly and pulmonary edema or pleural/abdominal effusion

Class IV: Severe heart failure with clinical signs at rest or with minimal activity; marked radiographic signs of congestive heart failure (CHF) and cardiomegaly

Forrester Classification

Class I: Normal cardiac output and pulmonary venous pressure

Class II: Pulmonary congestion but normal cardiac output

Class III: Low cardiac output and peripheral hypoperfusion with no pulmonary congestion

Class IV: Low cardiac output with pulmonary congestion

Clinical Findings

Low-Output Signs
Exercise intolerance
Syncope
Weak arterial pulses
Tachycardia
Arrhythmias
Cold extremities
Prerenal azotemia
Cyanosis

Signs Related to Poor Skeletal Muscle Function
Weight loss
Exercise intolerance
**Dyspnea**
Decreased muscle mass

**Signs Related to Fluid Retention**

**Left-Sided Heart Failure (Pulmonary Edema)**
- Dyspnea/orthopnea
- Exercise intolerance
- Wet lung sounds
- Tachypnea
- Gallop rhythm
- Functional mitral regurgitation
- Cyanosis
- Cough

**Right-Sided Heart Failure**
- Ascites
- Subcutaneous edema
- Jugular distension/pulsation
- Hepatomegaly
- Splenomegaly
- Hepatojugular reflux
- Gallop rhythm
- Cardiac arrhythmias

**Bilateral Signs**
- Pleural effusion (dyspnea, muffled heart sounds, cough)

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**Heartworm Disease**

**Clinical Findings**

**Historical Findings**
- Asymptomatic
- Cough
- Dyspnea
- Weight loss
- Lethargy
- Exercise intolerance
- Poor condition
- Syncope
- Abdominal distension (ascites)

**Physical Findings**
- Weight loss
- Right-sided murmur (tricuspid insufficiency)
- Split-second heart sound
- Gallop rhythm
- Cough
Pulmonary crackles
Dyspnea
Muffled breath sounds
Cyanosis
Right-sided heart failure
  • Jugular distension/pulsation
  • Hepatosplenomegaly
  • Ascites
Pulmonary thromboembolism
  • Dyspnea/tachypnea
  • Fever
  • Hemoptysis
Cardiac arrhythmias/conduction disturbances (rare)
Caval syndrome
  • Hemoglobinuria
  • Anemia
  • Disseminated intravascular coagulation (DIC)
  • Icterus
  • Collapse/death

Clinicopathologic Findings
  Eosinophilia
  Nonregenerative anemia
  Neutrophilia
  Basophilia
  Proteinuria
  Hyperbilirubinemia
  Azotemia
  Thrombocytopenia

Radiographic Signs
  Right ventricular enlargement
  Prominent main pulmonary artery segment
  Increased pulmonary artery size
  Tortuous pulmonary vessels
  Caudal vena cava enlargement
  Hepatosplenomegaly
  Ascites
  Pleural effusion
  Bronchial/interstitial lung disease

Diagnosis in Dogs
  *Antigen Test Positive and Modified Knott's or Filter Test Negative*
  • Perform complete blood count, serum chemistry panel, urinalysis, thoracic radiography
  • Start preventative and adulticidal therapy
• Antigen test positive and Modified Knott’s or filter test positive
• Perform complete blood count, serum chemistry panel, urinalysis, and thoracic radiography
• Start “slow kill” macrolide and adulticidal therapy

**Antigen Test Negative**
• No infection or low heartworm burden
• Start preventative

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**Hypertension**

**Pulmonary Hypertension**

**Potential Clinical Signs**
- Ascites
- Jugular venous distension/pulsation
- Subcutaneous edema
- Cachexia
- Nonspecific respiratory signs
  - Coughing
  - Tachypnea
  - Respiratory distress
  - Increased bronchovesicular sounds
  - Hemoptysis
- Cyanosis
  - Right-to-left cardiac shunts
  - Severe respiratory disease
- Split or loud pulmonic component to second heart sound
- Right or left apical systolic murmurs (tricuspid or mitral regurgitation)

**Radiographic Signs**
- Cardiomegaly
- Right ventricular enlargement
- Dilated central pulmonary arteries with tapering toward periphery
- Eisenmenger complex (pulmonary undercirculation and right-sided heart enlargement)
- Left atrial enlargement and perihilar to caudodorsal pulmonary infiltrates (left-sided congestive heart failure)

**Echocardiographic Signs**
- Right ventricular concentric hypertrophy and dilation
- Main pulmonary artery and main branch dilation
- Systolic flattening of interventricular septum
Paradoxical septal motion
Reduced left ventricular dimensions in severe pulmonary hypertension caused by ventricular underfilling

**Laboratory Values**
Acidosis
Rule out heartworm disease

**Systemic Hypertension**

**Causes of Systemic Hypertension in Dogs and Cats**
Renal failure (chronic or acute)
Hyperadrenocorticism
Diabetes mellitus
Pheochromocytoma
Hyperthyroidism
Liver disease
Hyperaldosteronism
Intracranial lesions (↑ intracranial pressure)
High-salt diet
Obesity
Chronic anemia (cats)

**Clinical Signs of Systemic Hypertension**

**Ocular Findings**
Hypertensive choroidopathy (edema, vascular tortuosity, hemorrhage, focal ischemia)
Hypertensive retinopathy (edema, vascular tortuosity, hemorrhage, focal ischemia, atrophy)
Intraocular hemorrhage (retinal, vitreal, hyphema)
Papilledema
Blindness
Glaucoma
Secondary corneal ulcers

**Neurologic Findings**
Edema (↑ intracranial pressure)
Hypertensive encephalopathy (lethargy, behavioral changes)
Cerebrovascular accident (focal ischemia, hemorrhage)
Seizures/collapse

**Renal**
Polyuria/polydipsia
Glomerulosclerosis/proliferative glomerulitis
Renal tubular degenerative and fibrosis
Further deterioration in renal function
**Cardiac**
- Left ventricular hypertrophy
- Murmur or gallop sound
- Aortic dilation
- Aneurysm or dissection rare

**Other**
- Epistaxis

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**Laryngeal and Pharyngeal Disease**

**Differential Diagnosis**
- Laryngeal paralysis
- Brachycephalic airway syndrome
- Acute laryngitis
- Laryngeal neoplasia
- Nasopharyngeal polyp
- Abscess
- Tonsillitis
- Pharyngitis
- Obstructive laryngitis
- Laryngeal collapse
- Trauma
- Foreign body
- Extrapulmonary mass
- Elongated soft palate
- Cleft palate
- Soft palate hypoplasia
- Pharyngeal neoplasia
- Granuloma
- Pharyngeal mucoceles
- Web formation
- Nasopharyngeal stenosis

**Causes of Laryngeal Paralysis**

**Idiopathic**

**Polyneuropathy and Polymyopathy**
- Idiopathic
- Immune-mediated
- Endocrinopathy
  - Hypothyroidism
  - Hypoadrenocorticism
- Toxicity
- Congenital disease
Ventral Cervical Lesion
Nerve trauma
- Direct trauma
- Inflammation
- Fibrosis
Neoplasia
Other inflammatory or mass lesion

Anterior Thoracic Lesion
Neoplasia
Trauma
- Postoperative
- Other
Other inflammatory or mass lesion

Myasthenia Gravis

Lower Respiratory Tract Disease
Differential Diagnosis

Disorders of Trachea and Bronchi
- Canine infectious tracheobronchitis
- Collapsing trachea
- Bacterial infection
- Mycoplasmal infection
- Bronchial asthma
- Neoplasia
- Allergic bronchitis
- Feline bronchitis
- Bronchial compression
  - Left atrial enlargement
  - Hilar lymphadenopathy
- Acute bronchitis
- Canine chronic bronchitis/bronchiectasis
- Parasites (Oslerus osleri, Filaroides osleri)
- Tracheal tear
- Primary ciliary dyskinesia
- Airway foreign body
- Chronic aspiration

Disorders of Pulmonary Parenchyma
Infectious disease
- Viral pneumonia (canine influenza, canine distemper virus, canine adenovirus, canine parainfluenza, feline calicivirus, feline infectious peritonitis, pneumonia secondary to feline leukemia virus or feline immunodeficiency virus)
• Bacterial pneumonia
• Protozoal pneumonia (toxoplasmosis)
• Fungal pneumonia (blastomycosis, histoplasmosis, coccidioidomycosis)
• Rickettsial disease (*Rickettsia rickettsii*, *Ehrlichia* spp.)
• Parasitism
  • Heartworm disease
  • Pulmonary parasites (*Paragonimus, Aelurostrongylus, Capillaria, Crenosoma* spp.)
  • Larval migration of *Toxocara canis*

Aspiration pneumonia
Pulmonary infiltrates with eosinophils
Eosinophilic pulmonary granulomatosis
Aspiration pneumonia
Pulmonary neoplasia (primary, metastatic, lymphosarcoma, lymphomatoid granulomatosis, malignant histiocytosis)
Pulmonary hypertension
Pulmonary contusions
Pulmonary thromboembolism
Pulmonary edema
Acute respiratory distress syndrome
Lung lobe torsion
Pulmonary fibrosis
Pickwickian syndrome (obesity)
Idiopathic interstitial pneumonias

### Mediastinal Disease

**Differential Diagnosis of Lesions Associated with Focal Mediastinal Enlargement**

- Pneumomediastinum
- Mediastinitis (*Histoplasma, Cryptococcus, Actinomyces, Nocardia, Spirocerca* spp.)
- Mediastinal hemorrhage
- Mediastinal cysts
- Nonneoplastic mediastinal masses (fungal pyogranulomas, abscesses, granulomas, lymphadenopathy, hematomas)
- Mediastinal neoplasia (lymphosarcoma)
- Thymoma
- Obesity
- Thymic hemorrhage
- Heart base mass
- Neurogenic tumor
- Tracheal mass
- Esophageal mass, foreign body, or dilatation
Ectopic thyroid tissue
Mediastinal edema
Vascular mass (aorta, cranial vena cava)
Paraspinal or spinal mass
Aortic stenosis
Patent ductus arteriosus
Left atrial enlargement
Main pulmonary artery mass (poststenotic dilatation)
Hiatal hernia
Diaphragmatic hernia or mass
Aortic aneurysm
Gastroesophageal intussusception
Peritoneopericardial diaphragmatic hernia

Myocardial Diseases

Differential Diagnosis, Dogs

Dilated Cardiomyopathy

*Primary (idiopathic, most common)*

Genetic (Doberman Pinscher, Boxer, Cocker Spaniel, Great Dane, Portuguese Water Dog, Newfoundland, Dalmatian, Irish Wolfhound)

*Secondary*

Nutritional Deficiencies

L-Carnitine (Boxer, Doberman Pinscher, Great Dane, Irish Wolfhound, Newfoundland, Cocker Spaniel)
Taurine

Myocardial Infection

Viral myocarditis (acute viral infections, e.g., parvovirus)
Bacterial myocarditis (secondary to bacteremia from infections elsewhere in body)
Lyme disease: *Borrelia burgdorferi*
Protozoal myocarditis (*Trypanosoma cruzi [Chagas disease], Toxoplasma gondii, Neospora caninum, Babesia canis, Hepatozoon canis*)
Fungal myocarditis (rare, *Aspergillus, Cryptococcus, Coccidioides, Histoplasma, Paecilomyces* spp.)
Rickettsial myocarditis (rare, *Rickettsia rickettsii, Ehrlichia canis, Bartonella* spp.)
Algae-like organisms (rare, *Prototheca* spp.)
Nematode larval migration (*Toxocara* spp.)
SECTION I Cardiopulmonary Disorders

Trauma
Ischemia
Infiltrative Neoplasia
Hyperthermia
Irradiation
Electric Shock
Cardiotoxins
  Doxorubicin; ethyl alcohol; plant toxins such as foxglove, black locust, buttercup, lily of the valley, and gossypol; cocaine; anesthetic drugs; catecholamines; monensin

Hypertrophic Cardiomyopathy (uncommon in dogs)

Arrhythmogenic Right Ventricular Cardiomyopathy (rare)

Noninfective Myocarditis
  Catecholamines; heavy metals; antineoplastic drugs (doxorubicin, cyclophosphamide, 5-fluorouracil, interleukin-2, interferon-α); stimulant drugs (thyroid hormone, cocaine, amphetamines, lithium)
  Immune-mediated diseases, pheochromocytoma
  Wasp and scorpion stings, snake venom, spider bite

Differential Diagnosis, Cats

Hypertrophic Cardiomyopathy
  Primary (Idiopathic)
    Maine Coon, Persian, Ragdoll, and American shorthair may be predisposed.
  Secondary
    Hyperthyroidism
    Hypersomatotropism (acromegaly)
    Infiltrative myocardial disease (lymphoma)

Restrictive Cardiomyopathy

Dilated Cardiomyopathy
  Taurine-deficient diets
  Doxorubicin
  End stage of other myocardial metabolic, toxic, or infectious process

Arrhythmogenic Right Ventricular Cardiomyopathy

Myocardiitis
  Viral (coronavirus, other viruses)
Bacterial (bacteremia, *Bartonella* spp.)
Protozoal (*Toxoplasma gondii*)

## Murmurs

### Clinical Findings

#### Systolic Murmurs

- Functional murmurs (point of maximal impulse [PMI] over left-sided heart base, decrescendo or crescendo-decrescendo)
  - Innocent puppy murmurs
  - Physiologic murmurs (anemia, fever, high sympathetic tone, hyperthyroidism, peripheral arteriovenous fistula, marked bradycardia, hypoproteinemia, athletic heart)

- Mitral valve insufficiency (left apex, typically holosystolic)

- Ejection murmurs (typically left-sided heart base)
  - Subaortic stenosis (low left base and right base)
  - Pulmonic stenosis (high left base)
  - Dynamic muscular obstruction

- Right-sided murmurs (usually holosystolic)
  - Tricuspid insufficiency (right apex, may see jugular pulse)
  - Ventricular septal defect (PMI over right sternal border)

#### Diastolic Murmurs

- Aortic insufficiency from bacterial endocarditis (left-sided heart base)
  - Aortic valve congenital malformations (left base)
  - Aortic valve degenerative disease (left base)
  - Pulmonic insufficiency (left base)

#### Continuous Murmurs

- Patent ductus arteriosus (PMI high left base above pulmonic area)

#### Concurrent Systolic and Diastolic Murmurs (To-and-Fro Murmurs)

- Subaortic stenosis with aortic insufficiency
- Pulmonic stenosis with pulmonic insufficiency

### Grading

**Grade 1**: Very soft murmur; heard only in quiet surroundings after minutes of listening
**Grade II:** Soft murmur but easily heard  
**Grade III:** Moderate-intensity murmur  
**Grade IV:** Loud murmur; no precordial thrill  
**Grade V:** Loud murmur with palpable precordial thrill  
**Grade VI:** Very loud murmur; can be heard with stethoscope off chest wall; palpable precordial thrill

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**Pericardial Effusion**

**Differential Diagnosis**

**Bacterial Pericarditis**  
Secondary to foxtail (*Hordeum* spp.) migration  
Secondary to penetrating animal bite  
Disseminated tuberculosis

**Fungal Pericarditis**  
Coccidioidomycosis  
Aspergillosis  
Actinomycosis

**Viral Pericarditis**  
Feline infectious peritonitis (FIP)  
Canine distemper virus

**Protozoal Pericarditis**  
Toxoplasmosis  
Other systemic protozoal infections

**Left Atrial Rupture (Secondary to Mitral Valve Disease)**

**Neoplasia**  
Hemangiosarcoma  
Mesothelioma  
Heart base tumor (aortic body tumor or chemodectoma, ectopic thyroid tumor, ectopic parathyroid tumor, connective tissue neoplasms)  
Lymphomasarcoma  
Rhabdomyosarcoma

**Other**  
Penetrating trauma  
Pericardioperitoneal diaphragmatic hernia  
Hypoalbuminemia  
Pericardial cyst  
Coagulation disorders  
Congestive heart failure  
Uremia  
Idiopathic
Pleural Effusion

Differential Diagnosis

Transudates and Modified Transudates
- Right-sided heart failure
- Pericardial disease
- Hypoalbuminemia
- Neoplasia
- Diaphragmatic hernia

Nonseptic Exudates
- Feline infectious peritonitis (FIP)
- Neoplasia
- Diaphragmatic hernia
- Lung lobe torsion

Septic Exudates
- Pyothorax

Chylous Effusion
- Chylothorax

Hemorrhage
- Trauma
- Bleeding disorder
- Neoplasia
- Lung lobe torsion

Diagnostic Approach in Dogs and Cats with Pleural Effusion Based on Fluid Type

Pure and Modified Transudates
- Right-sided heart failure, pericardial effusion (evaluate pulses, auscultation, ECG, thoracic radiography, echocardiography)
- Hypoalbuminemia (serum albumin concentration)
- Neoplasia, diaphragmatic hernia (thoracic radiography, thoracic ultrasound, CT, thoracoscopy, thoracotomy)

Nonseptic Exudates
- Feline infectious peritonitis (pleural fluid cytology [most reliable test], CBC, serum chemistry, ophthalmoscopic examination, serum or fluid electrophoresis, coronavirus antibody titer, PCR of tissues or effusion)
- Neoplasia, diaphragmatic hernia (thoracic radiography, thoracic ultrasound, CT, thoracoscopy, thoracotomy)
- Lung lobe torsion (thoracic radiography, ultrasound, bronchoscopy, thoracotomy)
**Septic Exudates**
- Pyothorax (Gram stain, aerobic and anaerobic culture, cytology)

**Chylous Effusion**
- Chylothorax (protein concentration, nucleated cell count, cytology, triglyceride)

**Hemorrhagic**
- Trauma (history)
- Bleeding disorder (systemic examination, coagulation tests, platelet count)
- Neoplasia (thoracic radiography, thoracic ultrasound, CT, thoracoscopy, thoracotomy)
- Lung lobe torsion (thoracic radiography, ultrasound, bronchoscopy, thoracotomy)

**Pulmonary Disease**

**Differential Diagnosis Based on Radiographic Patterns**

**Alveolar Pattern**
- Pulmonary edema (cardiogenic or noncardiogenic)
- Infectious pneumonia (bacterial, parasitic, protozoal, viral)
- Aspiration pneumonia
- Atelectasis
- Drowning
- Smoke inhalation
- Hemorrhage
  - Neoplasia (primary and metastatic)
  - Fungal pneumonia (severe)
  - Pulmonary contusion
  - Thromboembolic disease
  - Systemic coagulopathy

**Bronchial Pattern**
- Feline bronchitis/asthma
- Allergic bronchitis
- Bacterial bronchitis
- Canine chronic bronchitis
- Bronchiectasis
- Pulmonary parasites
- Bronchial calcification

**Vascular Pattern**

*Enlarged Arteries*
- Heartworm disease
Thromboembolic disease
Pulmonary hypertension

**Enlarged Veins**
Left-sided heart failure

**Enlarged Arteries and Veins (Pulmonary Overcirculation)**

**Left-to-Right Shunts**
Patent ductus arteriosus
Ventricular septal defect
Atrial septal defect

**Small Arteries and Veins**
Pulmonary Undercirculation
Cardiovascular shock
Hypovolemia
  - Severe dehydration
  - Blood loss
  - Hypoadrenocorticism
Pulmonic valve stenosis

Hyperinflation of Lungs
Feline bronchitis
Allergic bronchitis

**Nodular Interstitial Pattern**
Mycotic infection
  - Blastomycosis
  - Histoplasmosis
  - Coccidioidomycosis
Neoplasia
Pulmonary parasites
  - Aelurostrongylus infection
  - Paragonimus infection
Pulmonary abscess
  - Bacterial pneumonia
  - Foreign body
Pulmonary infiltrates with eosinophils
Miscellaneous inflammatory diseases
Inactive lesions

**Reticular Interstitial Patterns**
Infection
  - Viral pneumonia
  - Bacterial pneumonia
  - Toxoplasmosis
  - Mycotic pneumonia
Parasitic infestation
Neoplasia
Pulmonary fibrosis
Pulmonary infiltrates with eosinophils
Miscellaneous inflammatory diseases
Hemorrhage (mild)
Old dog lung

**Pulmonary Edema**

**Causes**

**Vascular Overload**
Cardiogenic
- Left-sided heart murmur
- Left-to-right shunt
Overhydration

**Decreased Plasma Oncotic Pressure**
Hypoalbuminemia
- Gastrointestinal loss
- Renal loss (glomerular disease)
- Liver disease (lack of production)
- Iatrogenic overhydration

**Increased Vascular Permeability**
Sepsis
Shock
Drugs or toxins
Snake envenomation
Cisplatin (cats)
Trauma
- Pulmonary
- Multisystemic
Inhaled toxins
- Smoke inhalation
- Gastric acid aspiration
- Oxygen toxicity
Electrocution
Pancreatitis
Uremia
Virulent babesiosis
Disseminated intravascular coagulation
Inflammation/Vasculitis

**Other Causes**
Thromboembolism
Postobstruction (strangulation, laryngeal paralysis, pulmonary reexpansion)
Near-drowning
Neurogenic edema
• Seizures
• Head trauma
Lung lobe torsion
Bacterial pneumonia
Pulmonary contusion
Hyperoxia
High altitude
Air embolus
Pheochromocytoma

Lymphatic Obstruction (rare)
Neoplasia

**Pulmonary Thromboembolism**

**Causes**

Embolization of Thrombi (any condition that predisposes to venous stasis, endothelial injury, and hypercoagulability)
- Heartworm disease
- Immune-mediated hemolytic anemia
- Systemic inflammatory disease
- Neoplasia
- Cardiac disease
- Cardiomyopathy
- Endocarditis
- Congestive heart failure
- Protein-losing nephropathy
- Protein-losing enteropathy
- Hyperadrenocorticism
- Pancreatitis
- Disseminated intravascular coagulation
- Anatomic abnormality (e.g., aneurysm, A-V fistula)
- Hyperviscosity (polycythemia, leukemia, hyperglobulinemia)
- Hypoviscosity (anemia)
- Sepsis
- Shock
- Intravenous catheterization
- Injection of irritating substance
- Prolonged recumbency
- Reperfusion injury
- Atherosclerosis/Arteriosclerosis
- Trauma
- Recent surgery
- Hyperhomocysteinemia
Embolization of Parasites
   Heartworm disease

Embolization of Fat

Embolization of Neoplastic Cells

Tachycardia, Sinus

Causes
   Anxiety/fear
   Excitement
   Exercise
   Pain
   Hyperthyroidism
   Hyperthermia/fever
   Anemia
   Hypoxia
   Shock
   Hypotension
   Sepsis
   Drugs (anticholinergics, sympathomimetics)
   Toxicity (e.g., chocolate, hexachlorophene)
   Electric shock
Dermatologic Disorders

Allergic Skin Disease
Alopecia, Endocrine
Claw Disorders
Erosions and Ulcerations of Skin or Mucous Membranes
Folliculitis
Otitis Externa, Chronic
Parasitic Dermatoses
Pigmentation
Pyoderma

Allergic Skin Disease

Clinical Findings

Flea Allergy

Dogs
Papular rash
Caudal distribution of lesions most common

Cats
Miliary dermatitis, especially over caudal back, around neck and chin
Eosinophilic granuloma complex

Atopy and Cutaneous Signs of Food Hypersensitivity
Signs of these two types of allergy are similar. Atopy tends to occur primarily in young adults, whereas food hypersensitivity can begin at any age. Atopy is usually seasonal at first but may become less seasonal.

Dogs
Papular rash
Pruritus and self-trauma
Lesions of face, ears, feet, and perineum
Recurrent otitis externa
Excoriation
Lichenification
Pigmentary changes
Secondary pyoderma

Cats
Miliary dermatitis
Eosinophilic dermatitis
Allergic Contact Dermatitis
Rarest of allergic dermatoses
Lesions tend to be confined to hairless or sparsely haired skin (ventral abdomen, neck, and chest; ventral paws but not pads; perineum; lateral aspect of pinnae).
*Acutely:* Erythema, macules, papules, vesicles
*Chronically:* Alopecic plaques, hyperpigmentation, hypopigmentation, excoriation, lichenification

**Alopecia, Endocrine**

**Causes**

- Hypothyroidism
- Hyperadrenocorticism
- Diabetes mellitus
- Adrenal sex hormone deficiency (Alopecia X)
- Growth hormone deficiency (pituitary dwarfism)
- Growth hormone-responsive dermatosis in adult dogs
- Castration-responsive dermatosis

**Hyperestrogenism**
- Sertoli cell tumor (male dog)
- Intact female dog

**Hypoestrogenism** (poorly understood)
- Estrogen-responsive dermatosis of spayed female dogs
- Feline endocrine alopecia

**Hypoandrogenism**
- Testosterone-responsive dermatosis (male dog)
- Feline endocrine alopecia

**Telogen defluxion** (effluvium): often after recent pregnancy or diestrus

Progestin excess (excess of progesterone or 17-hydroxyprogesterone)

**Clinical Findings**

**Nonspecific Features of Endocrine Disease**

- Bilaterally symmetric alopecia
- Follicular dilation, follicular keratosis, follicular atrophy
- Orthokeratotic hyperkeratosis
- Predominance of telogen hair follicles
- Sebaceous gland atrophy
- Epidermal atrophy
- Thin dermis
- Epidermal melanosis
- Dermal collagen atrophy
Features Suggestive of Specific Endocrine Disorder

Hypothyroidism
- Vacuolated and/or hypertrophied arrector pili muscles, increased dermal mucin content, thick dermis

Hyperadrenocorticism
- Calcinosis cutis, comedones, absence of erector pili muscles

Hyposomatotropism
- Decreased amount and size of dermal elastin fibers

Growth hormone and castration-responsive dermatoses
- Excessive trichilemmal keratinization (flame follicles)

Claw Disorders

Differential Diagnosis for Abnormal Claws

Bacterial Claw Infection—almost always secondary to an underlying cause
- Trauma—usually one claw affected
- Hypothyroidism
- Hyperadrenocorticism
- Allergies
- Autoimmune disorders
- Symmetrical lupoid onychodystrophy
- Neoplasia

Fungal Claw Infection
- Typically caused by dermatophytes

Symmetrical Lupoid Onychodystrophy
- Suspected to be immune mediated. German shepherds and Rottweilers may be predisposed. Acute onset of claw loss, initially 1-2 but eventually all claws slough. Replacement claws are misshapen, soft or brittle, discolored, and friable and usually slough again. Feet are painful and pruritic. Paronychia is uncommon unless secondary bacterial infection is present.

Drug Eruption

Vasculitis

Diagnostic Tests for Abnormal Claws
- Cytology—suppurative to pyogranulomatous inflammation with bacteria
- Bacterial culture of exudates from claw or claw fold. Mixed infections common. *Staphylococcus* spp. usually isolated
- Fungal culture—*Trichophyton* spp. most commonly isolated but may also see *Microsporum* spp. or *Malassezia* spp.
- Radiography—rule out osteomyelitis
• Dermatohistopathology—(P3 amputation), only recommended to rule out neoplasia. With symmetric lupoid onychodystrophy, see basal cell hydropic degeneration, degeneration or apoptosis of individual keratinocytes in the basal layer, pigmentary incontinence, and lichenoid interface dermatitis. Systemic lupoid onychodystrophy is most commonly diagnosed by typical history and clinical signs along with ruling out other differentials.

## Erosions and Ulcerations of Skin or Mucous Membranes

### Differential Diagnosis, Dogs

**Excoriation from Any Pruritic Skin Disease**

**Infection**

- **Bacterial Pyoderma**
  - Surface (pyotraumatic moist dermatitis, intertrigo)
  - Deep (folliculitis, furunculosis, bacterial stomatitis)

- **Fungal**
  - Yeast infection (*Malassezia pachydermatis, Candida* spp.)
  - Dermatophytosis
  - Systemic fungal infection (blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, others)
  - Subcutaneous mycoses (pythiosis, zygomycosis, phaeohyphomycosis, sporotrichosis, eumycotic mycetoma, others)

- **Parasitic**
  - Demodicosis

**Neoplasia**

- Squamous cell carcinoma
- Epitheliocytic lymphoma

**Metabolic Derangements**

- Uremia/renal failure
- Necrolytic migratory erythema
- Calcinosis cutis (hyperadrenocorticism)

**Physical/Chemical Injury**

- Drug reactions
- Urine scald
- Thermal injury (burn, freeze)
- Solar injury

**Immune-Mediated Disorders**

- Discoid lupus erythematosus (DLE)
- Pemphigus
Uveodermatologic syndrome
Miscellaneous autoimmune subepidermal vesiculobullous diseases (bullous pemphigoid, epidermolysis acquisita, linear IgA bullous disease, mucocutaneous pemphigoid, bullous systemic lupus type 1)

Miscellaneous
Arthropod bites
Dermatomyositis
Dystrophic epidermolysis bullosa, junctional epidermolysis bullosa
Idiopathic ulceration of Collies
Toxic epidermal necrolysis, erythema multiforme

Differential Diagnosis, Cats

Infection
Viral
Caliciviruses
Herpesviruses

Bacterial
Atypical mycobacterioses

Fungal
Cryptococcosis
Systemic and subcutaneous mycoses
Sporotrichosis

Neoplasia
Squamous cell carcinomas (especially white, outdoor cats)
Fibrosarcoma
Cutaneous lymphoma

Metabolic Derangements
Uremia/renal disease

Physical/Chemical Injury
Thermal
Drug reactions

Immune-Mediated Disorders
Bullous pemphigoid
Pemphigus foliaceus
Plasma cell pododermatitis
Toxic epidermal necrolysis

Inflammatory/Allergic Disorders
Eosinophilic plaque
Indolent ulcer
Arthropod bites
Miscellaneous/Idiopathic
Dystrophic epidermolysis bullosa
Idiopathic ulceration of dorsal neck
Junctional epidermolysis bullosa

Folliculitis

Differential Diagnosis

Superficial Folliculitis
Inflammation of hair follicles
- Bacterial pyoderma
- Fungal (dermatophytosis)
- Parasitic (demodicosis, *Pelodera* dermatitis)

Deep Folliculitis/Furunculosis
Inflammation of hair follicles with subsequent follicular rupture into dermis and subcutaneous tissues
- Deep pyodermas

Otitis Externa, Chronic

Primary Causes

Allergy
- Atopy
- Adverse reactions to foods
- Contact dermatitis

Parasites
- *Otodectes cynotis*
- *Notoedres cati*
- *Sarcoptes scabiei*
- *Demodex* spp.
- Chiggers
- Flies
- Ticks (spinous ear tick)

Dermatophytes

Endocrine Disorders
- Hypothyroidism

Foreign Bodies
- Foxtails, hair, etc.

Glandular Conditions
- Ceruminous gland hyperplasia
- Sebaceous gland hyperplasia or hypoplasia
- Altered type or rate of secretions
**Autoimmune Diseases**
- Systemic lupus erythematosus (SLE)
- Pemphigus foliaceus/erythematosus
- Cold agglutinin disease
- Juvenile cellulitis

**Viruses**
- Distemper

**Miscellaneous**
- Solar dermatitis
- Frostbite
- Vasculitis/vasculopathy
- Eosinophilic dermatitis
- Sterile eosinophilic folliculitis
- Relapsing polychondritis

**Predisposing Factors**

**Conformation**
- Stenotic canals
- Hair in canals
- Pendulous pinnae
- Hairy, concave pinna

**Excessive Moisture**
- Swimmer's ear
- High-humidity climate

**Excessive Cerumen Production**
- Secondary to underlying disease
- Primary (idiopathic)

**Treatment Effects**
- Trauma from cotton swabs
- Topical irritants
- Superinfections from altering microflora

**Obstructive Ear Disease**
- Polyps
- Granulomas
- Tumors

**Systemic Disease**
- Immunosuppression
- Debilitation
- Negative catabolic states
Perpetuating Factors

Bacteria (most commonly *Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas* spp., *Proteus*, *Escherichia coli*)

Yeast (*Malassezia pachydermatis*)

Progressive Pathologic Changes
- Hyperkeratosis
- Hyperplasia
- Epithelial folds
- Apocrine gland hypertrophy
- Hidradenitis
- Fibrosis

Otitis Media
- Purulent
- Caseated or keratinous
- Cholesteatoma
- Proliferative
- Destructive osteomyelitis

Parasitic Dermatoses

Classification

Fleas (*Ctenocephalides felis* most common)
- Flea infestation
- Flea allergy dermatitis
  - Caudal distribution of lesions (dogs)
  - Miliary dermatitis (cats)

Demodicosis
- Follicular infection (*Demodex canis*, *Demodex felis*)
- Epidermal infection (*Demodex gatoi*, short-tailed demodectic mite of dogs)

Sarcoptic Mange
- *Sarcoptes scabiei* (dogs, rarely cats)
- *Notoedres catti* (cats, rarely dogs)

Ear Mites
- *Otodectes cynotis* (common in both dogs and cats)

Cheyletiellosis
- *Cheyletiella yasguri* (primary host is dogs)
- *C. blakei* (primary host is cats)
C. parasitovorax (primary host is rabbits)
All Cheyletiella species freely contagious from one species to another

Chiggers
Larval stage (six-legged bright red or orange) is the parasitic stage; nymph and adult are free living.

Ticks
Brown dog tick (*Rhipicephalus sanguineus*)
American dog tick (*Dermacentor variabilis*)
Rocky Mountain wood tick (*Dermacentor andersoni*)
Lone star tick (*Amblyomma americanum*)
Deer tick (*Ixodes dammini*): primary vector of *Borrelia burgdorferi*
Spinous ear tick (*Otobius megnini*)

Lice
Sucking lice of dogs (*Linognathus setosus*)
Biting lice of dogs (*Trichodectes canis, Heterodoxus springer*)
Lice of cats (*Felicola subrostrata*)

Insects of Order Diptera
Mosquitoes: eosinophilic dermatitis (especially cats)
Black flies, stable flies, horn flies, houseflies: attack ear pinnae of dogs
Myiasis (development of fly larvae in skin or haircoat): screwworm, blow flies, flesh flies
*Cuterebra* fly larva

Helminth Parasites
Hookworm dermatitis (*Ancylostoma, Uncinaria*)
Pelodera dermatitis (*Peloderma strongyloides*)
Dracunculiasis (*Dracunculus insignis*)

### Pigmentation

**Differential Diagnosis for Changes in Skin Pigmentation**

**Hypopigmentation**
Vitiligo (Tervuren, Rottweiler, Doberman Pinscher, Newfoundland, Collie, German Shorthaired Pointer, Old English Sheepdog, Siamese cat)
Uveodermatologic syndrome (northern breeds such as Siberian Husky, Samoyed, Akita)
Acquired idiopathic hypopigmentation of nose (Labrador Retriever, Golden Retriever, Malamute, Siberian Husky, Samoyed, Poodle, German Shepherd)
Discoid lupus (German Shepherd, Collie, others)
Dermatomyositis (Collie, Shetland Sheepdog, Beauceron Shepherd)

**Hyperpigmentation**

*Postinflammatory Hyperpigmentation*
- Any Chronic Pruritic Skin Disease
- Atopy
- Adverse food reactions
- Pyoderma
- Malassezia dermatitis
- Sarcoptic mange
- Erythema multiforme
- Many others

**Demodicosis**

**Endocrinopathies**
- Hypothyroidism
- Hyperadrenocorticism

**Dermatophytosis**

**Nevus**

**Lentigo**

**Neoplasia (melanoma)**

## Pyoderma

### Differential Diagnosis

#### Surface Pyoderma
- Pyotraumatic dermatitis (acute moist dermatitis, “hot spot”)
- Intertrigo (skin fold dermatitis)

#### Superficial Pyoderma
- Impetigo (subcorneal pustules of sparsely haired skin)
  - Puppy pyoderma
  - Bullous impetigo
  - Hyperadrenocorticism, hypothyroidism, diabetes mellitus
- Mucocutaneous pyoderma
  - Dogs (German Shepherds predisposed)
  - Superficial bacterial folliculitis
    - Staphylococcus pseudintermedius most common
    - Local trauma secondary to pruritus (allergy, fleas, scabies, demodicosis, etc.)
- Dermatophilosis (rare, actinomycotic superficial crusting dermatitis) methicillin-resistant *Staphylococcus pseudintermedius*
Deep Pyoderma
Always secondary to predisposing problem
Localized lesion (laceration, penetrating wound, animal bite, foreign body)
Generalized (suspect underlying systemic disease)
Clinical syndromes associated with deep pyoderma
- Deep folliculitis, furunculosis, cellulitis
- Pyotraumatic folliculitis
- Muzzle folliculitis and furunculosis
- Pododermatitis (interdigital pyoderma)
- German Shepherd dog folliculitis, furunculosis, cellulitis
- Acral lick furunculosis
- Anaerobic cellulites
- Subcutaneous abscesses
- Bacterial pseudomycetoma
- Mycobacterial granulomas
  - Cutaneous tuberculosis (*Mycobacterium tuberculosis*, *M. bovis*)
  - Feline leprosy (*M. lepraemurium*)
- Opportunistic mycobacterial granulomas
- Actinomycosis
- Actinobacillosis
- Nocardiosis

Miscellaneous Bacterial Infections
Brucellosis, plague, borreliosis, *trichomycosis axillaris*, L-form infections
Acromegaly
In dogs, acromegaly is caused by endogenous progesterone from the luteal phase of the estrous cycle or by exogenous progesterone used for estrous prevention. Elevated progesterone, in turn, stimulates excessive growth hormone secretion of mammary origin. In cats, acromegaly is caused by a pituitary adenoma, usually a macroadenoma, which secretes excessive amounts of growth hormone. Physical changes are less pronounced in cats than in dogs.

Clinical Findings, Dogs
- Hypertrophy of mouth, tongue, and pharynx
- Thick skin folds, myxedema, hypertrichosis
- Prognathism
- Wide interdental spacing
- Visceral organomegaly
- Insulin-resistant diabetes mellitus
- Polyuria
- Polyphagia
- Elevated alkaline phosphatase
Clinical Findings, Cats

Physical changes most pronounced on head, but all the physical changes listed for dogs may be seen.
Insulin-resistant diabetes mellitus (severe)
Degenerative arthropathy/lameness
Polyuria/polydipsia
Polyphagia
Panting
Lethargy/exercise intolerance
Dyspnea secondary to hypertrophic cardiomypathy and heart failure
Neurologic signs when macroadenoma becomes large
  • Lethargy, stupor
  • Adipsia
  • Anorexia
  • Temperature deregulation
  • Circling
  • Seizures
  • Pituitary dysfunction
    • Hypogonadism
    • Hypothyroidism
    • Hypoadrenocorticism (feline acromegaly may also coexist with pituitary-dependent hyperadrenocorticism)

Adrenal Tumors

Differential Diagnosis

Nonfunctional Adrenal Tumor (dog, rarely cat)
  No hormone secreted
  Diagnosis by exclusion
  Histopathology

Functional Adrenocortical Tumor
  **Cortisol-Secreting Tumor**
  Hyperadrenocorticism (Cushing syndrome) (dog, rarely cat)
  Diagnosis by adrenocorticotropic hormone (ACTH) stimulation test, low-dose dexamethasone suppression test, adrenal ultrasound, CT scan

  **Aldosterone-Secreting Tumor**
  Hyperaldosteronism (Conn syndrome) (cat, rarely dog)
  Diagnosis by assessing Na/K, ACTH stimulation test (measure aldosterone)

  **Progestrone-Secreting Tumor**
  Mimics hyperadrenocorticism (cat, less commonly dog)
  Diagnosis by measuring serum progesterone
**Steroid Hormone Precursor–Secreting Tumor**

- 17-hydroxyprogesterone
- Mimics hyperadrenocorticism (dog)
- Diagnosis by ACTH stimulation test (measure steroid hormone precursors)
- Deoxycorticosterone
- Mimics hyperadrenocorticism (dog)
- Diagnosis by ACTH stimulation test (measure steroid hormone precursors)

**Functional Adrenomedullary Tumor**

*Epinephrine-Secreting Tumor*

- Pheochromocytosis (dog, rarely cat)
- Diagnosis by exclusion, histopathology

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**Cretinism (Hypothyroidism in Puppies)**

**Clinical Findings**

- Dwarfism
- Short, broad skull with short thick neck
- Enlarged cranium
- Shortened limbs
- Shortened mandible
- Mental dullness
- Alopecia
- Retention of puppy coat
- Kyphosis
- Inappetence
- Hypothermia
- Constipation
- Gait abnormalities
- Delayed dental eruption
- Macroglossia
- Dry coat
- Thick skin
- Lethargy
- Dyspnea
- Goiter

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**Diabetes Insipidus**

**Differential Diagnosis**

Features of diabetes insipidus include polyuria, polydipsia, and a near-continuous demand for water. Only the following three disorders can cause the degree of polyuria and dilute urine seen with diabetes insipidus:
• Central diabetes insipidus
• Nephrogenic diabetes insipidus
• Primary polydipsia

Causes in Dogs and Cats

Central Diabetes Insipidus

Idiopathic
Traumatic
Neoplasia
• Primary pituitary neoplasm
• Meningioma
• Craniopharyngioma
• Chromophobe adenoma
• Chromophobe adenocarcinoma
• Metastatic neoplasia

Pituitary malformation
Cysts
Inflammation
Parasitic lesions
Complication of pituitary surgery
Familial?

Nephrogenic Diabetes Insipidus

Polyuria caused by nonresponsiveness to antidiuretic hormone (ADH).

Primary idiopathic
Primary familial (Husky)
Secondary acquired
• Renal insufficiency or failure
• Hyperadrenocorticism
• Hypoadrenocorticism
• Hepatic insufficiency
• Pyometra
• Hypercalcemia
• Hypokalemia
• Postobstructive diuresis
• Diabetes mellitus
• Normoglycemic glucosuria
• Hyperthyroidism
• Iatrogenic or drug induced
• Renal medullary solute washout

Diabetic Ketoacidosis

Clinical Findings

No signs may be seen early with diabetic ketoacidosis.
Historical Findings
- Lethargy
- Anorexia
- Vomiting

Physical Examination Findings
- Dehydration
- Depression
- Weakness
- Tachypnea
- Vomiting
- Acetone odor on breath
- Slow, deep breaths (secondary to metabolic acidosis)
- Abdominal pain/abdominal distension secondary to concurrent pancreatitis

Clinicopathologic Findings
- Hyperglycemia
- Metabolic acidosis
- Hypercholesterolemia/lipemia
- Increased alkaline phosphatase (ALP)
- Increased alanine aminotransferase (ALT)
- Increased blood urea nitrogen (BUN)/creatinine
- Hyponatremia
- Hypochloremia
- Hypokalemia
- Increased amylase/lipase
- Hyperosmolality
- Glycosuria
- Ketonuria
- Urinary tract infection

Diabetes Mellitus

Potential Factors in Etiopathogenesis
- Obesity
- Pancreatitis
- Immune-mediated insulitis
- Concurrent hormonal disease
  - Hyperadrenocorticism
  - Diestrus-induced excess of growth hormone
  - Hypothyroidism
- Genetics (dog, possibly cat)
- Drugs
  - Glucocorticoids
  - Megestrol acetate (cat)
- Infection
Concurrent illness
- Renal insufficiency
- Cardiac disease
- Hyperlipidemia (dog, possibly cat)
- Islet amyloidosis

Clinicopathologic Abnormalities, Uncomplicated Diabetes Mellitus

Complete Blood Count
Often normal
Leukocytosis if pancreatitis or infection present

Serum Chemistry
Hyperglycemia
Mild increase in alkaline phosphatase (ALP) and alanine aminotransferase (ALT)
Hypercholesterolemia/hypertriglyceridemia

Urinalysis
Urine specific gravity normal to mildly decreased (>1.025)
Glycosuria
Variable ketonuria
Bacteriuria
Proteinuria

Ancillary Tests
Increased amylase/lipase if pancreatitis present
Normal serum trypsin-like immunoreactivity (TLI)
Low TLI with exocrine pancreatic insufficiency
High TLI with acute pancreatitis
Normal to high TLI with chronic pancreatitis
Low to normal serum insulin with insulin-dependent diabetes mellitus
Low, normal, or increased serum insulin with non-insulin-dependent diabetes mellitus

Potential Complications
Common
Iatrogenic hypoglycemia
Polyuria/polydipsia
Weight loss
Cataracts (dog)
Anterior uveitis
Bacterial infections (especially urinary tract infection)
Ketoacidosis
Pancreatitis
Peripheral neuropathy (cat)
Hepatic lipidosis
Uncommon
- Peripheral neuropathy (dog)
- Glomerulopathy
- Glomerulosclerosis
- Retinopathy
- Exocrine pancreatic insufficiency
- Gastric paresis
- Diabetic diarrhea
- Diabetic dermatopathy

Causes of Insulin Resistance or Ineffectiveness in Dogs and Cats

Caused by Insulin Therapy
- Improper administration
- Inadequate dose
- Inactive insulin
- Diluted insulin
- Somogyi effect
- Inappropriate insulin administration
- Impaired insulin absorption
- Antiinsulin antibody excess

Caused by Concurrent Disorder
- Obesity
- Diabetogenic drugs
- Hyperadrenocorticism
- Hypothyroidism (dog)
- Hyperthyroidism (cat)
- Urinary tract infection
- Oral infections
- Chronic inflammation/pancreatitis
- Diestrus (bitch)
- Acromegaly (cat)
- Renal insufficiency
- Hepatic insufficiency
- Cardiac insufficiency
- Glucagonoma
- Pheochromocytoma
- Exocrine pancreatic insufficiency
- Hyperlipidemia
- Neoplasia

Clinical Findings Associated with Insulin-Secreting Tumors
- Seizures
- Weakness
- Collapse
- Ataxia
Polyphagia
Weight gain
Muscle fasciculations
Posterior weakness (neuropathy)
Lethargy
Nervousness
Unusual behavior

Gastrinoma (Zollinger-Ellison Syndrome)

Clinical Findings

Clinical Signs
Vomiting
Weight loss
Anorexia
Diarrhea
Gastric and duodenal ulceration
Hematochezia
Hematemesis
Melena
Obstipation
Lethargy/depression
Abdominal pain
Esophageal pain and ulceration
Regurgitation
Fever
Polydipsia
Thin body condition
Pallor

Clinicopathologic Findings
Regenerative anemia
Hypoproteinemia
Neutrophilic leukocytosis
Hypoalbuminemia
Hypocalcemia
Mild increases in hepatic enzymes
Hypochloremia
Hypokalemia
Hyponatremia
Metabolic acidosis
Metabolic acidosis (secondary to vomiting)
Hyperglycemia, hypoglycemia (uncommon)
Glucagonoma

Clinical Findings in Dogs

Clinical Signs
Necrolytic migratory erythema (crusting skin rash of elbows, hocks, nose, scrotum, flank, ventral abdomen, distal extremities, and mucocutaneous junctions of mouth, eyes, prepuce and vulva)
Footpad lesions
Glucose intolerance/diabetes mellitus (caused by excess glycogenolysis and gluconeogenesis)
Oral ulcerations
Lethargy
Weight loss
Decreased appetite
Muscle atrophy
Peripheral lymphadenopathy

Clinicopathologic Findings
Hyperglycemia
Nonregenerative anemia
Increased hepatic enzymes
Decreased albumin
Decreased globulin
Decreased blood urea nitrogen (BUN)
Decreased cholesterol
Glucosuria
Abdominal ultrasound lesions
• Increased echogenicity of portal and hepatic vein walls
• Diffuse hyperechogenicity
• Multiple small hypoechoic foci

Hyperadrenocorticism

Clinical Findings

Potential Clinical Signs
Polyuria/polydipsia
Alopecia
Pendulous abdomen
Hepatomegaly
Polyphagia
Muscle weakness
Muscle atrophy
Pyoderma
Comedones
Panting
Pacing/restlessness
Hyperpigmentation
Systemic hypertension
Testicular atrophy
Anestrus
Calcinosis cutis
Facial nerve paralysis
Pulmonary thromboembolism

**Potential Clinicopathologic Findings**
Urinary tract infection/pyelonephritis
Decreased urine specific gravity
Increased serum alkaline phosphatase (ALP)
Increased alanine aminotransferase (ALT)
Hypercholesterolemia
Hypertriglyceridemia
Hyperglycemia (mild to moderate)
Diabetes mellitus (uncommon)
Increased serum bile acids
Decreased BUN and creatinine (secondary to diuresis)
Hypophosphatemia
Stress leukogram
  • Neutrophilia
  • Lymphopenia
  • Eosinopenia
  • Monocytosis
Thrombocytosis
Mild erythrocytosis
Decreased total serum thyroxine (T4) or free T4
Urolithiasis

**Hyperglycemia**

**Differential Diagnosis**
Diabetes mellitus
Stress (physiologic in cat)
Hyperadrenocorticism
Drug therapy
  • Glucocorticoids
  • Progestagens
  • Megestrol acetate
  • Thiazide diuretics
Dextrose-containing fluids
Parenteral nutrition
Postprandial effect (diets containing monosaccharides, disaccharides, propylene glycol)
Exocrine pancreatic neoplasia
Pancreatitis
Renal insufficiency
Acromegaly (cat)
Pheochromocytoma (dog)
Diestrus (bitch)
Head trauma

### Hypoadrenocorticism

#### Potential Clinical Findings

**Clinical Signs**
- Lethargy/depression
- Episodic weakness
- Vomiting
- Anorexia
- Waxing and waning illness
- Weight loss/failure to gain weight
- Bradycardia
- Dehydration/hypovolemia
- Diarrhea
- Polyuria or polydipsia
- Collapse
- Syncope
- Restlessness/shaking/shivering
- Regurgitation
- Muscle cramping
- Gastrointestinal hemorrhage/melena
- Abdominal pain

**Potential Clinicopathologic Findings**
- Hyponatremia
- Hyperkalemia
- Hypochloremia
- Decreased sodium/potassium ratio (<24:1)
- Azotemia
  - Increased blood urea nitrogen (BUN)
  - Increased creatinine
  - Increased phosphate
- Decreased bicarbonate and total CO₂ concentrations
- Hypercalcemia
- Hypoglycemia
- Hypoalbuminemia
- Increased hepatic enzymes
Metabolic acidosis
Lymphocytosis
Eosinophilia
Relative neutropenia
Anemia (usually nonregenerative)
Variable urine specific gravity (<1.030)

Hypoglycemia

Differential Diagnosis

Excess Secretion of Insulin or Insulin-Like Factors
Insulinoma
Extrapancreatic tumor
Islet cell hyperplasia

Decreased Glucose Production
Toy breeds
Néonates
Malnutrition
Pregnancy
Fasting
Hypoadrenocorticism
Hypopituitarism
Growth hormone deficiency
Liver disease (portal caval shunt, chronic fibrosis/cirrhosis)
Glycogen storage diseases

Excess Glucose Consumption
Sepsis
Extreme exercise

Drug-Associated Causes
Insulin
Oral hypoglycemics
Many other drugs reported to cause hypoglycemia in humans

Spurious
Blood cells not promptly separated from serum

Hyponatremia/Hyperkalemia

Differential Diagnosis

Hypoadrenocorticism
Renal or Urinary Tract Disease
Urethral obstruction
Acute renal failure
Chronic oliguric or anuric renal failure
Postobstructive diuresis
Nephrotic syndrome

Severe Gastrointestinal Disease
Parasitic infestation
• Whipworm (trichuriasis)
• Roundworm (ascariasis)
• Hookworm (ancylostomiasis)
Salmonellosis
Viral enteritis
• Parvovirus
• Canine distemper virus
Gastric dilatation/volvulus
Gastrointestinal perforation
Severe malabsorption
Hemorrhagic gastroenteritis
Pancreatic disease

Severe Hepatic Failure
Cirrhosis
Neoplasia

Severe Metabolic or Respiratory Acidosis

Congestive Heart Failure

Massive Release of Potassium into Extracellular Fluid
Crush injury
Aortic thrombosis
Rhabdomyolysis
• Heat stroke
• Exertional
Massive sepsis
Massive hemolysis

Pleural Effusion
Pregnancy
Lymphangiosarcoma

Pseudohyperkalemia
Akitas and related breeds
Severe leukocytosis (>100,000/mm³)
Severe thrombocytosis (>1 million/mm³)

Diabetes Mellitus

Primary Polydipsia

Inappropriate Antidiuretic Hormone (ADH) Secretion

Drug Induced
Potassium-sparing diuretics
Nonsteroidal antiinflammatory drugs (NSAIDs)
Angiotensin-converting enzyme (ACE) inhibitors
Potassium-containing fluids

**Insulinoma**

**Differential Diagnosis for Insulin-Secreting Beta-Cell Neoplasia**

**Excess Insulin or Insulin-Like Factors**
- Insulinoma
- Extrapancreatic tumor
- Islet cell hyperplasia

**Decreased Glucose Production**
- Hypoadrenocorticism
- Hypopituitarism
- Growth hormone deficiency
- Liver disease
- Glycogen storage diseases
- Neonates
- Toy breeds
- Fasting
- Malnutrition
- Pregnancy

**Excess Glucose Consumption**
- Sepsis
- Extreme exercise

**Drug-Associated Causes**
- Insulin
- Oral hypoglycemics (sulfonylurea)
- Salicylates (e.g., aspirin)
- Acetaminophen
- β-blockers
- β₂-agonists
- Ethanol
- Monoamine oxidase inhibitors
- Tricyclic antidepressants
- Angiotensin-converting enzyme (ACE) inhibitors
- Antibiotics (e.g., tetracycline)
- Lidocaine overdose
- Lithium

**Factitious Hypoglycemia**
- Failure to separate blood cells from serum promptly
- Severe polycythemia or leukocytosis when serum separation delayed
Parathyroidism

Hyperparathyroidism, Primary—Clinical Findings

Clinical Signs
Polyuria/polydipsia
Weight loss
Anorexia
Lethargy, listlessness
Urinary tract infection (UTI)
Urolithiasis
Vomiting
Constipation
Mental dullness, obtundation, coma
Weakness, muscle wasting, shivering

Clinicopathologic Findings
Hypercalcemia
Increased ionized calcemia
Low normal to low serum phosphorus
Decreased urine specific gravity
Hematuria
Pyuria
Crystalluria
Bacteriuria

Hypoparathyroidism—Clinical Findings

Clinical Signs
Seizures
Facial rubbing, biting at feet
Splinted abdomen
Stiff gait
Intermittent lameness
Muscle fasciculations, cramping, tremors
Fever
Paroxysmal tachyarrhythmias
Muffled heart sounds
Weak pulses
Disorientation

Clinicopathologic Findings
Hypocalcemia
Hyperphosphatemia
Decreased serum parathyroid hormone concentration

Electrocardiographic Findings
Deep, wide T waves
Prolonged QT interval
Bradycardia
Pheochromocytoma

Clinical Findings

- Intermittent weakness
- Intermittent collapse
- Panting
- Tachypnea
- Seizures
- Tachycardia
- Lethargy
- Inappetence
- Cardiac arrhythmias
- Restlessness
- Exercise intolerance
- Weak pulses
- Vomiting
- Diarrhea
- Weight loss
- Muscle wasting
- Polyuria/polydipsia
- Abdominal distension
- Rear limb edema
- Pale mucous membranes
- Abdominal pain
- Hemorrhage (epistaxis, surgical incision sites)
- Palpable abdominal mass

Pituitary Dwarfism

Clinical Findings

Musculoskeletal Signs
- Stunted growth
- Delayed growth plate closure
- Thin skeleton
- Immature facial features
- Square, chunky contour as adult
- Bone deformities
- Delayed dental eruption

Dermatologic Signs
- Soft, woolly haircoat
- Lack of guard hairs
- Alopecia; bilaterally symmetric trunk, neck, and proximal extremities
- Hyperpigmentation
- Thin, fragile skin
Wrinkles
Scales
Comedones
Papules
Pyoderma
Seborrhea sicca
Retention of secondary hairs

**Reproductive Signs**
Testicular atrophy
Unilateral or bilateral cryptorchidism
Flaccid penile sheath
Failure to have estrous cycles

**Other Signs**
Mental dullness
Shrill, puppy-like bark
Signs of secondary hypothyroidism
Signs of secondary adrenal insufficiency

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**Thyroid Disease**

**Hyperthyroidism, Feline—Clinical Findings**

**Clinical Signs**
Weight loss/thin body condition
Polyphagia
Hyperactivity
Palpable thyroid nodule (goiter)
Tachycardia
Vomiting
Cardiac murmur
Premature beats
Gallop rhythm
Aggressiveness
Panting
Pacing
Restlessness
Increased nail growth
Alopecia
Polyuria/polydipsia
Diarrhea
Increased fecal volume
Muscle weakness
Congestive heart failure (CHF)
Dyspnea
Ventroflexion of neck
Unkempt coat/alopecia
Tremor
Weakness
Anorexia

**Hypothyroidism, Canine—Clinical Findings**

**Clinical Signs**
- Lethargy/exercise intolerance
- Weight gain
- Cold intolerance
- Mental dullness

**Dermatologic signs**
- Alopecia
- Superficial pyoderma
- Seborrhea sicca or oleosa
- Dry, scaly skin
- Changes in haircoat quality and color
- Hyperkeratosis
- Hyperpigmentation
- Comedones
- Hypertrichosis
- Ceruminous otitis
- Myxedema (cutaneous mucinosis)
- Poor wound healing
- Slow regrowth of hair

**Reproductive abnormalities**
- Male: decreased libido, testicular atrophy, hypospermia
- Female: delayed estrus, silent estrus, failure to cycle, abortion, small litters, uterine inertia, weak or stillborn puppies

**Peripheral neuropathies**
- Generalized peripheral neuropathies
- Specific peripheral neuropathies (especially cranial nerves, facial, trigeminal, vestibulocochlear)

**Cerebral dysfunction (myxedema coma [rare])**

**Cardiovascular signs**
- Sinus bradycardia, weak apex beat, low QRS voltages, inverted T waves, hypercholesterolemia leading to atherosclerosis (rare)

**Ocular abnormalities** (corneal lipidosis, corneal ulceration, uveitis, secondary glaucoma, lipemia retinalis, retinal detachment, and keratoconjunctivitis sicca reported, but causal relationship not proven)
Clinicopathologic Changes

- Nonregenerative anemia
- Hypercholesterolemia
- Hypertriglyceridemia
- Mild increases in hepatic enzymes
SECTION IV

Gastroenterologic Disorders

Chronic Constipation, Feline
Diarrhea
Dental and Oral Cavity Diseases
Diseases of the Tongue
Salivary Gland Disease
Esophageal Disease
Stomach Disorders
Small Intestinal Disease
Large Intestinal Disease
Ileus
Malabsorptive Disease
Perianal Disease
Protein-Losing Enteropathy
Fecal Incontinence

Chronic Constipation, Feline

Differential Diagnosis

Neuromuscular Dysfunction
• Colonic smooth muscle: idiopathic megacolon, aging
• Spinal cord disease: lumbosacral disease, cauda equina syndrome, sacral spinal cord deformities (Manx cat)
• Hypogastric or pelvic nerve disorders: traumatic injury, malignancy, dysautonomia

Mechanical Obstruction
• Intraluminal: foreign material, neoplasia, rectal diverticula, perineal hernia, anorectal strictures
• Intramural: neoplasia
• Extraluminal: pelvic fractures, neoplasia

Inflammation
• Perianal fistula, proctitis, anal sac abscess, anorectal foreign bodies, perianal bite wounds

Metabolic and Endocrine
• Metabolic: dehydration, hypokalemia, hypercalcemia
• Endocrine: hypothyroidism, obesity, nutritional secondary hyperparathyroidism

Environmental and Behavioral
• Soiled litter box, inactivity, hospitalization, change in environment
Diarrhea

Causes of Diarrhea

Gastrointestinal Disease
- Diffuse gastrointestinal disease (e.g., inflammation or lymphoma)
- Gastric disease (achlorhydria, dumping syndromes)
- Intestinal disease (primary small intestinal disease, primary large intestinal disease, dietary-induced such as food poisoning, gluttony, or sudden change of diet)

Nongastrointestinal Disease
- Pancreatic disease (exocrine pancreatic insufficiency, pancreatitis, pancreatic carcinoma, gastrinoma or Zollinger-Ellison syndrome)
- Liver disease (hepatocellular failure, intrahepatic and extrahepatic cholestasis)
- Endocrine disease (classical hypoadrenocorticism, atypical hypoadrenocorticism, hyperthyroidism, hypothyroidism)
- Renal disease (uremia, nephrotic syndrome)
- Polysystemic infection (e.g., distemper, leptospirosis, infectious canine hepatitis in dogs, FIP, FeLV, FIV in cats)
- Miscellaneous (toxemias such as pyometra and peritonitis, congestive heart failure, autoimmune disease, metastatic neoplasia, various toxins and drugs)

Classification of Diarrhea

Mechanistic
- Secretory
- Osmotic
- Permeability (exudative)
- Dysmotility
- Mixed

Temporal
- Acute
- Chronic

Anatomic
- Extraintestinal
- Small intestinal
- Large intestinal
- Diffuse
Pathophysiologic
• Biochemical
• Allergic
• Inflammatory
• Neoplastic

Etiologic
• Bacteria
• Dietary
• Fungal
• Idiopathic
• Parasitic
• Viral

Causal
• Exocrine pancreatic insufficiency, salmonellosis, lymphoma, other

Clinical
• Acute, nonfatal, mild, self-limiting
• Acute, severe potentially fatal
• Acute systemic disease
• Chronic
• Chronic protein-losing

Dental and Oral Cavity Diseases

Differential Diagnosis

Trauma
Fractures
• Crown
• Root
• Mandible
• Maxillary
Avulsion
Pulp injury
Temporomandibular luxation

Caries

Feline Dental Resorptive Lesions

Periodontal Disease
Gingivitis
Gingival recession
Bone loss, osteomyelitis
Tooth loss

Tooth Root Abscess

Oronasal Fistula
Stomatitis (Faucitis, Glossitis, Pharyngitis)
Feline immunodeficiency virus, feline leukemia virus, feline syncytium-forming virus
Feline calicivirus, feline herpesvirus, feline infectious peritonitis
Candidiasis
Uremia
Trauma (foreign objects, caustic agents, electric cord bite)
Autoimmune disease (pemphigus, lupus, idiopathic vasculitis, toxic epidermal necrolysis)
Feline idiopathic gingivitis/pharyngitis

Neoplasia

*Malignant*
- Fibrosarcoma
- Squamous cell carcinoma
- Melanoma
- Salivary gland neoplasms

*Benign*
- Epulis
  - Fibromatous
  - Acanthomatous
  - Ossifying
  - Papilloma
- Fibroma
- Lipoma
- Chondroma
- Osteoma
- Hemangioma
- Hemangiopericytoma
- Histiocytoma

Eosinophilic Granuloma Complex
- Linear granuloma
- Eosinophilic ulcer (usually on maxillary lips)

Sialocele

Diseases of the Tongue

Differential Diagnosis

Trauma
- Mechanical injury (sharp objects)
- Chemical injury
- Electric shock (electric cord)
• Foreign body (plant material, porcupine quill, linear foreign bodies)
• Sublingual hyperplastic tissue (gum chewer’s disease)

Viral
• Calicivirus
• Herpes virus
• Papillomavirus

Neoplasia
• Malignant melanoma
• Squamous cell carcinoma
• Benign tumors (lipoma, plasma cell tumor, granular cell tumors, fibroma)

Metabolic Disease (Uremia)

Sublingual Mucocele (Ranula)

Immune Mediated
• Mucous membrane pemphigoid
• Pemphigus vulgaris
• Bullous pemphigoid
• Systemic lupus erythematosus
• Autoimmune vasculopathies (idiopathic, infectious, food allergies, drug reaction, neoplasia)

Eosinophilic granulomas

Contact Mucosal Ulceration from Calculus Contact

Calcinosis Circumscripta

Salivary Gland Disease

Differential Diagnosis

Salivary Neoplasia (more common in cats than dogs)
• Adenocarcinoma
• Squamous cell carcinoma
• Undifferentiated sarcoma
• Mucoepidermoid tumor
• Malignant mixed tumor
• Sarcoma
• Acinic cell carcinoma
• Adenoid cystic carcinoma

Salivary Mucocele
• Sublingual gland most commonly

Sialoadenitis

Sialadenosis
Esophageal Disease

Differential Diagnosis

**Congenital**

**Obstruction**
- Persistent right aortic arch
- Persistent right or left subclavian artery
- Other vascular ring anomaly

**Idiopathic**

**Acquired**

**Obstruction**
- Foreign body
- Cicatrix/stricture
- Neoplasia
  - Carcinoma
  - *Spirocerca lupi*-induced sarcoma
  - Leiomyoma of lower esophageal sphincter
  - Extraesophageal neoplasia
    - Thyroid carcinoma
    - Pulmonary carcinoma
    - Mediastinal lymphosarcoma
- Achalasia of lower esophageal sphincter (rare)
- Gastroesophageal intussusception (rare)

**Weakness**
- Myasthenia (generalized or localized)
- Hypoadrenocorticism
- Esophagitis
- Persistent vomiting
- Hiatal hernia
- Gastroesophageal reflux/anesthesia-associated reflux
- Caustic ingestion (doxycycline, disinfectants, chemicals, etc.)
- Foreign body
- Excess gastric acidity (gastrinoma, mast cell tumor)
- Fungal organisms (e.g., pythiosis)

**Spirocerca lupi Infection**

**Myopathies/Neuropathies**
- Hypothyroidism
- Systemic lupus erythematosus (SLE)
- Others

**Miscellaneous Causes**
- Lead poisoning
- Chagas disease
PART TWO Systemic Approach to Differential Diagnosis

Canine distemper
Dermatomyositis (principally in Collies)
Dysautonomia
Tetanus

*Idiopathic*

**Stomach Disorders**

**Differential Diagnosis**

**Gastritis**

*Acute Gastritis*
- Dietary indiscretion
- Dietary intolerance or allergy
- Foreign body
- Drugs and toxins (nonsteroidal antiinflammatory drugs [NSAIDs], corticosteroids, antibiotics, plants, cleaners, bleach, heavy metals)
- Systemic disease (uremia, hepatic disease, hypoadrenocorticism)
- Parasites (*Ollulanus* spp., *Physaloptera* spp.)
- Bacterial (bacterial toxins, *Helicobacter* spp.)

*Hemorrhagic Gastroenteritis*

*Chronic Gastritis*
- Lymphocytic/plasmacytic gastritis (inflammatory reaction to a variety of antigens such as *Helicobacter* spp. or *Physaloptera rara*)
- Eosinophilic gastritis (allergic reactions to food antigens)
- Granulomatous gastritis (e.g., *Ollulanus tricuspis*)
- Atrophic gastritis

**Gastric Outflow Obstruction/Gastric Stasis**
- Benign muscular pyloric hypertrophy (pyloric stenosis)
- Gastric antral mucosal hypertrophy
- Foreign body
- Idiopathic gastric hypomotility
- Bilious vomiting syndrome

**Gastric Ulceration/Erosion**

*Iatrogenic*
- NSAIDs
- Corticosteroids
- NSAID/corticosteroid combinations
Foreign Body

*Helicobacter* spp.

**Stress Ulceration**
- Hypovolemic shock
- Septic shock
- After gastric dilatation/volvulus
  - Neurogenic shock
- Hyperacidity
  - Mast cell tumor
  - Gastrinoma (rare)
- Other causes
  - Hepatic disease
  - Renal disease
  - Hypoadrenocorticism
  - Inflammatory disease

**Infiltrative Disease**
- Neoplasia
- Inflammatory bowel disease
- Pythiosis (young dogs, southeastern United States)

**Gastric Dilatation/Volvulus**

**Causes of Acute Abdomen**

**Gastrointestinal (GI) Causes**
- Acute pancreatitis
- Gastroenteritis (parvoviral, bacterial, toxic, hemorrhagic gastroenteritis, etc.)
- Gastric dilatation/volvulus
- Intestinal obstruction/intussusception/volvulus
- Colitis
- Obstipation
- Necrosis, rupture, ulceration, or perforation of GI tract
- Surgical wound dehiscence
- Mesenteric torsion
- Duodenocolic ligament entrapment
- Pancreatic abscess
- Pancreatic neoplasia

**Hepatobiliary Causes**
- Acute hepatitis/cholangiohepatitis
- Biliary obstruction
- Necrotizing cholecystitis
- Hepatic abscess
- Bile peritonitis
Liver lobe torsion
Hepatic trauma/rupture
Hepatobiliary neoplasia

**Urogenital Causes**
Urethral or ureteral obstruction/rupture
Pyelonephritis
Renal neoplasia
Acute nephrosis/nephritis
Cystic, renal, ureteral, or urethral calculi
Prostatitis/prostatic abscess/prostatic cyst/prostatic neoplasia
Dystocia
Pyometra/uterine rupture
Acute metritis
Renal abscess
Testicular torsion
Ovarian cyst, ovarian neoplasia
Uterine torsion
Uroabdomen
Vaginal rupture

**Other Causes**
Penetrating wound, crush injury
Peritonitis (septic, chemical, urine, bile)
Mesenteric traction (large masses)/lymphadenitis/lymphadenopathy/volvulus/avulsion/artery thrombosis
Hemoabdomen (parenchymatous organ rupture)
Neoplasia
Splenic torsion/abscess/mass/rupture
Strangulated hernia
Adhesions with organ entrapment
Pansteatitis
Retroperitoneal hemorrhage
Evisceration
Surgical contamination

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**Small Intestinal Disease**

**Clinical Findings**

Diarrhea
Vomiting
Inappetence/anorexia
Malabsorption
Protein-losing enteropathy
Weight loss
Dehydration
Hematemesis  
Melena  
Polyphagia  
Coprophagia  
Abdominal distension  
Abdominal pain  
Borborygmus/flatulence  
Ascites  
Edema  
Shock  
Halitosis  
Polydipsia  
Ileus

**Differential Diagnosis**

**Acute Diarrhea**  
Acute enteritis  
Dietary indiscretion  
Enterotoxemia

**Infectious Diarrhea**  
Canine paroviral enteritis  
Clostridial disease  
Feline paroviral enteritis (panleukopenia)  
Canine coronavirus enteritis  
Feline coronavirus enteritis  
Feline leukemia virus–associated panleukopenia  
Feline immunodeficiency virus–associated diarrhea  
Salmon poisoning (*Neorickettsia helminthoeca*)  
Campylobacteriosis  
Salmonellosis  
Histoplasmosis  
Miscellaneous *bacteria* (*Yersinia enterocolitica*, *Aeromonas hydrophila*, *Plesiomonas shigelloides*)  
Protothecosis (algae)

**Alimentary Tract Parasites**  
Roundworms (*Toxocara* spp.)  
Hookworms (*Ancylostoma, Uncinaria* spp.)  
Tapeworms (*Dipylidium caninum*, *Taenia* spp., *Mesocestoides* spp.)  
Strongyloides stercoralis (in puppies)  
Coccidiosis  
Cryptosporidiosis  
Giardiasis  
Trichomoniasis  
*Heterobilharzia*
Maldigestive Disease
   Exocrine pancreatic insufficiency

Malabsorptive Disease
   Dietary-responsive disease (allergy, intolerance)
   Inflammatory bowel disease (lymphocytic/plasmacytic enteritis canine eosinophilic gastroenteritis)
   Feline eosinophilic enteritis/hypereosinophilic syndrome
   Granulomatous enteritis
   Immunoproliferative enteropathy in Basenjis
   Enteropathy in Shar-Peis
   Antibiotic-responsive enteropathy

Protein-Losing Enteropathy
   Intestinal lymphangiectasia
   Protein-losing enteropathy in Soft-Coated Wheaten Terriers

Irritable Bowel Syndrome

Intestinal Obstruction
   Simple intestinal obstruction
   Incarcerated intestinal obstruction
   Mesenteric torsion/volvulus
   Linear foreign object

Intussusception
   Ileocolic
   Jejunojejunual

Short-Bowel Syndrome

Neoplasia
   Alimentary lymphoma
   Intestinal adenocarcinoma
   Intestinal leiomyoma/leiomyosarcoma

Breed Susceptibilities, Dogs
   Basenji: lymphocytic/plasmacytic enteritis (immunoproliferative disease)
   Beagle: cobalamin deficiency
   Border Collie: cobalamin deficiency
   German Shepherd: idiopathic antibiotic-responsive small intestinal disease, inflammatory bowel disease (lymphoplasmacytic, eosinophilic)
   Giant Schnauzer: defective cobalamin absorption
   Irish Setter: gluten-sensitive enteropathy
Lundehund: lymphangiectasia  
Retrievers: dietary allergy  
Rottweiler: increased susceptibility to parvoviral enteritis  
Soft-Coated Wheaten Terrier: protein-losing enteropathy/nephropathy  
Shar-Pei: lymphocytic/plasmacytic enteritis, cobalamin deficiency  
Yorkshire Terrier: lymphangiectasia  
Toy breeds: hemorrhagic gastroenteritis

**Large Intestinal Disease**

**Differential Diagnosis**

**Inflammation of Large Intestine**  
Acute colitis/proctitis  
Chronic colitis  
- Lymphocytic/plasmacytic colitis  
- Eosinophilic enterocolitis  
- Chronic ulcerative colitis  
- Histiocytic ulcerative colitis (Boxers)  
Irritable bowel syndrome

**Dietary Intolerance or Food Allergy**

**Parasites**  
Whipworms (*Trichuris* spp.)  
*Tritrichomonas* spp. (cats)  
Giardiasis  
Hookworms (*Ancylostoma* spp.)  
*Heterobilharzia americanum*

**Bacterial Colitis**  
Clostridial colitis  
*Campylobacter* colitis  
*Escherichia coli*  
*Salmonell* a spp.  
*Brachyspira pilosicoli*

**Fungal Colitis**  
Histoplasmosis  
Pythiosis

**Viral Colitis**  
Feline leukemia virus (FeLV)  
Infections secondary to FeLV and feline immunodeficiency virus (FIV)
Algae (*Prototheca* spp.)

Cecocolic Intussusception

Rectal Prolapse

Neoplasms of Large Intestine
   - Adenocarcinoma
   - Lymphoma
   - Rectal polyps

Constipation
   - Pelvic canal obstruction caused by malaligned healing of pelvic fractures
   - Benign rectal stricture
   - Dietary indiscretion leading to constipation
   - Idiopathic megacolon

Ileus

Causes

Physical
   - Intestinal obstruction (foreign body, intussusception, neoplasia, granuloma, torsion, volvulus, incarceration in hernia)
   - Overdistension by aerophagia

Metabolic
   - Uremia
   - Diabetes mellitus
   - Hypokalemia
   - Endotoxemia

Inflammatory
   - Parvovirus
   - Peritonitis
   - Other inflammatory causes

Functional
   - Abdominal surgery
   - Peritonitis
   - Pancreatitis
   - Ischemia

Neuromuscular
   - Anticholinergic drugs
   - Spinal cord injury
   - Visceral myopathies/neuropathy
   - Dysautonomia
**Malabsorptive Diseases**

**Causes**

- Food intolerance or allergy
- Parasitism
  - Giardiasis
- Bacterial overgrowth
- Inflammatory bowel disease
  - Lymphocytic/plasmacytic enteritis
  - Eosinophilic enteritis
  - Idiopathic villous atrophy
  - Purulent enteritis
- Gastrointestinal lymphoma
- Lymphangiectasia
- Obstruction caused by neoplasia, infection, or inflammation
- Portal hypertension
- Pythiosis
- Exocrine pancreatic insufficiency
- Cholestatic liver disease/biliary obstruction
- Brush border enzyme deficiencies
- Brush border transport protein deficiencies
- Hyperthyroidism
- Gastric hypersecretion

**Perianal Disease**

**Differential Diagnosis**

- Perineal hernia
- Perianal fistulae
- Anal sacculitis
- Anal sac impaction
- Abscessed anal sac
- Anal sac (apocrine gland) adenocarcinoma
- Perianal gland tumors
  - Adenoma (common)
  - Adenosarcoma (rare)

**Protein-Losing Enteropathy**

**Differential Diagnosis**

- Gastrointestinal Hemorrhage
  - Hemorrhagic gastroenteritis
  - Ulceration
  - Neoplasia
Endoparasites
   *Giardia* spp.
   *Ancylostoma* spp.
   Coccidia
   Others

Inflammation
   Lymphocytic/plasmacytic
   Eosinophilic
   Granulomatous

Infection
   Parvovirus
   Salmonellosis
   Histoplasmosis
   Phycomycosis

Structural
   Intussusception

Neoplasia
   Lymphosarcoma

Lymphangiectasia
   Primary lymphatic disorder
   Venous hypertension (e.g., right heart failure)
   Hepatic cirrhosis

Fecal Incontinence

Causes

Nonneurologic Disease

*Colorectal Disease*
   Inflammatory bowel disease
   Neoplasia
   Constipation

*Anorectal Disease*
   Perianal fistula
   Neoplasia
   Surgery (anal sacculectomy, perianal herniorrhaphy, rectal resection and anastomosis)

Miscellaneous
   Decreased mentation
   Old age
   Severe diarrhea
   Irritable bowel disease
Neurologic Disease

**Sacral Spinal Cord Disease**
- Discospondylitis
- Neoplasia
- Degenerative myelopathy
- Congenital vertebral malformation
- Sacrococcygeal hypoplasia of Manx cats
- Sacral fracture
- Sacrococcygeal subluxation
- Lumbosacral instability
- Lumbosacral nerve root compression
- Meningomyelocele
- Viral meningomyelitis
- Cauda equina syndrome
- Vertebral fracture

**Peripheral Neuropathy**
- Trauma
- Penetrating wounds
- Repair of perineal hernia
- Perineal urethrostomy
- Hypothyroidism?
- Diabetes mellitus?
- Dysautonomia

**Central Nervous System**
- Infectious (distemper, feline infectious peritonitis)
- Neoplasia
- Vascular compromise
Hematologic Disorders

Anemia
Coagulopathies, Inherited and Acquired
Expected Hemostatic Test Results in Selected Diseases
Leukocyte Disorders
Platelet Dysfunction
Splenitis/Splenomegaly
Thrombocytopenia

Anemia

Hemolytic Anemia

Causes/Triggers of Immune-Mediated Hemolytic Anemia

Infection
- Viral
  - Feline leukemia virus (FeLV), feline immunodeficiency
    virus (FIV), feline peritonitis virus (FIP), chronic
    upper respiratory or gastrointestinal (GI) disease
- Bacterial
  - Leptospirosis, *Mycoplasma haemophilus* infection,
    salmonellosis, acute and chronic infections (e.g.,
    abscess, pyometra, discospondylitis)
- Parasitic
  - Babesiosis, anaplasmosis, leishmaniasis,
    dirofilariasis, ehrlichiosis, *Ancylostoma caninum*,
    *Trichuris vulpis* infection, bartonellosis

Immune Disorders
- Systemic lupus erythematosus (SLE)
- Hypothyroidism
- Primary and secondary immunodeficiencies

Drugs/Toxins
- Vaccines
- Sulfonamides
- Methimazole
- Procainamide
- Cephalosporins
- Penicillins
- Propylthiouracil
- Carprofen
- Levamisole
Griseofulvin
Bee-sting envenomation

Oxidants
Acetaminophen
Phenothiazines
Vitamin K
Methylene blue
Methionine
Propylene glycol

Inflammation
Pancreatitis
Prostatitis/cystitis

Neoplasia
Leukemias
Lymphoma
Multiple myeloma
Mast cell tumor
Splenic hemangioma
Solid tumors

Genetic Predisposition
American Cocker Spaniel (most common breed),
English Springer Spaniel, Old English Sheepdog,
Irish Setter, Poodle, Dachshund, Alaskan Malamute,
Schnauzer

Differentiating Blood Loss from Hemolytic Anemia

Blood Loss
Serum or plasma protein concentration normal to low
Clinical evidence of hemorrhage
No icterus, hemoglobinemia, spherocytosis,
hemosiderinuria, autoagglutination, splenomegaly,
or red blood cell (RBC) changes
Negative direct Coombs test

Hemolysis
Serum or plasma protein concentration normal to high
Rarely clinical evidence of hemorrhage
Icterus common
Hemoglobinuria/hemoglobinemia
Spherocytosis
Hemosiderinuria
Autoagglutination sometimes seen
Direct Coombs test usually positive
Splenomegaly
RBC changes numerous
Nonregenerative Anemia

Differential Diagnosis

**Anemia of Chronic Disease**

- Erythropoietin-Related Conditions
  - Renal disease
  - Hypothyroidism
  - Hypoadrenocorticism
  - Panhypopituitarism
  - Growth hormone deficiency
  - Reduced oxygen requirement
  - Increased oxygen release

- Iron Deficiency Anemia
  - Chronic inflammation
  - Chronic hemorrhage
  - Dietary iron deficiency

**Marrow Disorders**

- Toxic Red Cell Aplasia
  - Estrogen related
  - Phenylbutazone related
  - Other drugs

- Hyperestrogenism (iatrogenic, neoplastic)

- Infection
  - Feline leukemia virus (FeLV)
  - Feline immunodeficiency virus (FIV)
  - Parvovirus
  - Ehrlichiosis
  - Babesiosis
  - *Mycoplasma haemofelis*
  - Endotoxemia

- Immunotherapy

- Myelofibrosis
  - Feline leukemia virus (FeLV) infection
  - Pyruvate kinase deficiency anemia
  - Idiopathic

- Myelophthisic Disease
  - Acute leukemias
  - Chronic leukemias
  - Multiple myeloma
  - Lymphoma
  - Systemic mast cell disease
  - Malignant histiocytosis
  - Metastatic carcinoma
  - Histoplasmosis
Myelodysplasia
  Idiopathic
  FeLV/FIV
  Preleukemic syndrome

Pure Red Cell Aplasia

**Ineffective Erythropoiesis**

Macrocytic (rare)
  Intrinsic marrow disease
  Vitamin B₁₂ deficiency
  Folic acid deficiency

Normocytic
  Myelofibrosis
  Intrinsic erythroid disease

Microcytic
  Iron deficiency
  Globin or porphyrin deficiency

Time Related
  Hemolysis or hemorrhage (during the first 3-5 days)

**Diagnosis**

**Nonregenerative Anemias without Other Cytopenias**

Examine bone marrow.

Severe Erythroid Hypoplasia
  Pure red cell aplasia

Normal to Mild Erythroid Hypoplasia
  Inflammatory disease
  Renal disease
  Neoplasia
  Hepatic disease
  Hypothyroidism
  Hypoadrenocorticism

Hypercellular Bone Marrow
  Less than 30% blast forms: consider myelodysplastic syndrome
  Greater than 30% blast forms: consider hemopoietic neoplasia

**Nonregenerative Anemias with Leukopenia and/or Thrombocytopenia**

Examine bone marrow.

Panhypoplasia
  Aplastic anemia
Disease Determined by Core Biopsy
  - Myelonecrosis
  - Myelofibrosis

Hypercellular Bone Marrow
  - Less than 30% blast forms: myelodysplastic syndrome
  - More than 30% blast forms: hemopoietic neoplasia

Regenerative Anemia

Differential Diagnosis

**Hemolysis**
  - Immune mediated
    - Intravascular
    - Extravascular

**Blood Loss Anemia**
  - Trauma
  - Coagulopathy
    - Clotting factor deficiency
    - Disseminated intravascular coagulation (DIC)
    - Platelet disorders
    - Anticoagulant rodenticides
  - Endoparasites
  - GI blood loss
  - Severe ectoparasites (fleas)

**Oxidative Injury (Heinz Body)**
  - Onion ingestion
  - Acetaminophen (cats)
  - Zinc ingestion (pennies minted after 1982, zinc oxide ointment, zinc-plated bolts and screws)
  - Benzocaine ingestion (dogs)
  - D-L Methionine (cats)
  - Phenolic compounds (mothballs)
  - Phenazopyridine (cats)

**Erythrocytic Parasites**
  - *Haemobartonella* spp.
  - *Babesia* spp.
  - *Cytauxzoon* spp.

**Fragmentation (Microangiopathic)**
  - Disseminated intravascular coagulation (DIC)
  - Heartworm disease
  - Hemangiosarcoma
  - Vasculitis
  - Hemolytic-uremic syndrome
  - Diabetes mellitus


**Other**
- Copper toxicity
- Neonatal isoerythrolysis
- Hereditary nonspherocytic hemolytic anemia
- Pyruvate kinase deficiency
- Feline porphyria
- Hemolysis in Abyssinian and Somali cats

**Coagulopathies, Inherited and Acquired**

**Differential Diagnosis**

**Inherited Clotting Factor Deficiencies**
- Hemophilia A (factor VIII deficiency)
- Hemophilia B (factor IX deficiency)
- Factor XII deficiency (Hageman trait) (Miniature and Standard Poodle, Shar-Pei, German Shorthair Pointer, cats)
- Vitamin K–dependent factor deficiency: factors II, VII, IX, X (Devon Rex cats)
- Factor I: hypofibrinogenemia or dysfibrinogenemia (St. Bernard, Borzoi)
- Factor II: hypoprothrombinemia (Boxer, Otterhound, English Cocker Spaniel)
- Factor VII: hypoproconvertinemia (Beagle, Malamute, Boxer, Bulldog, Miniature Schnauzer)
- Factor X deficiency (Cocker Spaniel, Parson Russell Terrier)
- Hemophilia C (factor XI deficiency: English Springer Spaniel, Great Pyrenees, Kerry Blue Terrier)
- Prekallikrein deficiency (Fletcher factor)

**Acquired Clotting Factor Deficiency**
- Liver disease
  - Decreased clotting factor production
  - Qualitative disorders
- Cholestasis
- Vitamin K antagonists
- Autoimmune disease (lupus anticoagulant)
- Disseminated intravascular coagulation (DIC)
- Neoplasia

**Clinical Manifestations of Primary and Secondary Hemostatic Defects**

**Primary Hemostatic Defects**
- Thrombocytopenia and diseases that cause platelet dysfunction such as uremia, von Willebrand disease, monoclonal gammopathies,
and vector-borne diseases)—typically see manifestations of superficial bleeding
• Petechiae, ecchymoses
• Bleeding from mucosal surfaces (e.g., bleeding from gingiva, melena, hematochezia, epistaxis, hematuria)
• Bleeding in skin
• Hematomas rare
• Prolonged bleeding immediately after venipuncture

Secondary Hemostatic Defects
Clotting factor deficiencies, rodenticide poisoning, liver disease—typically see manifestations of deep bleeding
• Petechiae, ecchymoses rare
• Hematomas common
• Bleeding into body cavities, joints, muscles
• Delayed bleeding after venipuncture

Expected Hemostatic Test Results in Selected Diseases

• Thrombocytopenia—increased buccal mucosal bleeding time (BMBT), decreased platelet count (PLT), normal activated partial thromboplastin time (APTT), normal prothrombin time (PT), normal fibrin degradation products (FDP)
• Platelet dysfunction (e.g., aspirin treatment)—increased BMBT, normal PLT, increased APTT, normal, PT, normal FDP
• Intrinsic pathway defect (e.g., hemophilia A or B)—normal BMBT, normal PLT, increased APTT, normal PT, normal FDP
• Factor VII deficiency—normal BMBT, normal PLT, normal APTT, increased PT, normal, FDP
• Multiple factor defects (e.g., vitamin K antagonism)—normal BMBT, normal PLT, increased APTT, increased PT, normal FDP
• Common pathway defect (e.g., factor X deficiency)—normal BMBT, normal PLT, increased APTT, increased PT, normal FDP
• Disseminated intravascular coagulation (DIC) —increased BMBT, decreased PLT, increased APTT, increased PT, increased FDP
• von Willebrand disease—increased BMBT, normal PLT, normal APTT, normal PT, normal FDP
**Leukocyte Disorders**

**Differential Diagnosis**

- Pelger-Huët anomaly (many breeds of dogs and cats)
  - Neutrophil function not altered
- Chédiak-Higashi syndrome (blue smoke-colored Persian cats)
- Canine leukocyte adhesion deficiency: fatal defect (Irish Setter and Irish Setter crosses)
- Cyclic hemopoiesis (cyclic neutropenia): fatal defect (gray Collies)
- Birman cat neutrophil granulation anomaly: neutrophil function not altered
- Hypereosinophilic syndrome (cats): may eventually be fatal
- Severe combined immunodeficiency of Parson Russell Terriers: fatal defect
- Canine X-linked severe combined immunodeficiency: fatal defect (many breeds)
- Defective neutrophil function in Doberman Pinscher: need frequent antimicrobial therapy
- Immunodeficiency of Shar-Pei
- Immunodeficiency of Weimaraners
- Lysosomal storage diseases (many types described, all rare, many breeds)

**Platelet Dysfunction**

**Differential Diagnosis**

**Acquired Platelet Dysfunction**

*Drugs*

- Prostaglandin inhibitors (NSAIDs)
- Vaccines
- Antibiotics
- Antifungals
- Phenothiazines
- Aminophylline
- Diltiazem
- Isoproterenol

*Secondary to Disease*

- Renal disease
- Liver disease
- Myeloproliferative disorders
Systemic lupus erythematosus (SLE)
Dysproteinemias

Hereditary
von Willebrand disease (many breeds)
Canine thrombopathia (Basset Hound, Foxhound, Spitz)
Canine thrombasthenic thrombopathia (Otterhound, Great Pyrenees)
Collagen deficiency diseases/Ehler-Danlos syndrome (many breeds)

Splenitis/Splenomegaly

Differential Diagnosis for Splenomegaly

Splenic Mass (Asymmetric Splenomegaly)
Nodular hyperplasia (lymphoid, fibrohistiocytic)
Hematoma
Neoplasia
• Hemangiosarcoma
• Hemangioma
• Leiomyosarcoma
• Fibrosarcoma
• Histiocytic sarcoma
• Leiomyoma
• Myelolipoma
• Metastatic disease
Abscess
Extramedullary hematopoiesis
Granuloma

Uniform Splenomegaly

Congestion
Drugs
Portal hypertension
Right-sided heart failure
Splenic torsion

Hyperplasia
Chronic infection
Inflammatory bowel disease
Systemic lupus erythematosus (SLE)
Polycythemia vera

Extramedullary Hematopoiesis
Chronic anemia
Immune-mediated hemolytic anemia
Immune-mediated thrombocytopenia
**Neoplasia**
- Lymphoma
- Systemic mastocytosis
- Primary mast cell tumor
- Metastatic neoplasia
- Multiple myeloma
- Acute and chronic leukemias
- Malignant histiocytosis
- Polycythemia vera

**Nonneoplastic Infiltrative Disease**
- Amyloidosis
- Hypereosinophilic syndrome (cats)

**Inflammation**
- Suppurative
- Sepsis
- Bacterial endocarditis
- Infectious canine hepatitis
- Foreign body
- Penetrating wounds
- Toxoplasmosis

**Granulomatous**
- Cryptococcosis
- Histoplasmosis
- Mycobacteriosis
- Leishmaniasis

**Pyogranulomatous**
- Feline infectious peritonitis (FIP)
- Blastomycosis
- Sporotrichosis

**Eosinophilic**
- Eosinophilic gastroenteritis
- Hypereosinophilic syndrome
- Neoplasia

**Lymphoplasmacytic**
- Ehrlichiosis
- Hemotropic mycoplasmosis
- Lymphoplasmacytic enteritis
- Pyometra
- Brucellosis
- Anaplasmosis

**Necrotic Tissue**
- Torsion
- Necrotic center of neoplasms
Infectious canine hepatitis
Anaerobic infection
Systemic calicivirosis
Tularemia
Salmonellosis

**Infectious Causes**

**Viral**
- Feline leukemia virus (FeLV)
- Feline immunodeficiency virus (FIV)
- Feline infectious peritonitis (FIP)
- Infectious canine hepatitis

**Bacterial**
- Canine brucellosis
- Mycoplasmosis
- Borreliosis
- Plague
- Tularemia
- Streptococcosis
- Staphylococcosis
- Salmonellosis
- *Francisella* infection
- Endotoxemia

**Fungal**
- Cryptococcosis
- Histoplasmosis
- Blastomycosis

**Rickettsial**
- Ehrlichiosis
- Rocky Mountain spotted fever
- Q fever (*Coxiella burnetii*)
- *Mycoplasma haemofelis*

**Protozoal**
- Toxoplasmosis
- Cytauxzoonosis (cat)
- Babesiosis (*Babesia canis* and *B. gibsoni*)
- Leishmaniasis (dog)

**Thrombocytopenia**

**Differential Diagnosis**

**Increased Platelet Destruction/Sequestration/Utilization**
- Immune-mediated thrombocytopenia
- Drug-induced thrombocytopenia
Infectious (*Anaplasma* spp., *Bartonella* spp., sepsis)
Microangiopathy
Disseminated intravascular coagulation
Neoplasia (immune-mediated, microangiography)
Live viral vaccine–induced thrombocytopenia
Hemolytic uremic syndrome/thrombotic thrombocytopenic purpura
Vasculitis
Splenomegaly
Splenic torsion
Endotoxemia
Acute hepatic necrosis
Hemorrhage

**Decreased Platelet Production**
Drug-induced megakaryocytic hypoplasia (estrogen, phenylbutazone, melphalan, lomustine, β-lactams)
Myelophthisis
Idiopathic bone marrow aplasia
Retroviral infection (FeLV/FIV)
Immune-mediated megakaryocytic hypoplasia
Cyclic thrombocytopenia
Idiopathic bone marrow aplasia
Ehrlichiosis
Autoimmune Skin Diseases

Differential Diagnosis

**Generalized Pustular/Crusting Dermatosis**
- Pemphigus foliaceus (PF) (nose, ear pinna, and footpad typically affected)
- Superficial pustular drug reactions (nasal and footpad lesions may be absent)
- Others: rare presentation—systemic lupus erythematosus (SLE), sterile eosinophilic pustulosis, linear immunoglobulin A (IgA) pustular dermatosis, subcorneal pustular dermatosis

**Focal Pustular/Crusting Dermatosis**
- Face, footpads: PF
- Face and ears only: PF (early), pemphigus erythematosus (PE), drug eruptions, lupus erythematosus
- Nasal only: discoid lupus erythematosus (DLE), PF (early), PE

**Mucocutaneous and Mucosal Ulcerations**
- Pemphigus vulgaris (may also have oral lesions)
- Mucous membrane bullous pemphigoid
- Epidermolysis bullosa acquisita
- Erythema multiforme (target lesions, cutaneous lesions)
- Bullous SLE
- Drug reactions
- Linear IgA bullous dermatosis, toxic epidermal necrolysis (rare)

**Nonmucosal Ulcerations (Axillae, Inguinae, Pinnae, Other Haired Areas)**
- Bullous pemphigoid
Epidermolysis bullosa acquisita
Linear IgA bullous dermatosis
Bullous SLE
Canine vesicular cutaneous lupus erythematosus (idiopathic ulcerative dermatosis of Collies, Shetland Sheepdogs)
Erythema multiforme (EM)
Toxic epidermal necrolysis
Drug eruptions
Pemphigus vulgaris

Depigmenting Skin Diseases
Nasal only: DLE, vitiligo-like syndrome, uveodermatologic syndrome, early PF or PE
Nose, footpad, lip, eyelid, mucocutaneous area: uveodermatologic syndrome (uveitis also)
Haircoat or skin: idiopathic leukotrichia or leukoderma

Miscellaneous
Focal alopecia: alopecia areata, rabies vaccine, focal vasculitis
Widespread noninflammatory alopecia: alopecia areata, pseudopelade
Erythematous target lesions: erythema multiforme
Nodular ulcerative lesions: nodular panniculitis
Purpura, hemorrhage, punched-out lesions
Ear margin necrosis, dependent edema: vasculitis, proliferative necrotizing otitis of kittens, cryoglobulinemia and cryofibrinogenemia, proliferative thrombovascular necrosis of the pinnae

Immune-Mediated Disease

Laboratory Diagnosis

Direct Coombs Test
Immune-mediated hemolytic anemia
Hemolytic anemia in systemic lupus erythematosus (SLE)

Antiplatelet Antibodies
Immune-mediated thrombocytopenia

Antineutrophil Antibodies
Immune-mediated neutropenia

Thyroxin and Thyroglobulin Autoantibodies
Hypothyroidism

Acetylcholine Receptor Autoantibodies
Myasthenia gravis
2M Myofiber Autoantibodies
Masticatory muscle myositis

Antinuclear Antibody
SLE
Chronic antigenic stimulation

Rheumatoid Factor
Rheumatoid arthritis (RA)

Direct Immunofluorescence
Antibody-complement deposition

Differential Diagnosis for Immune-Mediated Arthritis

Erosive Immune-Mediated Arthritides
RA (dog, rarely in cat)
Periosteal proliferative polyarthritis (cat, rarely in dog)

Nonerosive Immune-Mediated Arthritides
Idiopathic polyarthritis
- **Type I:** uncomplicated idiopathic arthritis (most common)
- **Type II:** idiopathic arthritis associated with infection remote from joints—respiratory tract, tonsils, conjunctiva (chlamydia in cats), urinary tract, uterus, skin, oral cavity
- **Type III:** idiopathic arthritis associated with gastroenteritis
- **Type IV:** idiopathic arthritis associated with malignant neoplasia—squamous cell carcinoma, heart base tumor, leiomyoma, mammary carcinoma, myeloproliferative disease (cats)

SLE
Drug-induced polyarthritis
- Sulfas, lincomycin, erythromycin, cephalosporins, penicillins, trimethoprim-sulfa (especially Doberman Pinscher)

Vaccination reaction
Polyarthritis/polymyositis syndrome
Polyarthritis/meningitis syndrome
Familial renal amyloidosis in Chinese Shar-Peis
Polyarthritis in adolescent Akitas
Polyarthritis nodosa (-inflammatory condition of small arteries—histopathologic diagnosis)
Immune System Components

Function

Humoral immunity

*B Lymphocytes and Plasma Cells*

Production of immunoglobulins

Cellular Immunity

*T Lymphocytes*

Production of lymphokines

- Helper T cells
- Stimulate immune reactivity

Suppressor T cells

- Suppress immune reactivity

Antibody-dependent cell-mediated cytotoxicity

Natural killer cells

- Direct cytotoxicity

Phagocytic Cells

*Mononuclear Phagocytic Cells*

Antigen presentation

Phagocytosis of particles

*Neutrophils and Eosinophils*

Phagocytosis of particles

Antibody-dependent cell-mediated cytotoxicity

Mechanisms of Immunopathologic Injury

Type I (immediate)

- Humoral immune system (T-helper cells and B cells), IgE, mast cells, inflammatory mediators
- Skin, respiratory tract, GI tract commonly affected
- Examples include acute anaphylactic reaction, atopy, allergic bronchitis, feline asthma

Type II (cytotoxic)

- Humoral immune system (IgG and IgM)
- Hematologic systems, neuromuscular junctions, and skin commonly affected
- Examples include immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, myasthenia gravis, pemphigus foliaceus
Type III (immune complex)
- Soluble immune complexes
- Kidney, joints, and skin commonly affected
- Examples include glomerulonephritis, systemic lupus erythematosus, rheumatoid arthritis

Type IV (delayed type)
- Sensitized T lymphocytes, cytokines, neutrophils, and macrophages
- Endocrine glands, muscle commonly affected
- Examples include lymphocytic thyroiditis, myositis

Organ Systems Affected by Autoimmune Disorders in the Dog and Cat

Differential Diagnosis

Hematologic
- Immune-mediated hemolytic anemia
- Pure red cell aplasia
- Immune-mediated thrombocytopenia
- Idiopathic neutropenia

Joints (see Differential Diagnosis for Immune-Mediated Arthritis)

Skin (see Autoimmune Skin Diseases)

Eye
- Uveitis
- Retinitis

Kidney
- Glomerulonephritis

Respiratory Tract
- Allergic rhinitis
- Allergic bronchitis (asthma)
- Pulmonary infiltrates with eosinophils

Gastrointestinal Tract
- Feline stomatitis, gingivitis
- Lymphocytic, plasmacytic enteritis
- Anal furunculosis (perianal fistula)

Neurologic System
- Myasthenia gravis
- Myositis
- Polyradiculoneuritis
- Granulomatous meningoencephalitis
- Polyarteritis
Endocrine Glands
- Thyroiditis (hypothyroidism)
- Adrenalitis (hypoadrenocorticism)
- Insulitis (diabetes mellitus)

Multisystemic Immune Disease
- Systemic lupus erythematosus

Systemic Lupus Erythematosus (SLE)

Organs and Tissues Affected
- Red blood cells
  - Immune-mediated hemolytic anemia
  - Pure red cell aplasia
- Platelets
  - Immune-mediated thrombocytopenia
- Glomeruli
  - Glomerulonephritis
- Synovium
  - Nonerosive polyarthritis
- Blood vessels
  - Vasculitis
- Epidermis
  - Dermatitis
  - Neutrophils
  - Immune-mediated neutrophilia
- Clotting factors
  - Coagulopathy
- Central nervous system
  - Seizures, focal signs
- Skeletal muscle/nerve end plate
  - Polymyositis
  - Polyneuritis
  - Myasthenia gravis

Criteria for Diagnosis in Dogs and Cats
SLE is diagnosed when three or more of the following criteria are manifested simultaneously or at any time:
- Antinuclear antibodies (ANAs)
  - Abnormal ANA titer in the absence of drugs or infectious or neoplastic conditions known to be associated with abnormal titers
- Cutaneous lesions
  - Depigmentation, erythema, erosions, ulcerations, crusts, scaling, with biopsy findings consistent with SLE
Oral ulcers
• Oral or nasopharyngeal ulceration, usually painless
Arthritis
• Nonerosive, nonseptic arthritis involving two or more peripheral joints
Renal disorders
• Glomerulonephritis or persistent proteinuria in the absence of urinary tract infection
Anemia/thrombocytopenia
• Hemolytic anemia/thrombocytopenia in the absence of offending drugs
Leukopenia
• Low total white cell count
Polymyositis or myocarditis
• Inflammatory disease of skeletal or cardiac muscles
Serositis
• Presence of a nonseptic inflammatory cavity effusion (abdominal, pleural, or pericardial)
Neurologic disorders
• Seizures or psychosis in the absence of known disorders
Antiphospholipoids
• Prolongation of activated partial thromboplastin time (APTT) that fails to correct with a 1:1 mixture of patient’s and normal plasma, in the absence of heparin or fibrin degradation products (FDPs)
Infectious Disease

Anaplasmosis, Canine
Bacterial Infections, Systemic
Bartonellosis, Canine
Bartonellosis, Feline
Anaplasmosis
Anaplasma Platys
Ehrlichiosis, Canine
Influenza, Canine
Neorickettsiosis Canine
Mycoses, Systemic
Polysystemic Protozoal Diseases
Rocky Mountain Spotted Fever
Sepsis and Systemic Inflammatory Response Syndrome (SIRS)
Vaccines, Recommended Core vs. Noncore
Viruses, Canine
Viruses, Feline

Anaplasmosis, Canine

Clinical Signs

Infection may be subclinical
Fever
Depression
Inappetence
Scleral injection
Lameness, stiffness, reluctance to move
Coughing (soft and nonproductive)
Lymphadenopathy
Splenomegaly
Neutrophilic polyarthritis (rare)
CNS signs?
Vomiting/diarrhea
May be more susceptible to other infections

Laboratory Abnormalities

Thrombocytopenia
Lymphopenia
Eosinopenia
Mild regenerative anemia
Hypoalbuminemia
Mild to moderately elevated hepatic enzymes
Leptospirosis
Hepatic dysfunction, renal dysfunction, fever, anterior uveitis, icterus
Coagulation abnormalities, vomiting/diarrhea, icterus, polyuria/polydipsia, anorexia
Some cases may be subclinical

Borreliosis (Lyme Disease)
Fever, inappetence/lethargy, lymphadenopathy, polyarthritis
Glomerulonephritis/acute, progressive renal failure, mild dermatologic lesions
Meningitis/encephalitis (rare), myocarditis

Mycobacteriosis
Often asymptomatic, skin lesions, dermal nodules, draining tracts, lymphadenopathy, bronchopneumonia, pulmonary nodules, hilar lymphadenopathy, vomiting, diarrhea secondary to intestinal malabsorption, feline leprosy

Brucellosis (Dogs)
Clinical signs may be mild to absent
Fever, lymphadenopathy
Epididymitis, scrotal enlargement, scrotal dermatitis, infertility in males
Abortion, early embryonic death, fetal resorption, in pregnant bitches
Discospondylitis
Rarely uveitis, glomerulonephritis, meningoencephalitis

Tetanus
Localized tetanus, especially cats; stiffness in a muscle of limb
Generalized tetanus stiff gait, outstretched or dorsally curved tails, extreme muscle rigidity, hypersensitivity to touch, light, and sounds
Ears erect, lips drawn back (sardonic grin), protrusion of globe, enophthalmos
Trismus (lockjaw), laryngeal spasm, regurgitation, megaesophagus leading to aspiration pneumonia, seizures
Botulism
Generalized lower motor neuron and parasympathetic dysfunction, cranial nerve signs, mentation is normal. Quadriplegia, megaesophagus, respiratory paralysis; may lead to death.

Feline Plague (*Yersinia pestis*)
Spread by fleas
May show signs of bubonic, septicemic, and pneumonic plague
Depression
Cervical swellings, draining tracts
Dyspnea or cough

Mycoplasmosis/Ureaplasmosis (Cats)
Conjunctivitis, sneezing, mucopurulent nasal discharge, coughing, dyspnea, fever, lameness, swollen joints, subcutaneous abscessation

Members of the Order Rickettsiales of Clinical Importance in Dogs and Cats

Rickettsioses (Spotted Fever Group Rickettsiae)
*Rickettsia rickettsii*
Species of the following tick genera transmit spotted-fever group agents: *Dermacentor, Rhipicephalus, Haemaphysalis*, and *Amblyomma*

Ehrlichiosis (Canine)
*Ehrlichia canis, E. chaffeensis, E. ewingii, E. muris, and E. ruminantium*

Anaplasmosis (Canine and Feline)
*Anaplasma phagocytophilium*
*Anaplasma platys* (canine cyclic thrombocytopenia: mildly pathogenic)

Neorickettsiosis
*Neorickettsia helminthoeca, N. risticii*

Bartonellosis, Canine

Clinical Findings
- Many species of *Bartonella* are suspected to cause disease in dogs (e.g., *B. vinsonii, B. henselae, B. claridgeae, B. elizabethae*)
- Fever
- Endocarditis, myocarditis, arrhythmias
• Epistaxis
• Intermittent lameness
• Bone pain
• Granulomatous lymphadenitis
• Dermatologic lesions/cutaneous vasculitis
• Anterior uveitis
• Polyarthritis
• Meningoencephalitis
• Immune-mediated hemolytic anemia
• Thrombocytopenia
• Eosinophilia
• Peliosis hepatitis
• Granulomatous hepatitis
• Chronic weight loss

**Bartonellosis, Feline**

**Subclinical Disease in Most Cats**

Uveitis? 
Endocarditis?

**Anaplasmosis**

*Anaplasma phagocytophilum*, formally known as *Ehrlichia equi*, *E. phagocytophila*

**Cause of Canine Granulocytic Ehrlichiosis**

**Clinical Signs**

- Fever
- Depression
- Inappetence
- Scleral injection
- Lameness/polyarthritis
- Coughing
- Lymphadenopathy
- Splenomegaly
- Vomiting/diarrhea
- Lymphopenia, eosinopenia, mild nonregenerative anemia
- Hypoalbuminemia, elevated hepatic enzymes

**Anaplasma Platys**

**Cause of Canine Thrombocytic Anaplasmosis**

Forms morula that can be visualized in platelets

**Clinical Signs**

Majority of cases in United States have been mild or subclinical
More severe signs in European or South American cases include:
- Fever
- Splenomegaly
- Hemorrhage

**Ehrlichiosis, Canine**

**Clinical Findings**

**Acute**
- Fever
- Anorexia/weight loss
- Depression
- Serous or purulent oculonasal discharge
- Lymphadenopathy/splenomegaly
- Peripheral edema
- Petechial and ecchymotic hemorrhages
- Neurologic signs (ataxia, seizures, vestibular signs, hyperesthesia, cranial nerve defects)
- Dyspnea
- History of recent or present tick bite
- Thrombocytopenia
- Leukopenia followed by leukocytosis and monocytosis
- Low-grade nonregenerative anemia, unless hemorrhage
- Variable *Ehrlichia* titer, polymerase chain reaction (PCR) positive

**Subclinical**
- No clinical abnormalities apparent
- Hyperglobulinemia, thrombocytopenia, neutropenia, lymphocytosis, monocytosis
- Positive *Ehrlichia* titer, PCR positive

**Chronic**
- Depression
- Pale mucous membranes
- Weight loss
- Abdominal pain
- Splenomegaly
- Epistaxis, retinal hemorrhage, petechia and ecchymoses, melena, hematochezia, hematuria, and other examples of hemorrhage
- Lymphadenopathy
- Stiffness, swollen/painful joints, polymyositis
- Hepatomegaly
- Dyspnea, interstitial or alveolar lung infiltrates
Perivascular retinitis, hyphema, retinal detachment, anterior uveitis, corneal edema
Seizures, paresis, meningeal pain, cranial nerve deficits
Arrhythmias
Polyuria/polydipsia
Secondary opportunistic infection (viral papillomatosis, protozoal infections, bacteriuria)
Monocytosis, lymphocytosis, thrombocytopenia, nonregenerative anemia, hyperglobulinemia, hypoalbuminemia, hypocellular bone marrow, proteinuria, polyclonal or monoclonal gammopathy, nonseptic suppurative polyarthritis, cerebrospinal fluid (CSF) mononuclear pleocytosis
Increased alanine aminotransferase (ALT) and alkaline phosphatase (ALP)
Positive *Ehrlichia* titer, PCR positive

**Influenza, Canine**

**Clinical Features**

- Most outbreaks in group housed dogs (race tracks, animal shelters)
- Individual pets often had a recent history of exposure to other dogs
- Mild form may cause a harsh cough similar to cough heard with infectious tracheobronchitis
- More commonly cough is soft and moist, cough may persist for as long as a month
- Fever
- Mucopurulent nasal discharge
- Increased respiratory rate progressing to respiratory distress
- May progress to overt pneumonia
- Mortality rate less than 5%. Very young and very old are most at risk

**Neorickettsiosis Canine**

*Neorickettsia helminthoea* (salmon poisoning disease)
Restricted to western slopes of Cascade Mountains from northern California to southern Vancouver Island
Vector is a fluke *Nanophyetus salmincola*. Dogs become infected from ingesting parasitized fish.

**Clinical Signs**

- Fever
- Anorexia/weight loss
- Depression
- Lymphadenopathy
Vomiting
Diarrhea
Hematochezia
Neutrophilia with left shift, lymphopenia, monocytosis, thrombocytopenia
Electrolyte derangements, elevated hepatic enzymes, hypoalbuminemia

Neorickettsia risticii
Cause of equine Potomac horse fever
Vector is suspected to be a fluke Acantharium oregonense
Has been identified by culture and PCR in dogs with the following signs:
Lethargy
Intermittent vomiting
Bleeding tendencies
Polyarthritis
Neurologic signs
Dependent edema
Anemia
Thrombocytopenia

Myocoses, Systemic

Clinical Findings

Blastomycosis
Restricted primarily to Mississippi, Ohio, Missouri, Tennessee, and St. Lawrence River valleys plus the southern Great Lakes and the southern Mid-Atlantic states
Sporting breeds predisposed because of greater exposure, males more than females
Anorexia, depression, weight loss, cachexia, fever, mild to severe dyspnea, cyanosis, cough, chylothorax, diffuse lymphadenopathy, papules, plaques and ulcerative nodules, paronychia, chorioretinitis, conjunctivitis, keratitis, iridocyclitis, anterior uveitis, subretinal granulomas, retinal detachment, secondary glaucoma, lameness from osteomyelitis, splenomegaly
Radiographically, infiltrative bronchointerstitial and alveolar disease, hilar lymphadenopathy

Histoplasmosis
Restricted primarily to Mississippi, Missouri, and Ohio River valleys and Mid-Atlantic states
Sporting breeds predisposed because of greater exposure
Common clinical signs include anorexia, fever, depression, weight loss, cough, dyspnea, diarrhea (large bowel diarrhea most often, may see protein-losing
enteropathy), hepatosplenomegaly, icterus, ascites, and lymphadenopathy.
Less common signs include lameness secondary to osteomyelitis or polyarthritis, chorioretinitis, central nervous system (CNS) disease, and cutaneous lesions.

**Differential Diagnosis for Gastrointestinal Signs Seen in Dogs and Cats with Histoplasmosis**

**Large Intestinal Disease**

**Diet-Associated Colitis**
- Dietary hypersensitivity
- Foreign material–induced colitis

**Idiopathic Colitis**
- Lymphocytic-plasmacytic colitis
- Eosinophilic colitis
- Granulomatous colitis
- Histioctytic ulcerative colitis of Boxer dogs
- Suppurative colitis

**Parasitic and Protozoal Colitis**
- Trichuriasis (whipworm)
- Ancylostomiasis (hookworm)
- Entamebiasis
- Balantidiasis
- Giardiasis

**Bacterial colitis**
- Salmonellosis
- Campylobacter jejuni
- Yersinia enterocolitica, Y. pseudotuberculosis
- Mycobacteria
- Clostridium perfringens, C. difficile

**Fungal colitis**
- Candidiasis
- GI pythiosis
- Protothecosis

**Cecocolic or ileocolic intussusception**

**Pancreatitis-associated colitis**

**Small Intestinal Disease**

**Idiopathic inflammatory bowel disease**
- Lymphocytic-plasmacytic enteritis
- Eosinophilic enteritis
- Granulomatous enteritis

**Intestinal lymphosarcoma**

**Parasitic enteritis**
- Ancylostomiasis
- Toxocariasis
- Chronic giardiasis
Infectious enteritis
• Small intestinal bacterial overgrowth
• GI pythiosis
Lymphangiectasia
Exocrine pancreatic insufficiency
Partial intestinal obstruction
Chronic enteropathy of Shar-Peis
Immunoproliferative enteritis of Basenjis

Coccidioidomycosis
Primarily southwestern United States, California, Mexico, Central and South America
Common clinical signs include lameness with swollen and painful joints and bones, cough, dyspnea, anorexia, weakness, pleural effusion, and cutaneous lesions over infected bones.
Less common signs include myocarditis, icterus, renomegaly, splenomegaly, hepatomegaly, orchitis, epididymitis, keratitis, iritis, granulomatous uveitis, glaucoma, seizures, ataxia, and central vestibular disease.

Cryptococcosis
Found worldwide, more common in southern United States, most common in cats
Common clinical signs include upper respiratory signs, unilateral to bilateral nasal discharge, soft masses in nasal cavity or over bridge of nose, ulcerative skin lesions, lymphadenopathy, granulomatous chorioretinitis, and retinal detachment.
Less common signs include fever, lung involvement, CNS involvement caused by invasion through cribriform plate, depression, seizures, circling, ataxia, blindness, head pressing, and paresis.

Aspergillosis
Dogs affected more often than cats
Nasal turbinate destruction, frontal sinus osteomyelitis, mucoid to hemorrhagic nasal discharge, epistaxis
May lead to masticatory muscle atrophy and CNS disease by erosion through cribriform plate
In rare cases, disseminates and causes multiple-organ disease

Pythiosis, Lagenidiosis (Pythium insidiosum, Lagenidium giganteum)
Severe, often fatal, chronic gastrointestinal and cutaneous diseases

Zygomycosis (Multiple Fungi in Class Zygomycetes)
Nasopharyngeal involvement, poorly responsive to therapy
Differential Diagnosis for Systemic Manifestations

Multisystemic granulomatous, neoplastic, and immune-mediated diseases must be differentiated from disseminated systemic mycoses.

Differential Diagnosis for Nodular Skin Disease

**Bacteria Skin Disease**
- Actinomycosis
- Mycobacteriosis
- Botryomycosis
- Brucellosis
- *Rhodococcus equi* infection
- *Bartonella vinsonii* subsp. *Berkhoffi* infection

**Mycotic and Miscellaneous Infectious Skin Disease**
- Cryptococcosis
- Blastomycosis
- Coccidioidomycosis
- Sporotrichosis
- Basidiobolomycosis
- Conidiobolomycosis
- Phaeohyphomycosis
- Hyalohyphomycosis
- Eumycotic mycetoma
- Dermatophytic mycetoma
- Protothecosis
- Pythiosis
- Lagenidiosis
- Nodular leishmaniasis

**Noninfectious Pyogranulomatous Skin Disease**
- Foreign body reaction
- Idiopathic nodular panniculitis
- Sebaceous adenitis (nodular form)
- Canine cutaneous sterile pyogranulomatous/granuloma syndrome

**Neoplasia**
- Squamous cell carcinoma
- Cutaneous lymphoma
- Mycosis fungoides (cutaneous T-cell lymphoma)
- Cutaneous histiocytosis

**Miscellaneous Diseases**
- Systemic lupus erythematosus
- Systemic vasculitis
- Cutaneous embolic disease
Differential Diagnosis for Chorioretinitis, Exudative Retinal Detachment, and Panophthalmitis

**Fungal**
- Blastomycosis
- Cryptococcosis
- Coccidioidomycosis
- Geotrichosis
- Histoplasmosis
- Aspergillosis

**Neoplasia**
- Lymphosarcoma
- Metastatic neoplasia

**Miscellaneous Infectious Causes**
- Protothecosis
- Brucellosis
- Toxoplasmosis
- *Neospora caninum* infection
- Leishmaniasis

Lymphadenopathy must be differentiated from numerous causes including lymphosarcoma, other fungal infections, rickettsial diseases, brucellosis, mycobacteriosis, protothecosis, and leishmaniasis. Solitary bone lesions must be differentiated from primary or metastatic neoplasia and other fungal or bacterial osteomyelitis.

**Polysystemic Protozoal Diseases**

**Clinical Findings**

**Feline Toxoplasmosis**
- Acute toxoplasmosis: may induce a self-limiting, small bowel diarrhea
- Disseminated toxoplasmosis: overwhelming intracellular replication of tachyzoites after primary infection—depression, anorexia, fever, hypothermia, peritoneal effusion, icterus, dyspnea, death—coinfeciton with feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), and others may predispose to disseminated toxoplasmosis
- Chronic toxoplasmosis: anterior or posterior uveitis, fever, muscle hyperesthesia, weight loss, anorexia, seizures, ataxia, icterus, diarrhea, pancreatitis
Canine Toxoplasmosis
Respiratory, gastrointestinal, neuromuscular signs: fever, vomiting, diarrhea, dyspnea, icterus, ataxia, seizures, tremors, cranial nerve deficits, paresis, paralysis, myositis, lower motor neuron disease, myocardial disease, chorioretinitis, anterior uveitis, iridocyclitis, optic neuritis (ocular lesions less common in dogs than cats)

Neosporosis
Most common in neonates but can be seen at any age
Ascending paralysis, hyperextension of hind limbs, muscle atrophy, polymyositis, multifocal CNS disease, myocarditis, dysphagia, ulcerative dermatitis, pneumonia, hepatitis

Babesiosis
Anemia, fever, pale mucous membranes, tachycardia, tachypnea, depression, anorexia, weakness, icterus, petechiae, hepatosplenomegaly, disseminated intravascular coagulation (DIC), metabolic acidosis, renal disease

Cytauxzoonosis
Fever, anorexia, dyspnea (pneumonitis), depression, icterus, pale mucous membranes, death

Hepatozoonosis (*Hepatozoon canis and H. americanum*)
Most common in puppies and immunosuppressed dogs, but *H. americanum* can be primary
Fever, weight loss, severe hyperesthesia, anorexia, anemia, depression, oculonasal discharge, bloody diarrhea

Leishmaniasis
Weight loss, normal to increased appetite, polyuria/polydipsia, muscle wasting, depression, vomiting, diarrhea, cough, epistaxis, sneezing, melena, splenomegaly, facial alopecia, rhinitis, dermatitis, icterus, swollen and painful joints, uveitis, conjunctivitis
Dermatologic lesions include hyperkeratosis, scaling, mucocutaneous ulcers, and intradermal nodules on muzzle, ears, and footpads.

American Trypanosomiasis (*Trypanosoma cruzi*)
Acute infection: myocarditis, heart failure—lymphadenopathy, pale mucous membranes, tachycardia, pulse deficits, hepatomegaly, abdominal distension, anorexia, diarrhea, neurologic signs
Chronic infection: Those that survive acute infection may present with chronic dilative cardiomyopathy—right-sided heart failure, conductive disturbances, supraventricular arrhythmias.
Rocky Mountain Spotted Fever

Clinical Findings

- Depression/lethargy
- Fever
- Anorexia
- Myalgia/arthralgia
- Lymphadenopathy
- Vestibular deficits
- Conjunctivitis/scleral congestion/hyphema/iridal and retinal hemorrhage
- Pneumonitis/dyspnea/cough
- Abdominal pain
- Edema of face and extremities
- Epistaxis
- Melena
- Hematuria
- Anterior uveitis
- Rash/petechiae
- Nausea/vomiting
- Diarrhea
- Vasculitis/thrombocytopenia/disseminated intravascular coagulation (DIC)
- Hyperesthesia/spinal cord signs
- Seizures
- Cardiac arrhythmias
- Icterus
- Acute renal failure
- Coma/stupor
- Polyuria/polydipsia

Sepsis and Systemic Inflammatory Response Syndrome (SIRS)

Definitions

*Bacteremia:* the presence of viable bacteria in the bloodstream

*Sepsis:* infection-induced systemic inflammation

*Severe sepsis:* organ dysfunction and manifestations of hypoperfusion or hypotension secondary to sepsis

*Septic shock:* hypotension secondary to sepsis, not responsive to intravenous (IV) fluid therapy

*SIRS:* systemic inflammation caused by either infectious or noninfectious processes. Diagnosis of SIRS is based on fulfillment of at least two of four criteria (tachycardia,
tachypnea, hypothermia, or hyperthermia and either
leucocytosis, leucopenia, or bands)

*Multiple organ dysfunction syndrome (MODS)*: altered
function of two or more organs secondary to SIRS
such that homeostasis cannot be maintained without
intervention

*Acute respiratory distress syndrome (ARDS)*: a pulmonary
inflammatory disorder characterized by noncardiogenic
pulmonary edema, neutrophilic inflammation, and
hypoxemia

### Noninfectious Causes of SIRS

- Pancreatitis
- Tissue trauma
- Heat stroke
- Ischemia
- Burns
- Pansystemic neoplasia

### Infectious Causes of SIRS (Sepsis)

- Peritonitis
- Pyometra
- Prostatitis
- Prostatic abscess
- Pyelonephritis
- Pneumonia
- Pyothorax
- Gastroenteritis
- Endocarditis
- Nosocomial infections (IV catheters, urinary catheters, etc.)

### Clinical Findings of Sepsis and SIRS

- Fever or hypothermia
- Tachycardia, tachypnea
- Neutrophilia with left shift or leukopenia
- Anemia
- Depression
- Bounding or diminished pulses
- Brick-red mucus membranes or pallor
- Hypothermia
- Thrombocytopenia
- Hypoalbuminemia, hypoglycemia
- Disseminated intravascular coagulation (DIC)
- Bilirubinemia
- Elevated hepatic enzymes
- Azotemia
- Oliguria
Lactic acidosis
Hypoxemia
Signs related to underlying condition

Vaccines, Recommended Core vs. Noncore

Core Vaccines for Dogs
- Distemper
- Parvovirus
- Adenovirus-2
- Rabies

Core Vaccines for Cats
- Parvovirus (panleukopenia)
- Herpesvirus-1
- Calicivirus
- Rabies

Noncore Vaccines for Dogs
Need determined by individual clinician after assessment of patient risk
- Bordetellosis
- Parainfluenza
- Canine influenza
- Leptospirosis
- Lyme borreliosis
- *Crotalus atrax*
- *Porphyromonas* spp.

Noncore Vaccines for Cats
Need determined by individual clinician after assessment of patient risk
- Feline leukemia virus (FeLV)
- Feline immunodeficiency virus (FIV)
- *Chlamydomphila felis* (formerly, *Chlamydia psittaci*)
- Bordetellosis

Viruses, Canine

Common Viral Agents of Diseases of Dogs

Parvovirus
- May be asymptomatic or fulminant disease
- Anorexia, lethargy, fever, vomiting, hemorrhagic diarrhea, myocarditis (rare)
- Worse in very young and parasitized puppies
- Neutropenia, hypoalbuminemia, severe dehydration, secondary septicemia
Coronavirus
Diarrhea (infrequently blood in feces), vomiting, anorexia, lethargy, often self-limiting
Canine respiratory coronavirus, part of “kennel cough” complex
Coughing, sneezing, nasal discharge
Canine pancytotropic coronavirus
Severe clinical disease in puppies and juvenile dogs
Fever, lethargy, anorexia, vomiting, hemorrhagic diarrhea, ataxia, seizures

Rotavirus
Vomiting, diarrhea (rarely bloody), anorexia, typically recover after 5-7 days

Adenovirus Type 1 (Infectious Canine Hepatitis)
Fever, anorexia, lethargy, depression, abdominal pain, pale mucous membranes, tonsillitis, pharyngitis, coughing, hepatomegaly
Severe cases: coagulation abnormalities, petechiae, ecchymosis, DIC, rarely icterus, hepatic encephalopathy
Anterior uveitis and glomerulonephritis secondary to immune complex deposition

Canine Distemper Virus (See the next section)

Canine Influenza A Subtype H3N8 Virus
Acute onset of coughing, sneezing, nasal discharge, ocular discharge
Lowgrade fever
Secondary commensal bacterial infections leading to mucopurulent discharge and productive cough
May lead to pneumonia with high fever, inappetence, productive cough, and increased respiratory effort

Rabies Virus
Variable incubation period, prodromal phase: nervousness, anxiety, paresthesia
Progress to forebrain signs (“furious” form of rabies): irritability, restlessness, pica, photophobia, increased saliva production with decreasing ability to swallow, hyperesthesia progressing to incoordination, seizures, and death
May also progress to “dumb” form: paralysis, lower motor disease, leading to coma, respiratory paralysis, and death

Pseudorabies
Suspected to be result from ingestion of infected raw pork
Neurologic dysfunction: ataxia, abnormal papillary light response, restlessness, trismus, cervical rigidity, ptyalism, tachypnea, excoration from pruritus of head and neck; vomiting, diarrhea; most dogs die within 48 hours

**Parainfluenza and Adenovirus Type 2**
Hacking cough with gagging, easily elicited with tracheal palpation; cough may be paroxysmal, usually subsides within 7-10 days, and may lead to secondary bacterial or mycoplasmal infection

**Canine Herpesvirus**
Abortion, stillbirths; puppies born live progress to crying, hypothermia, soft stools, petechiae, cessation of nursing, and death
Older puppies develop mild respiratory signs that may emerge later as neurologic disease (ataxia, blindness, central vestibular disease).
Adult dogs: usually asymptomatic, rhinitis, pharyngitis, vaginal or preputial hyperemia, hyperplasia of vaginal mucosal lymphoid follicles, submucosal hemorrhage

**Canine Oral Papillomavirus**
Oral papilloma (warts), may be quite extensive, spontaneously regress

**West Nile Virus**
Clinical disease is uncommon.

**Bornavirus**
Seropositivity in the absence of clinical signs appears possible.
Tremors, salivation, mydriasis, circling

**Canine Distemper Virus Infection, Clinical Findings**

**General Signs**
- Fever
- Lethargy
- Depression
- Anorexia
- Dehydration

**Respiratory Tract**
- Mucoid to mucopurulent discharge
- Bronchopneumonia
  - Coughing
  - Crackles on auscultation
  - Increased bronchovesicular sounds
  - Dyspnea
- Sneezing
Gastrointestinal Tract
   Vomiting
   Small bowel diarrhea

Ocular Disease
   Mucopurulent ocular discharge
   Chorioretinitis, medallion lesions, optic neuritis, retinal detachment
   Keratoconjunctivitis sicca
   Anterior uveitis

Neurologic Disease
   Spinal cord lesion: paresis and ataxia
   Central vestibular disease: head tilt, nystagmus, other cranial nerve and conscious proprioception deficits
   Cerebellar disease: ataxia, head bobbing, hypermetria
   Cerebral disease: seizures, blindness
   Chorea myoclonus: rhythmic jerking of single muscles or muscle groups

Miscellaneous
   Tonsillar enlargement
   Pustular dermatosis
   Hyperkeratosis of nose and footpads
   Enamel hypoplasia

In Utero Infection
   Stillbirth
   Abortion
   “Fading puppy” syndrome in neonatal period
   Central nervous system signs at birth

Viruses, Feline

American Association of Feline Practitioners Guidelines for Retroviral Testing in Cats

- Sick cats should be tested even if they have tested negative before.
- Cats and kittens should be tested when they are first acquired.
- Even cats not expected to live with other cats should be tested. This provides a health assessment of the individual, other cats may join the household, indoor cats may escape and expose other cats.
- Tests should be performed at adoption and negative cats should be retested a minimum of 60 days later.
• Cats with known recent exposure to a retrovirus-infected cat or a cat with unknown status, particularly via a bite wound, should be tested regardless of previous test results. Testing should be done immediately and, if negative, should be repeated after a minimum of 30 days for FeLV and after a minimum of 60 days for FIV (when the type of potential viral exposure is unknown, retesting for both viruses after 60 days is most practical).
• Cats living in households with other cats infected with FIV or FeLV should be tested annually.
• High-risk cats (cats in cat-dense neighborhoods or cats that fight and get cat-bite wounds and abscesses) should be tested regularly.
• Cats should be tested before initial vaccination against FeLV or FIV.
• Cats used for blood or tissue donation should have negative screening tests for FeLV and FIV and should be negative for real-time PCR tests.
• Intermittent retesting is not necessary for cats with confirmed negative infection status unless there is opportunity for exposure to infected cats or if they become ill.
• Each cat should be individually tested. Testing of one cat as a proxy for another or pooling samples from multiple cats for testing is inappropriate.

Clinical Signs of Rabies Virus Infection in Cats
• Initially signs are nonspecific: lethargy, inappetence, vomiting, diarrhea
• Rapid and continual deterioration of clinical conditions, no waxing and waning
• Behavioral changes: more reclusive or attention-seeking, may unpredictably attack animate, inanimate, or unseen objects
• Irrevocable progression to classic signs, ptalism with decreased ability to swallow leads to contamination of oral cavity, chin, and forelegs with potentially infectious saliva. Cranial nerve signs such as anisocoria, pupil dysfunction, facial or tongue paresis, and changes in phonation may occur.
• Auditory, visual, or tactile stimulation may elicit profound aggression to self-mutilation.
• Become profoundly moribund to comatose to death. 100% fatal
Feline Infectious Peritonitis (FIP, Feline Coronavirus Infection), Clinical Findings

**Signalment and History**
- Purebred cats from cattery
- Multicat households
- Younger than 5 years or older than 10 years of age
- Previous history of mild, self-limiting gastrointestinal or respiratory disease
- Anorexia, weight loss, depression
- Seizures, nystagmus, ataxia
- Acute, fulminant course in cats with effusive FIP
- Chronic, intermittent course in cats with noneffusive FIP

**Physical Examination Findings**
- Fever
- Weight loss
- Abdominal distension/fluid wave
- Abdominal mass (focal intestinal granuloma, lymphadenopathy)
- Icterus
- Muffled heart or lung sounds
- Dyspnea secondary to pleural effusion
- Hepatomegaly
- Chorioretinitis, iridocyclitis
- Splenomegaly
- Pale mucous membranes with or without petechiae
- Multifocal neurologic abnormalities
- Irregularly marginated kidneys
- Renomegaly

**Clinicopathologic Abnormalities**
- Complete blood count (CBC): nonregenerative anemia, neutrophilia with or without left shift, lymphopenia
- Serum chemistry: elevated alkaline phosphatase (ALP) and alanine aminotransferase (ALT), hyperbilirubinemia, hyperglobulinemia (polyclonal, rarely monoclonal gammopathy), azotemia (prerenal or renal)
- Urinalysis: proteinuria
- Nonseptic, pyogranulomatous exudate in peritoneal cavity, pleural space, and pericardium
- Positive coronavirus antibody titer (especially in noneffusive cases)
- Cerebrospinal fluid (CSF) tap: increased protein concentration, neutrophilic pleocytosis, coronavirus antibodies
- Histopathology: pyogranulomatous inflammation in perivascular locations of tissues
Positive for coronavirus on immunofluorescence or reverse-transcriptase polymerase chain reaction (RT-PCR) testing of abdominal or pleural effusions (although these tests do not differentiate between FIP-causing viruses and “harmless” feline enteric coronavirus)

**Feline Immunodeficiency Virus (FIV) Infection, Clinical Findings**

**Primary Phase of Infection**
- Low-grade fever
- Lymphadenopathy
- Neutropenia

**Latent Phase**
- No clinical signs for months to years

**Immunodeficiency Phase**

**Primary Viral Effects**
- Weight loss
- Nonregenerative anemia, neutropenia, thrombocytopenia
- Small bowel diarrhea
- Glomerulonephritis
- Myeloproliferative disorders
- Lymphoma
- Renal failure
- Anterior uveitis, pars planitis
- Behavioral abnormalities

**Opportunistic Infectious Agents**
- Cutaneous: atypical mycobacteriosis, demodicosis, *Notoedres* and *Otodectes* infestation, dermatophytosis, cryptococcosis, cowpox
- Gastrointestinal: cryptosporidiosis, coccidiosis, giardiasis, salmonellosis, campylobacteriosis, others
- Renal: bacterial infections, FIP, feline leukemia virus (FeLV)
- Urinary tract: bacterial infections
- Neoplasia: FeLV
- Hematologic: *Mycoplasma haemofelis*, FeLV, bartonellosis
- Neurologic: toxoplasmosis, cryptococcosis, FIP, FeLV
- Ophthalmologic: toxoplasmosis, FIP, cryptococcosis, herpesvirus, bartonellosis
- Pneumonia/pneumonitis: bacterial, toxoplasmosis, cryptococcosis
Pyothorax: bacterial
Stomatitis: calicivirus, bacterial, candidiasis, bartonellosis
Upper respiratory: herpesvirus, calicivirus, bacterial, cryptococcosis

**Feline Leukemia Virus (FeLV), Clinical Findings**

**Acute Phase**
- Fever
- Malaise
- Diarrhea
- Leukopenia

**General Signs**
- Anorexia
- Weight loss
- Depression
- Many FeLV positive cats are asymptomatic at diagnosis

**Neoplastic**
- Lymphoma: mediastinal, multicentric, alimentary, renal
- Leukemia: lymphocytic, myelogenous, erythroid, megakaryocytic
- Myeloproliferative disorders
- Fibrosarcoma

**Icterus**
- Prehepatic: immune-mediated red blood cell (RBC) destruction induced by FeLV or secondary infection with *Mycoplasma haemofelis*
- Hepatic: hepatic lymphoma, focal liver necrosis, hepatic lipidosis
- Posthepatic: alimentary lymphoma

**Bone marrow**
- Pure red cell aplasia
- Regenerative anemia (less common and often associated with coinfection with *Mycoplasma haemofelis*)
- Myeloproliferative disease (anemia, leukopenia, thrombocytopenia)

**Stomatitis**
- Bacterial infection
- Calicivirus infection

**Rhinitis/Pneumonia**
- Bacteria
- Herpesvirus and calicivirus
Renal
Glomerulonephritis
Renal failure
Urinary incontinence: sphincter incompetence or detrusor hyperactivity

Ocular Lymphoma
Aqueous flare, mass lesions, keratitic precipitates, lens luxations, glaucoma, anterior uveitis

Neurologic Polyneuropathy or lymphoma
Anisocoria, ataxia, weakness, tetraparesis, paraparesis, behavioral changes, urinary incontinence
Secondary infection with FIP, *Toxoplasma gondii*, *Cryptococcus neoformans*

In Utero Infection
Abortion, stillbirth, infertility, kitten mortality complex (“fading kitten” syndrome)

Lameness
Neutrophilic polyarthritis secondary to immune complex deposition
Multiple cartilaginous exostoses

**Feline Leukemia Virus, Possible Outcomes Following Exposure**

**Progressive Infection**
Viral replication in lymphoid tissue and bone marrow, spread to mucosal and glandular tissues, leading to shedding of virus. Most cats become persistently infected and frequently die of an FeLV-associated disease within a few years.

**Regressive Infection**
Effective immune response limits viral replication. FeLV antigen detectable in peripheral blood within 2-3 weeks after exposure but disappears 2-8 weeks later. May not ever develop antigenemia. Clinical relevance of regressive infection is not clear. May have persistent integration of FeLV DNA in their genome but are unlikely to develop FeLV-associated diseases. Do not shed virus.

**Abortive Exposure**
Seen infrequently following experimental FeLV inoculation characterized by negative results for culturable virus, antigen, viral RNA, and proviral DNA

**Focal Infections**
Rare events in which cats have FeLV infection restricted to certain tissues such as spleen, lymph nodes, small intestine, or mammary glands.
Other Feline Viral Diseases

Upper Respiratory Tract Viruses
- Herpesvirus type 1: ocular and nasal disease
- Calicivirus: ocular, nasal, and oral disease; rarely joint disease
- Reovirus: Conjunctivitis, respiratory lesions, diarrhea experimentally, no evidence of importance in the field

Enteric Viruses
- Feline parvovirus (panleukopenia virus): enteritis, panleukopenia, cerebellar hypoplasia, fetal death
- Feline coronavirus: mild enteritis, FIP
- Rotavirus: rare cause of mild diarrhea
- Astrovirus: uncommon cause of persistent watery diarrhea
- Torovirus: may be associated with protruding nictitating membrane and diarrhea syndrome

Miscellaneous
- Cowpox virus: mainly see skin lesions; sporadic disease in cats
- Hantavirus: zoonotic disease of wild rodents; clinical significance in cats not known
- Rabies virus
- Pseudorabies virus: cats are a rare host, severe behavioral changes, pruritus, paralysis, coma, death
- Feline herpesvirus type 2: possible association with feline idiopathic lower urinary tract disease
Differential Diagnosis: Infectious Arthritis

**Septic Arthritis**

*Bacterial Suppurative Arthritis*
- Penetrating wounds
- Animal bites
- Iatrogenic
- Infection during surgery, arthrocentesis
- Trauma (e.g., hit by car)
- Hematogenous
- Endocarditis
- Omphalophlebitis
- Pyoderma
- Other foci of infection

**Lyme Arthritis**

*Borrelia burgdorferi*

Transmitted by *Ixodes* ticks

**Bacterial L-Form Arthritis**

Cell wall–deficient bacteria

Causes suppurative arthritis and subcutaneous abscesses in cats

**Mycoplasma Arthritis**

Debilitated and immunosuppressed animals

*M. gatae, M. felis* in cats

**Fungal Arthritis (Rare)**

*Coccidioides immitis*

*Blastomyces dermatitidis*

*Cryptococcus neoformans*

*Sporothrix schenckii*

*Aspergillus terreus*
Rickettsial Arthritis
- Rocky Mountain spotted fever (*Rickettsia rickettsii*)
- *Ehrlichia canis*
- *Anaplasma phagocytophilum*

Protozoal Arthritis
- Leishmaniasis (*Leishmania* spp.)
- Toxoplasmosis (rare)
- Neosporosis (*Neospora caninum*): polyarthritis, polymyositis, neurologic disease
- Hepatozoonosis: polyarthritis and polymyositis in dog and cat
- Babesiosis (rare, more often causes severe anemia)

Viral Arthritis
- Calicivirus infection in cats

Differential Diagnosis of Noninfectious Arthritis

Nonerosive
- Immune-mediated polyarthritis
- Systemic lupus erythematosus
- Reactive polyarthritis (bacterial, fungal, parasitic, neoplastic, enterohepatic, drug reaction, vaccine induced)
- Breed-associated syndromes
  - Polyarthritis (Akita, Newfoundland, Weimaraner)
  - Polyarthritis/meningitis (Akita, Beagle, Bernese Mountain Dog, Boxer, German Shorthair Pointer)
  - Polyarthritis/polymyositis (spaniels)
- Familial Shar-Pei fever
- Lymphoplasmacytic synovitis

Erosive
- Rheumatoid-like arthritis
- Erosive polyarthritis of Greyhounds
- Feline chronic progressive polyarthritis

Bone Disorders

Differential Diagnosis: Congenital, Developmental, Genetic

Congenital
- Hemimelia, phocomelia, amelia: absence of portions or entire limb (amelia)
- Syndactyly: fusion of two or more digits; rarely clinically significant
Polydactyly: extra digits
Ectrodactyly: third metacarpal and digit missing forming a cleft (split or “lobster” claw)
Segmented hemiatrophy: limb hypoplasia

Developmental and Genetic
Osteopetrosis: rare; diaphysis remains filled with bone, marrow does not form, fragile bones
Osteogenesis imperfecta: heritable diseases—fragile bones
Mucopolysaccharidosis: rare lysosomal storage disease—Siamese cats—causes dwarfism, facial dysmorphism
Dwarfism
• Osteochondrodysplasias
• Pituitary dwarfism
• Congenital hypothyroidism
Retained cartilage cores
Craniomandibular osteopathy (West Highland White Terrier, Scottish Terrier, Cairn Terrier, Boston Terrier, other terriers)
Multiple cartilaginous exostoses

Differential Diagnosis: Metabolic, Nutritional, Endocrine, Idiopathic

Metabolic
Nutritional secondary hyperparathyroidism
Lead poisoning

Nutritional
Rickets (hypovitaminosis D)
Renal osteodystrophy
Hypervitaminosis A: causes osteopathy
Hypovitaminosis A: deformed bones secondary to impedance of bone remodeling
Hypervitaminosis D: skeletal demineralization
Zinc-responsive chondrodysplasia
Copper deficiency
Overnutrition of growing dogs

Endocrine
Primary hyperparathyroidism
Humoral hypercalcemia of malignancy
Hyperadrenocorticism
Hypogonadism: delay in physis closure after early gonadectomy
Hepatic osteodystrophy
Anticonvulsant osteodystrophy
Idiopathic
    Enostosis (panosteitis)
    Metaphyseal osteopathy (hypertrophic osteodystrophy)
    Avascular necrosis of femoral head (Legg-Calvé-Perthes disease)
    Secondary hypertrophic osteopathy (usually in response to thoracic neoplasia)
    Medullary bone infarction
    Bone cyst
    Aneurysmal bone cyst
    Subchondral bone cyst
    Fibrous dysplasia
    Central giant cell granuloma
Liver and Exocrine Pancreatic Disorders

Cholangitis and Cholangiohepatitis, Feline
Exocrine Pancreatic Disease
Gallbladder and Extrahepatic Biliary Disease
Hepatic Encephalopathy
Hepatic Lipidosis, Feline
Hepatobiliary Disease
Hepatomegaly and Microhepatica
Hyperlipidemia
Pancreatitis
Portosystemic Shunt, Congenital
Vacuolar Hepatopathy, Canine

**SECTION IX**

Liver and Exocrine Pancreatic Disorders

Cholangitis and Cholangiohepatitis, Feline
Exocrine Pancreatic Disease
Gallbladder and Extrahepatic Biliary Disease
Hepatic Encephalopathy
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**Cholangitis and Cholangiohepatitis, Feline**

**Comparative Clinical Findings**

**Suppurative (Neutrophilic) Cholangitis and Cholangiohepatitis**
- Middle-aged to older cats
- Often depressed and ill
- Anorexia (usually)
- Jaundice
- Neutrophilia
- Increased alanine aminotransferase (ALT)
- Increased alkaline phosphatase (ALP)
- Increased bilirubin (±)
- Increased serum and urine bile acids (±)
- Hyperechoic liver and bile stasis
- Primarily neutrophilic infiltrate
- Lesions surround bile ducts
- May be associated with pancreatitis and/or inflammatory bowel disease
- Respond to antibiotics and supportive nonspecific treatments

**Lymphocytic Cholangitis**
- Younger cats
- Persians
- Bright and alert
- Polyphagia (±)
Ascites (±)
Icterus (±)
Lymphadenopathy (±)
Hepatomegaly (±)
Neutrophilia (±)
Lymphopenia (±)
Bile acids (±)
Increased ALT
Increased ALP
Bilirubinemia/bilirubinuria (±)
Hyperglobulinemia
Hyperechoic liver (±)
Primarily lymphocytic infiltrate
Lesions found in portal areas
Variable fibrosis
Pancreatitis (may be present)
Positive response to immunosuppressive corticosteroids

Exocrine Pancreatic Disease

Differential Diagnosis

Pancreatitis
• Acute
• Chronic
Exocrine pancreatic insufficiency
Pancreatic pseudocyst
Pancreatic abscess
Exocrine pancreatic neoplasia
• Pancreatic adenoma
• Pancreatic adenocarcinoma
• Pancreatic sarcoma (spindle cell sarcoma, lymphosarcoma) rare
Nodular hyperplasia
Pancreatic parasites (cats)
• *Eurystrema procyonis* (pancreatic fluke)
• *Amphimerus pseudofelineus* (hepatic fluke)
Pancreatic bladder
• Abnormal extension of pancreatic duct (rare finding in cat)

Clinical Findings of Exocrine Pancreatic Insufficiency

Most often seen in young to middle-aged dogs; German Shepherds are predisposed
Chronic weight loss
Ravenous appetite
Coprophagia
Pica
Change in fecal character
• Voluminous
• Soft
• Watery
• May be normal
Poor haircoat quality
Borborygmus, flatulence
Coagulation disorder (caused by malabsorption of vitamin K, rare)

Gallbladder and Extrahepatic Biliary Disease

Differential Diagnosis

Obstructive Disease
Extrahepatic biliary obstruction
• Pancreatitis (most common etiology in dog)
• Biliary neoplasia
• Cholangitis
• Pancreatic neoplasia
Cholelithiasis/choledocholithiasis
Gallbladder mucocele

Nonobstructive Disease
Cholecystitis
• Bacterial cholecystitis (ascending infection—Escherichia coli most common)
• Necrotizing cholecystitis
• Emphysematous cholecystitis (E. coli, Clostridium perfringens)
Cholelithiasis/choledocholithiasis (does not always cause obstruction)
Parasites (mainly seen in cats) Tropical climates (seen in cats that eat lizards or toads)
• Platynosomum fastosum (a fluke)
• Amphimerus pseudofelineus
• Metorchis conjunctus
• Eurytrema procyonis
Gallbladder infarct

Neoplasia
Biliary cystadenoma
Bile duct carcinoma
Carolii Disease
Dilatation of intrahepatic and extrahepatic bile ducts

Gallbladder Rupture
Necrotizing cholecystitis
Obstruction
Iatrogenic
Blunt abdominal trauma
Gallbladder torsion

Clinical Findings of Gallbladder and Biliary Disease

Clinical Signs
Vomiting
Icterus
Anorexia
Fever
Abdominal pain
Depression
Weight loss
Ascites/bile peritonitis

Clinicopathologic Findings
Hyperbilirubinemia
Elevated alkaline phosphatase (ALP) levels
Elevated gamma glutamyltransferase (GGT) levels
Elevated serum bile acids
Elevated alanine aminotransferase (ALT) levels
Hypercholesterolemia
Stress leukogram
Nonregenerative anemia

Radiographic Findings
Hepatomegaly
Mass effect in area of gallbladder
Gas shadow in area of gallbladder
Choleliths radiopaque if they contain calcium (50% may not be seen on radiographs)

Ultrasonographic Signs
Dilated and tortuous bile ducts
Gallbladder distension
Thickened gallbladder wall
Cholelith visible
Pancreatic mass identified
Stellate appearance to contents of gallbladder
(characteristic of a gallbladder mucocele)
Hepatic Encephalopathy

Clinical Findings

General Systemic Clinical Signs
- Anorexia
- Depression
- Weight loss
- Lethargy
- Nausea
- Fever
- Ptyalism
- Intermittent vomiting
- Diarrhea

Central Nervous System Clinical Signs
- Tremors
- Ataxia
- Personality change (often toward aggression)
- Dementia
- Head pressing
- Pacing
- Circling
- Hysteria
- Cortical blindness
- Seizures
- Coma

Hepatic Lipidosis, Feline

Clinical Findings

Historical Findings
- Obesity
- Recent anorexia and rapid weight loss
  - Concurrent disease that causes anorexia (pancreatitis, diabetes mellitus, inflammatory hepatobiliary disease, inflammatory bowel disease, feline infectious peritonitis, chronic renal failure, neoplasia, cardiomyopathy, neurologic disease, etc.)
  - Stressful event
  - Abrupt diet change
- Typically indoor cats

Physical Findings
- Jaundice
- Vomiting
- Dehydration
Hepatic encephalopathy

- Depression
- Ptyalism

Hepatomegaly

**Clinicopathologic Findings**

Typical findings of cholestasis

- Moderate increase in alanine aminotransferase (ALT)
- Marked increase in alkaline phosphatase (ALP)
- Mild increase in gamma glutamyltransferase (GGT); disproportionately low compared with other feline cholestatic hepatopathies
- Elevated serum bile acids typical

Coagulation test abnormalities (especially in conjunction with acute pancreatitis)

**Cytology (Ultrasound-Guided Needle Aspirates) and Histopathology**

Reveal clear vacuolation of most hepatocytes, nonzonal in distribution; typically with absence of inflammatory cells

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**Hepatobiliary Disease**

**Clinical and Physical Findings**

**General Clinical Features**

- Depression
- Anorexia
- Lethargy
- Weight loss
- Poor haircoat, insufficient grooming
- Nausea, vomiting
- Diarrhea
- Dehydration
- Small body stature
- Polydipsia, polyuria

**Signs Specific but Not Pathognomonic for Hepatic Disease**

- Icterus
- Bilirubinuria
- Acholic feces
- Organomegaly
- Ascites
- Hepatic encephalopathy
  - Behavioral changes (aggression, dementia, hysteria)
  - Circling
  - Ataxia
• Staggering
• Pacing
• Head pressing
• Cortical blindness
• Ptyalism
• Tremors/seizures
• Coma
Coagulopathies
Polydipsia/polyuria

Causes of Elevated Serum Hepatobiliary Enzymes

Primary Hepatic Disease

Drug Induction
Corticosteroids (dogs)
Anticonvulsants (phenobarbital, phenytoin, primidone)

Endocrinopathies
Hyperadrenocorticism (dogs)
Hypothyroidism (dogs)
Hyperthyroidism (cats)
Diabetes mellitus

Bone Disorders
Growing animals
Osteosarcoma
Osteomyelitis

Neoplasia
Adenocarcinomas (pancreatic, intestinal, adrenocortical, mammary)
Sarcomas (hemangiosarcoma, leiomyosarcoma)
Hepatic metastasis

Muscle Injury
Acute muscle necrosis/trauma
Myopathies
Malignant hyperthermia

Hypoxia/Hypotension
Septic shock
Surgery
Congestive heart failure
Hypoadrenocorticism
Circulatory shock
Severe acute blood loss
Hypotensive crisis
Status epilepticus
Gastrointestinal Disease
Pancreatitis
Inflammatory bowel disease

Miscellaneous Causes
Systemic infections
Pregnancy (cats—increased placental alkaline phosphatase)
Colostrum-fed neonates (dogs)
Breed related (Scottish terrier)

Differential Diagnosis, Dogs

Inflammation
Chronic hepatitis complex
- Copper accumulation—Bedlington Terrier, Airedale Terrier, Bull Terrier, Bulldog, Cocker Spaniel, Collie, Dachshund, Dalmatian, Doberman Pinscher, German Shepherd, Golden Retriever, Keeshond, Kerry Blue Terrier, Labrador Retriever, Norwich Terrier, Old English Sheepdog, Pekingese, Poodle, Samoyed, Schnauzer, Skye Terrier, West Highland White Terrier, Wire Fox Terrier
- Drug induced: trimethoprim-sulfa, phenobarbital, diethylcarbamazine, oxibendazole, many others
- Familial hepatitis—Doberman Pinscher, West Highland White Terrier, Dalmatian, Skye Terrier, Cocker Spaniel

Fibrosis and cirrhosis (results from any severe or chronic hepatic insult)
Infectious agents: leptospirosis, canine adenovirus type 1 infection, bacterial hepatitis, histoplasmosis, Rocky Mountain spotted fever, ehrlichiosis, babesiosis, leishmaniasis
Cholangiohepatitis
Granulomatous hepatitis
- Rhodococcus, Borrelia, Bartonella, Histoplasma, Coccidioidomyces, Hepatozoon, Heterobilharzia Nocardia, Mycobacterium spp.
Acidophil cell hepatitis
Lobular dissecting hepatitis
Hepatic abscess

Acute Toxic or Drug-Induced Hepatopathy

Vacuolar Hepatopathy

Metabolic Liver Disease
Amyloidosis
Hyperlipidemia
Lysosomal storage disease
Vascular Hepatic Disease
- Congenital portosystemic venous anomaly
- Intrahepatic portal vein hypoplasia
- Intrahepatic arteriovenous fistula

Biliary Tract Disease

Neoplasia
- Primary: hepatocellular carcinoma, hepatocellular adenoma, hepatic hemangiosarcoma, biliary carcinoma
- Other hepatic tumors: leiomyosarcoma, liposarcoma, myxosarcoma, fibrosarcoma, biliary adenoma, hepatic carcinoid
- Hemolymphatic: lymphosarcoma, mast cell tumor, plasma cell tumor
- Metastatic neoplasia

Hepatic or Biliary Cysts

Differential Diagnosis, Cats

Hepatic Lipidosis

Inflammatory Hepatobiliary Disease
- Cholangitis/cholangiohepatitis complex
  - Suppurative (neutrophilic) cholangitis, cholangiohepatitis
  - Lymphocytic cholangitis
- Chronic cholangiohepatitis (later stage of acute cholangiohepatitis)
- Sclerosing cholangitis
- Lymphocytic portal hepatitis
- Feline infectious peritonitis (FIP)

Toxic Hepatopathy
- Antimicrobials (trimethoprim-sulfa, tetracycline)
- Anticonvulsants (phenobarbital)
- Diazepam
- Methimazole
- Griseofulvin
- Ketoconazole
- Pine oils (cleaning agents)
  - Amanita phalloides (death cap mushroom)
- Natural or herbal remedies
- Many others

Portosystemic Venous Anomaly

Lipoprotein Lipase Deficiency

Neoplasia

Primary Hepatic Neoplasia
- Biliary carcinoma
- Hepatocellular carcinoma
Hepatic hemangiosarcoma
Biliary cystadenoma
Myelolipoma
Hepatic carcinoid

**Hemolymphatic Neoplasia**
Lymphosarcoma
Mast cell tumor
Plasma cell tumor

**Metastatic Neoplasia**

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### Differential Diagnosis

#### Generalized Hepatomegaly
- Acute toxic hepatopathy
- Infiltrative hepatic disease
  - Neoplasia: primary or metastatic
  - Chronic hepatitis complex (dog)
  - Cholangiohepatitis (cat)
  - Extramedullary hematopoiesis
  - Mononuclear-phagocytic cell hyperplasia
  - Amyloidosis (rare)
- Passive congestion
  - Right-sided heart failure
  - Pericardial disease (dog)
  - Caval syndrome (dog)
  - Caudal vena cava obstruction (dog)
  - Budd-Chiari syndrome (rare)
- Hepatocellular hypertrophy
  - Hepatic lipidosis
  - Steroid hepatopathy
  - Anticonvulsant drug therapy
- Acute extrahepatic bile duct obstruction

#### Focal Hepatomegaly
- Neoplasia: primary or metastatic
- Nodular hyperplasia
- Chronic hepatic disease with fibrosis and nodular regeneration
- Hepatic abscess
- Hepatic cyst

#### Microhepatica
- Decreased hepatic mass
  - Chronic hepatic disease with progressive loss of hepatocytes
Decreased portal blood flow with hepatocellular atrophy
- Congenital portosystemic shunt
- Intrahepatic portal vein hypoplasia
- Chronic portal vein thrombosis

Hypovolemia
- Hypoadrenocorticism
- Shock

## Hyperlipidemia

### Differential Diagnosis

#### Postprandial Hyperlipidemia

**Primary**
- Idiopathic hyperlipoproteinemia of Miniature Schnauzers
- Feline familial hyperchylomicronemia
- Idiopathic hypercholesterolemia (rare—Doberman Pinscher, Rottweiler)
- Idiopathic hypercholesterolemia

**Secondary**
- Endocrine
  - Hypothyroidism
  - Diabetes mellitus
  - Hyperadrenocorticism
- Pancreatitis
- Nephrotic syndrome
- Hepatic insufficiency
- Cholestasis
- Drug induced
  - Glucocorticoids
  - Megesterol acetate

### Clinical Findings

**Severe Hyperlipidemia**
- Intermittent gastrointestinal signs
  - Vomiting
  - Diarrhea
  - Abdominal discomfort
- Seizures
- Pancreatitis
- Lipemia retinalis
- Cutaneous xanthomas
- Peripheral nerve paralysis
- Behavioral changes
Severe Hypercholesterolemia
Arcus lipoides corneae
Lipemia retinalis
Atherosclerosis

Pancreatitis

Clinical Findings of Acute Pancreatitis

Dogs

*Mild Acute Pancreatitis*
- Depression
- Anorexia
- Nausea, vomiting, diarrhea
- Ptyalism
- Mild right cranial abdominal pain
- Fever, dehydration, weakness

*Moderate to Severe Acute Pancreatitis*
- Depression
- Anorexia
- Vomiting
- Right cranial abdominal pain
- Hematemesis, hematochezia, melena
- Jaundice
- Respiratory distress
- Shock, fever, dehydration
- Hyperemic mucous membranes
- Tachycardia, tachypnea
- Abdominal effusion
- Mass effect in region of pancreas
- Petechiae, ecchymoses
- Cardiac arrhythmia
- Glossitis, glossal slough
- Extrahepatic biliary obstruction

Cats

Signs tend to be more subclinical and nonspecific.
May be associated with inflammatory bowel disease
May be component of multisystemic disease such as toxoplasmosis
Lethargy, anorexia, vomiting, dehydration, weight loss, jaundice, hypothermia
May present as acute necrotizing or acute suppurative form
Predisposing Factors

Nutritional
- Obesity
- High-fat diet
- After ingestion of large, fatty meal

Hypertriglyceridemia
- Hyperlipoproteinemia (Idiopathic in Miniature Schnauzers)
- Endocrine (diabetes mellitus, hyperadrenocorticism, hypothyroidism)

Drugs
- Chemotherapeutic agents
  - L-Asparaginase
  - Azathioprine
  - Others
- Organophosphates
- Asparaginase
- Thiazides
- Furosemide
- Estrogens
- Sulfa drugs
- Procainamide
- Potassium bromide
- Tetracyclines

Ischemia
- Hypovolemia
- Associated with disseminated intravascular coagulation (DIC)
- Vasoactive amine–induced vasoconstriction
- Surgery
- Gastric dilatation/volvulus
- Severe immune-mediated hemolytic anemia

Duodenal Reflex
- Increased intraluminal pressure during severe vomiting

Other
- Cholangitis
- Infection (toxoplasmosis, feline infectious peritonitis)
- Abdominal trauma
- Hypercalcemia
- Trauma
Clinicopathologic Findings in Dogs and Cats with Acute Pancreatitis

- **BUN/creatinine**—increased in 50 to 65% of dogs and in 33% (Cr) and 57% (BUN) in cats. Usually prerenal due to dehydration and hypotension. May be secondary to intrinsic renal failure (sepsis and immune-complex)
- **Potassium**—decreased in 20% of cases in dogs and 56% in cats. Increased loss in vomiting and due to renal loss with fluid therapy plus reduced intake and aldosterone release caused by hypovolemia
- **Sodium**—can be increased, decreased or normal. Increase usually caused by dehydration, decrease caused by losses secondary to vomiting
- **Calcium**—Commonly decreased in cats, rarely in dogs, rarely increased in both dogs and cats. Reduction is a poor prognostic indicator in cats but no prognostic significance in dogs. May be caused by saponification in peripancreatic fat and glucagon release stimulating calcitonin
- **Chloride**—Very commonly decreased in dogs. Loss in gastrointestinal secretions in vomiting
- **Phosphate**—Often increased in dogs, uncommonly increased or decreased in cats. Increase usually due to reduced renal excretion secondary to renal compromise. Decrease (in cats) due to treatment for diabetes mellitus
- **Glucose**—increased in 40-88% of dogs and decreased in up to 40%. Increased in 64% of cats, rarely decreased. Increase due to decreased insulin and increased glucagon, cortisol, and catecholamines. Decrease caused by sepsis or anorexia
- **Albumin**—Increased in 39-50% and decreased in 17% of dogs. Increased in 8-30% and decreased in 40% of cats. Increase due to dehydration. Decrease due to gut loss, malnutrition, concurrent hepatic disease, or renal loss
- **Hepatocellular enzymes (ALT, AST)**—increased in 61% of dogs and 68% of cats. Hepatic necrosis and vacuolation due to sepsis, local effects of pancreatitis +/− concurrent hepatic disease in cats
- **Cholestatic enzymes (ALP and GGT)**—Increased in 79% of dogs and 50% of cats. Biliary obstruction due to acute or chronic pancreatitis +/− concurrent cholangitis +/− lipidosis in cats; steroid-induced ALP in dogs
- **Bilirubin**—Increased in 53% of dogs and 64% of cats (same causes as GGT and ALP)
• Cholesterol—Increased in 48-80% of dogs and 64% of cats. Can be due to cholestasis; unclear if cause or effect
• Triglycerides—Commonly increased in dogs. Unclear if cause or effect
• Neutrophils—Increased in 55-60% of dogs, increased in 30% and decreased in 15% of cats. Increased due to inflammatory response. Decreased in some cats due to consumption, may be a poor prognostic indicator
• Hematocrit—Increased in about 20% and decreased in 20% of both dogs and cats. Increased due to dehydration and decreased due to anemia of chronic disease or gastric ulceration
• Platelets—Commonly decreased in severe cases in dogs. Decreased due to circulating proteases +/- disseminated intravascular coagulation

Portosystemic Shunt, Congenital

Clinical Findings

Signalment
Young animal, male or female, often purebred

History
Neurologic signs (dementia, circling, central blindness, personality change, head pressing, wall hugging, seizures)
Vomiting
Diarrhea
Ptyalism (especially cats)
Worsening of signs after eating
Improvement of signs with antimicrobial therapy
Prolonged recovery from anesthesia
Polydipsia/polyuria
Recurrent urate urolithiasis in breeds other than Dalmatian and English Bulldog

Physical Examination
Poor haircoat
Small stature
Cystic calculi
Cryptorchidism
Bilateral renomegaly
Copper-colored irises in non-Asian cat breeds
Other congenital anomalies
Clinicopathologic Findings
- Microcytosis
- Hypoalbuminemia
- Mild increases in hepatic enzymes
- Hypocholesterolemia
- Low BUN
- Normal to high resting bile acids/elevated postprandial bile acids
- Hyposthenuria
- Urate crystalluria and urolithiasis

Vacuolar Hepatopathy, Canine

Differential Diagnosis
- Hyperadrenocorticism
  - Pituitary dependent
  - Adrenal dependent
  - Iatrogenic (glucocorticoid therapy)
- Pancreatitis
  - Chronic
- Severe hypothyroidism
- Chronic stress
  - Illness of more than 4 months
- Chronic infection or inflammation (e.g., pyelonephritis, chronic dermatitis)
- Severe dental disease
  - Oral infection
- Disorders affecting lipid metabolism
  - Diabetes mellitus
  - Idiopathic hyperlipidemia
- Neoplasia
  - Lymphoma
- Congestive heart failure
- Abnormal sex hormone production
- Inflammatory bowel disease
  - Chronic, lymphoplasmacytic, eosinophilic
- Hepatocutaneous syndrome
Neoplasia

Chemotherapeutic Agent Toxicity
Corticosteroid Therapy
Histiocytic Disease
Humoral Hypercalcemia
Lymphoma
Paraneoplastic Syndromes
Sarcomas
Thyroid Neoplasms
Tumors

Chemotherapeutic Agent Toxicity

Most severely affects tissues with a growth fraction that approaches that of tumor cells

Clinical Findings

Myelosuppression
  Neutropenia: short-lived cells; nadir is 5-10 days postchemotherapy
  Thrombocytopenia: nadir is 7-14 days postchemotherapy
  Anemia: erythrocytes live longer; rarely clinically significant

Gastrointestinal Toxicity
  Nausea, vomiting
  Diarrhea
  Inappetence
  Anorexia

Cardiotoxicity
  Doxorubicin therapy
  Breeds susceptible to dilated cardiomyopathy (e.g., Doberman) most sensitive
  Most likely after cumulative dose of 180 mg/m²

Nephrotoxicity
  Cisplatin, streptozotocin
  Limit use of cisplatin in cases of preexisting renal disease.

Hepatopathy
  Irreversible hepatic toxicity may result if lomustine (CCNU) given in face of elevated ALT
PART TWO  Systemic Approach to Differential Diagnosis

Urothelial Toxicity
Sterile hemorrhagic cystitis
Cyclophosphamide, ifosfamide

Extravasation
Doxorubicin: severe local reaction leading to slough
Vincristine: usually minor tissue damage

Hypersensitivity
Doxorubicin: caused by histamine release from mast cells; prevented by slow administration
L-Asparaginase: less likely if given subcutaneously rather than intravenously
Etoposide, paclitaxel: caused by carrier solutions for these agents

Alopecia
Less of a problem in dogs and cats than in people
Worse in breeds that have hair (e.g., Poodles, Terriers, Old English Sheepdogs) than in dogs with fur
Loss of “feathers” (e.g., Golden Retrievers)
Loss of whiskers in cats

Neurologic Toxicity
Fatal neurotoxicity in cats with topical or systemic administration of 5-fluorouracil

Respiratory Toxicity
Fatal, acute pulmonary edema in cats with cisplatin therapy

Corticosteroid Therapy

Adverse Effects Associated with Glucocorticoid Administration

Polyuria/polydipsia
Polyphagia
Increased alkaline phosphatase (ALP) levels
Increased gamma glutamyltransferase (GGT) levels
Panting
Insomnia, agitation, behavioral changes
Immunosuppression
• Secondary infection
• Recrudescence of latent infection
• Worsening of existing infection
• Demodicosis
Vacuolar hepatopathy
Iatrogenic hyperadrenocorticism
Adrenocorticoid deficiency with rapid withdrawal after sustained use
Alopecia  
Calcinosism cutis  
Comedones  
Skin thinning  
Proteinuria  
Muscle atrophy/muscle wasting  
Myotonia/myopathy  
Delayed wound healing  
Colonic perforation  
Gastrointestinal ulceration  
Insulin resistance  
Diabetes mellitus  
Hyperlipidemia  
Abortion  
Growth suppression  
Hypercoagulable state  
Ligament and tendon rupture  
Psychosis/behavior change  
Lowered seizure threshold  
Osteopenia

Histiocytic Disease

Classification, Dogs

May be difficult to differentiate from lymphoproliferative, granulomatous, or reactive inflammatory disease by histopathology alone

**Cutaneous Histiocytoma**  
Benign, usually solitary lesion  
Typically young dogs  
Often spontaneously regress

**Langerhans Cell Histiocytoma**  
Rare, rapidly metastatic, cutaneous infiltration by histiocytes, may be limited to multiple cutaneous sites or may affect lymph nodes and internal organs

**Cutaneous Histiocytosis**  
Single or multiple lesions  
May spontaneously regress  
May respond to immunosuppressive drugs

**Systemic Histiocytosis**  
Familial disease of Bernese Mountain Dogs, rarely other breeds  
Similar lesions to cutaneous histiocytosis but may also affect mucous membranes, lymphoid organs, lung, bone marrow, and other organ systems  
Progressive, requires immunosuppressive therapy
Histiocytic Sarcoma
Bernese Mountain Dog, Rottweiler, Flat-Coated Retriever, Golden Retriever, rarely other breeds
Histiocytic sarcoma usually begins as a localized lesion in spleen, lymph nodes, lung, bone marrow, skin and subcutis, brain, and periarticular tissue of appendicular joints.
- Rapidly disseminates to multiple organs

Malignant Histiocytosis
Bernese Mountain Dog, Rottweiler, Flat-Coated Retriever, Golden Retriever, rarely other breeds
Multisystemic, rapidly progressive disease of multiple organs

Classification, Cats

Feline Progressive Histiocytosis
Rare, usually see multiple skin nodules, papules, plaques
Head, lower extremities, trunk
Poor long-term prognosis

Feline Histiocytic Sarcoma
Poorly demarcated tumors of subcutis or spleen
Poor prognosis

Humoral Hypercalcemia

Differential Diagnosis

Hematologic Cancers
- Lymphosarcoma
- Lymphocytic leukemia
- Myeloproliferative disease
- Myeloma

Solid Tumors with Bone Metastasis
- Mammary adenocarcinoma
- Nasal adenocarcinoma
- Epithelial-derived tumors
- Pancreatic adenocarcinoma
- Lung carcinoma

Solid Tumors without Bone Metastasis
- Apocrine gland adenocarcinoma of the anal sac
- Interstitial cell tumor
- Squamous cell carcinoma
- Thyroid adenocarcinoma
Lung carcinoma
- Pancreatic adenocarcinoma
- Fibrosarcoma

Lymphoma

Common Differential Diagnoses

Generalized Lymphadenopathy
- Disseminated infections
  - Bacterial, fungal, rickettsial, parasitic, viral
  - Systemic lupus erythematosus (SLE), polyarthritis
  - Vasculitis, dermatopathy
- Immune-mediated disease
  - Systemic lupus erythematosus (SLE), polyarthritis
  - Vasculitis, dermatopathy
- Other hematopoietic tumors
  - Leukemia, multiple myeloma, malignant or systemic histiocytosis
- Neoplasia metastatic to lymph nodes
- Benign reactive hyperplastic syndromes in cats

Alimentary Disease
- Inflammatory bowel diseases
  - Lymphocytic/plasmacytic, eosinophilic enteritis
  - Nonlymphoid intestinal neoplasia
  - Granulomatous enteritis
  - Granulated round cell tumors in cats
  - Gastrointestinal mast cell neoplasia in cats

Cutaneous Disease
- Infectious dermatitis (deep pyoderma, fungal dermatitis)
- Immune-mediated dermatitis (e.g., pemphigus foliaceus)
- Other cutaneous neoplasms

Mediastinal Disease
- Thymoma
- Chemodectoma (heart base tumor)
- Ectopic thyroid neoplasia
- Pulmonary lymphomatoid granulomatosis
- Granulomatous disease (e.g., hilar lymphadenopathy with blastomycosis)

Paraneoplastic Syndromes

Classification

General
- Cancer anorexia, cachexia
- Fever
Hematologic

Anemia
- Anemia of chronic disease
- Immune-mediated hemolytic anemia
- Bone marrow infiltration
- Blood loss anemia
- Hyperestrogenism
- Microangiopathic hemolytic anemia

Polycythemia (rare)
- Associated with renal neoplasia, nasal fibrosarcoma, lymphoma, bronchial carcinoma, cecal leiomyosarcoma, transmissible venereal tumor, schwannoma

Leukocytosis
- Neutrophilic
- Eosinophilic

Thrombocytopenia
- Increased consumption
- Decreased production (bone marrow neoplasia)
- Increased destruction (immune-mediated thrombocytopenia)

Thrombocytosis

Thrombocyte hyperaggregability/hypercoagulability

Pancytopenia

Coagulation disorders
- Disseminated intravascular coagulation (DIC)
- Coagulation-activating substances produced by tumor

Hyperproteinemia/hyperglobulinemia

Endocrine

Hypercalcemia of malignancy

Hypoglycemia

Syndrome of inappropriate antidiuretic hormone (ADH) secretion
- Hyponatremia, serum
- Hypoosmolality, urine
- Hyperosmolality

Hyperestrogenism (Sertoli cell tumor)

Gastrointestinal

Gastroduodenal ulceration
- Mast cell tumors, gastrinoma

Cancer cachexia

Renal

Glomerulonephritis

Hypercalcemic nephropathy
Cutaneous
- Superficial necrolytic dermatitis
- Nodular dermatofibrosis
- Feline paraneoplastic alopecia

Neuromuscular
- Myasthenia gravis
  - Dogs with thymoma
  - Peripheral neuropathy
  - Multiple myeloma, lymphoma, various carcinomas and sarcomas

Hypertrophic Osteodystrophy
- Space-occupying mass in thorax or rarely abdomen

Sarcomas

Classification of Soft Tissue Sarcomas
- Fibrosarcoma
- Mast cell tumor
- Undifferentiated sarcoma
- Hemangiosarcoma
- Hemangiopericytoma (peripheral nerve-sheath tumor)
- Myxosarcoma
- Leiomyosarcoma
- Malignant fibrous histiocytoma
- Schwannoma
- Neurofibrosarcoma
- Synovial cell sarcoma
- Rhabdomyosarcoma
- Liposarcoma
- Vaccine-associated fibrosarcoma (cats)

Clinical Findings for Hemangiosarcoma
- Older dogs and cats
- Many potential sites of origin
  - Spleen
  - Right atrium
  - Subcutis
  - Pericardium
  - Liver
  - Muscle
  - Lung
  - Skin
  - Bone
  - Kidney
  - Central nervous system
• Peritoneum
• Oral cavity
• Nasal cavity
• Eye
• Retroperitoneum
Hemoabdomen
Pericardial effusion
Cardiac tamponade
Sudden death
Anorexia, vomiting
Lethargy
Right-sided heart failure
Muffled heart sounds
Arrhythmias
Neurologic signs (may metastasize to brain)

### Thyroid Neoplasms

#### Classification and Clinical Findings

#### Cats

Hyperthyroidism: functional thyroid tumors
• Thyroid adenoma
• Thyroid adenocarcinoma

#### Dogs

**Nonfunctional Tumors (90%)**

Thyroid adenoma
Thyroid adenocarcinoma
• Swelling or mass in neck
• Dyspnea
• Cough
• Lethargy
• Dysphagia
• Regurgitation
• Anorexia
• Weight loss
• Horner syndrome
• Change in bark
• Facial edema

**Functional Tumors (10%)**

Thyroid adenoma
Thyroid adenocarcinoma
• Swelling or mass in neck
• Polyphagia/weight
• Hyperactivity
• Polyuria/polydipsia
• Panting
• Change in behavior (aggression)

## Tumors

### Bone and Joint Tumors, Classification

**Canine osteosarcoma**
- Appendicular
- Skull
- Scapular
- Pelvic
- Ribs
- Vertebral
- Nasal and paranasal
**Chondrosarcoma**
**Fibrosarcoma**
**Hemangiosarcoma**
**Multilobular osteochondrosarcoma**
**Osteoma**
**Canine multiple cartilaginous exostoses**
**Feline osteosarcoma**
**Feline multiple cartilaginous exostoses**
**Metastatic bone tumors**
- Transitional cell carcinoma
- Prostatic adenocarcinoma
- Mammary carcinoma
- Thyroid carcinoma
- Pulmonary carcinoma
- Nasal carcinoma
- Apocrine gland, anal sac adenocarcinoma
- Renal tumors
- Others
**Primary joint tumors**
- Synovial cell sarcoma
- Histiocytic sarcoma
- Malignant fibrous histiocytoma
- Synovial myxoma
- Myxosarcoma
- Osteosarcoma
- Fibrosarcoma
- Chondrosarcoma
- Hemangiosarcoma
- Liposarcoma
- Rhabdomyosarcoma
- Undifferentiated sarcoma
Hematopoietic Tumors, Classification

Lymphoma

*Feline*
- Alimentary
- Multicentric
- Mediastinal/thymic
- Nasal
- Renal
- Other
  - Feline leukemia virus (FeLV) associated

*Canine*
- Multicentric
- Others (alimentary, mediastinal, cutaneous)

Lymphoid Leukemia
- Acute lymphoblastic leukemia (in cats, often associated with FeLV infection)
- Chronic lymphocytic leukemia

Nonlymphoid Leukemias and Myeloproliferative Disorders
- Acute myelogenous leukemia (myeloblastic)
- Acute myelomonocytic leukemia (myeloblasts/monoblasts)
- Acute monocytic leukemia (monoblasts)
- Acute megakaryoblastic leukemia (megakaryoblasts)
- Erythroleukemia (erythroblasts)

Chronic Myeloproliferative Disorders
- Chronic myelogenous leukemia (neutrophils, late precursors)
- Primary thrombocythemia (platelets)
- Basophilic leukemia (basophils and precursors)
- Eosinophilic leukemia (eosinophils and precursors)
- Polycythemia vera (erythrocytes)

Plasma Cell Neoplasms
- Multiple myeloma
- Solitary plasmacytoma
- IgM (Waldenström macroglobulinemia)

Mast Cell Tumor (MCT) Disease, Clinical Findings

Clinical Appearance and Location of MCTs
- Extremely variable in appearance
- Soft, fluctuant, firm, discrete, diffuse, small, large, solitary, multiple, haired, hairless, dermal, or subcutaneous
- Erythema, bruising, ulceration
On trunk most often; also perineum, extremities, head, neck
Rarely oral cavity, nasal cavity, larynx, conjunctiva

**Systemic Signs of Disseminated Mastocytosis**
- Gastrointestinal ulceration
- Abdominal discomfort
- Vomiting
- Melena
- Hypotension
- Coagulation abnormalities
- Acute or chronic blood loss anemia

**Oral Cavity Tumors, Differential Diagnosis**

**Malignant Neoplasms**
- Melanoma
- Squamous cell carcinoma
- Fibrosarcoma
- Osteosarcoma
- Lingual carcinoma or sarcoma
- Histiocytic sarcoma
- Lymphoma
- Mast cell tumor

**Benign Neoplasms**
- Epulides (acanthomatous ameloblastoma)
  - Fibromatous
  - Ossifying
  - Acanthomatous (squamous): may be invasive but does not metastasize
- Papillomas: self-limiting
- Fibroma
- Lipoma
- Chondroma
- Osteoma
- Odontoma
- Cementoma
- Plasmacytoma
- Hemangioma
- Hemangiopericytoma
- Histiocytoma
- Eosinophilic granuloma

**Skin and Subcutaneous Tumors**

**Epithelial Tumors**
- Sebaceous gland adenoma/adenocarcinoma
- Squamous cell carcinoma
• Canine cutaneous squamous cell carcinoma
• Canine nasal planum squamous cell carcinoma
• Canine digital squamous cell carcinoma
• Feline cutaneous squamous cell carcinoma
• Feline multicentric squamous cell carcinoma in situ (Bowen disease)

Trichoepithelioma
Intracutaneous cornifying epithelioma
Basal cell tumors
• Benign tumors
• Basal carcinoma
Trichoblastoma
Pilomatrixoma
Papilloma
Perianal gland tumors (hepatoid gland tumors)
Sweat gland tumors (apocrine gland tumors)
Ceruminous gland tumors
Anal sac, apocrine gland tumors
Follicular stem cell carcinoma

Round Cell Tumors
Lymphoma
Mast cell tumor
Histiocytoma
Transmissible venereal tumor (TVT)
Plasmacytoma

Melanocytic Tumors
Melanoma
• Benign (typically melanomas of haired skin and eyelids)
• Malignant (typically those of digit or mucocutaneous junctions)

Urogenital Tumors, Classification

Kidney
Lymphoma (most common renal tumor in cats)
Primary renal carcinoma, adenoma/adenocarcinoma
Cystadenocarcinoma with concurrent nodular dermatofibrosis in German Shepherds
Tumors of embryonic origin (e.g., Wilm tumor)
Nephroblastoma
Transitional cell carcinoma

Urinary Bladder
Older female dogs, West Highland White Terrier, Scottish Terriers, Beagles, Dachshunds, Shetland Sheepdogs
Transitional cell carcinoma
Squamous cell carcinoma
Leiomyosarcoma
Leiomyoma
Rhabdomyosarcoma
Metastatic neoplasia
• Hemangiosarcoma
• Lymphoma
• Extension of prostate neoplasia

Prostate
Prostatic adenocarcinoma
Transitional cell carcinoma

Penis and Prepuce
Prepuce affected by tumors of haired skin seen elsewhere
Penile
• Transmissible venereal tumor
• Others

Testicular Neoplasia
Cryptorchid dogs are 13.6 times more likely to develop
Sertoli cell tumor or seminoma
Sertoli cell tumor (25-50% are functional and cause hyperestrogenemia)
Leydig cell (interstitial) tumor
Seminoma

Vagina and Vulva
Leiomyoma
Fibroleiomyoma
Fibroma
Polyps
Lipoma
Leiomyosarcoma (rare)
Transmissible venereal tumor (TVT)

Uterus
Leiomyoma
Leiomyosarcoma
Uterine adenocarcinoma

Ovary

Epithelial Tumors (50% of ovarian tumors)
Papillary adenoma
Cystadenoma
Papillary adenocarcinoma
Undifferentiated adenocarcinoma
Germ Cell Tumors (10% of ovarian tumors)
  - Dysgerminoma
  - Teratoma
  - Teratocarcinoma

Sex-Cord Stromal Tumors (40% of ovarian tumors)
  - Granulosa cell tumor
  - Benign thecoma
  - Benign luteoma

Mammary Gland
  - Fibroadenoma (mixed mammary tumor)
  - Solid carcinomas
  - Tubular adenocarcinoma
  - Sarcoma
  - Inflammatory carcinomas
  - Feline mammary adenocarcinomas
Neurologic and Neuromuscular Disorders

Brain Disease, Congenital or Hereditary
Cognitive Dysfunction
Cranial Nerve (CN) Deficits
Head Tilt
Inflammatory Disease of the Nervous System
Intracranial Neoplasms
Myasthenia Gravis
Myositis and Myopathies
Neurologic Examination
Paroxysmal Disorders Confused with Epileptic Seizures
Peripheral Neuropathies
Spinal Cord Disease
Spinal Cord Lesions
Systemic Disease
Vestibular Disease

Brain Disease, Congenital or Hereditary

Differential Diagnosis

Congenital Malformations
Failure of normal closure of neural tube: vary in severity from clinically inapparent (agenesis of corpus callosum) to severe (anencephaly)
Lissencephaly: failure of normal migration of neurons in development of cerebral cortex; leads to abnormal appearance of sulci and gyri (most often seen in Lhasa Apso)
Cerebellar hypoplasia: seen most often in cats after in utero panleukopenia infection; rarely seen with parvovirus infection of developing cerebellum in dogs; may be isolated malformation without infection
Chiari-like malformations: protrusion of cerebellar vermis through foramen magnum (Cavalier King Charles Spaniel, other dog breeds)
Hydrocephalus: congenital hydrocephalus seen most often in toy and brachycephalic breeds; suggests hereditary basis; often congenital stenosis or aplasia of mesencephalic aqueducts
Inborn errors of metabolism (hereditary): young, purebred animals with diffuse, symmetric signs of brain disease
- Organic acidurias
- Spongiform encephalopathies: may be hereditary or acquired (transmissible) disease
- Polioencephalopathies: metabolic defects that affect gray matter
- Neuroaxonal dystrophy: spheroids causing swelling within axons
- Leukoencephalopathies: disorders of myelin; affect white matter; often affect cerebellum and long tracts leading to tremors and dysmetria
- Lysosomal storage diseases: accumulation of metabolic products in lysosomes
- Ceroid lipofuscinosis: accumulation of proteins in lysosomes
- Neonatal encephalopathy: hereditary disease of Standard Poodles

### Movement Disorders
- Hereditary cerebellar hypoplasia
- Multisystem degeneration: diseases of cerebellum and basal ganglia—progressive neuronal abiotrophy of Kerry Blue Terriers and Chinese Crested dogs
- Dyskinesia and dystonias
- Paroxysmal dyskinesias (“Scotty cramp” or idiopathic cerebellitis)—Scottish Terriers

### Cognitive Dysfunction
**Clinical Findings**
Disorientation
Sleep/wake cycle alterations
House soiling problems
Change in activity levels
- Increased
- Stereotypic
- Decreased
Agitation
Anxiety
Altered responsiveness to stimuli
- Heightened
- Reduced
Changes in appetite
- Increased
- Decreased
Decreased ability to perform learned tasks
Changes in interaction with owners

**Cranial Nerve (CN) Deficits**

**Clinical Findings**

**CN I (Olfactory)**
Loss of ability to smell

**CN II (Optic)**
Loss of vision, loss of menace response, dilated pupil, loss of papillary light reflex (direct and consensual)

**CN III (Oculomotor)**
Loss of papillary light reflex on affected side (even if light shone in opposite eye), dilated pupil, ptosis, ventrolateral strabismus

**CN IV (Trochlear)**
Slight dorsomedial eye rotation

**CN V (Trigeminal)**
Atrophy of temporalis and masseter muscles, loss of jaw tone and strength, dropped jaw (if bilateral), analgesia of innervated areas

**CN VI (Abducens)**
Medial strabismus, impaired lateral gaze, poor retraction of globe

**CN VII (Facial)**
Lip, eyelid, and ear droop; loss of ability to blink; loss of ability to retract lip; possibly decreased tear production

**CN VIII (Vestibulocochlear)**
Ataxia, head tilt, nystagmus, deafness, positional strabismus

**CN IX (Glossopharyngeal)**
Loss of gag reflex, dysphagia

**CN X (Vagus)**
Loss of gag reflex, laryngeal paralysis, dysphagia, megaesophagus

**CN XI (Accessory)**
Atrophy of trapezius, sternoclephalicus, and brachiocephalicus muscles

**CN XII (Hypoglossal)**
Loss of tongue strength, inability to retract tongue if bilateral, atrophy of tongue
Head Tilt

Differential Diagnosis

Peripheral Vestibular Disease
- Otitis media/interna
- Feline idiopathic vestibular disease
- Geriatric canine vestibular disease
- Feline nasopharyngeal polyps
- Middle ear tumor
  - Ceruminous gland adenocarcinoma
  - Squamous cell carcinoma
- Trauma
- Aminoglycoside ototoxicity/chemical ototoxicity
- Hypothyroidism (possibly)

Central Vestibular Disease
- Trauma/hemorrhage
- Infectious inflammatory disease
  - Rocky Mountain spotted fever
  - Feline infectious peritonitis (FIP)
  - Others
- Granulomatous meningoencephalitis
- Neoplasia
- Vascular infarct
- Thiamine deficiency
- Metronidazole toxicity

Inflammatory Disease of the Nervous System

Differential Diagnosis

Steroid-responsive meningitis-arteritis (steroid-responsive suppurative meningitis) (juvenile to young adult large breed dogs: Bernese Mountain Dogs, Boxers, German Shorthaired Pointers, Nova Scotia Duck Tolling Retrievers)
- Granulomatous meningoencephalitis
  - Idiopathic inflammatory brain disease of dogs
  - Most commonly in small breed dogs
- Pug meningoencephalitis
  - Necrotizing meningoencephalitis of cerebral cortex
  - Maltese and Yorkshire terrier also
- Feline polioencephalomyelitis
  - Young cats, progressive course
- Feline immunodeficiency virus (FIV) encephalopathy
- Bacterial meningitis and myelitis
  - *Staphylococcus aureus*
  - *Staphylococcus epidermidis*
• *Staphylococcus albus*
• *Pasteurella multocida*
• *Actinomyces*
• *Nocardia*
• Others
Canine distemper virus
Rabies
Feline infectious peritonitis (FIP)
Toxoplasmosis
Neosporosis
Borreliosis
Mycotic infections
• *Cryptococcus neoformans, C. gattii*
• Other disseminated systemic mycoses
Rickettsial diseases
• Rocky Mountain spotted fever
• Ehrlichiosis
• *Ehrlichia ewingii, Anaplasma phagocytophilia*
Parasitic meningitis, myelitis, encephalitis
• Aberrant parasite migration

### Intracranial Neoplasms

#### Differential Diagnosis

**Meningioma**
Benign tumor of cells of meninges

**Neuroepithelial Tumors (Gliomas)**
Astrocytomas
Oligodendrogliomas
Choroid plexus tumors (choroid plexus papilloma, ependymal tumor)

**Central Nervous System (CNS) Lymphoma**
Primary: neoplasia of native CNS lymphocytes
Secondary: metastasis of systemic lymphoma

**Metastatic Neoplasia to CNS**
Local invasion: nasal adenocarcinoma
Hematogenous spread: melanoma, hemangiosarcoma, lymphosarcoma
Many other neoplasms may metastasize to CNS.

**Pituitary Tumors**
Functional tumors of pars distalis or pars intermedia:
cause pituitary-dependent hyperadrenocorticism;
generally cause little damage to surrounding tissue
Pituitary macrotumor
Myasthenia Gravis

*Congenital myasthenia gravis:* inherited deficiency of acetylcholine receptors at presynaptic membranes of skeletal muscle.

*Acquired myasthenia gravis:* antibodies made against nicotinic acetylcholine receptors of skeletal muscle.

**Clinical Findings**

- Appendicular muscle weakness
  - Worsens with exercise
  - Improves with rest
  - Tetraplegia
- Mentation, postural reactions, reflexes normal
- **Megaesophagus**
  - Salivation
  - Regurgitation
- **Dysphagia**
- Ventroflexion
- Urinary bladder distension
- Hoarse bark or meow
- Persistently dilated pupils
- Facial muscle weakness
- Aspiration pneumonia
- Respiratory weakness

Myositis and Myopathies

**Differential Diagnosis**

**Inflammatory Myopathies**

- Masticatory myositis
  - Immunoglobulin G (IgG) antibodies to type 2M myofibers
  - German Shepherd, retrievers, and Doberman Pinscher predisposed
  - Young to middle-aged dogs
- Canine idiopathic polymyositis
  - Large-breed dogs predisposed
- Feline idiopathic polymyositis
- Dermatomyositis
  - Herding breeds, especially Shetland Sheepdog and Collie
- Protozoal myositis
  - *Toxoplasma gondii*
  - *Neospora caninum Hepatozoon, Babesia, Leishmania,* or *Trypanosoma* infection
Bacterial myositis *Clostridium, Leptospira, Ehrlichia*, Rocky Mountain spotted fever
Extraocular myositis (dogs)
Feline immunodeficiency virus

**Metabolic Myopathies**
- Glucocorticoid excess
  - Hyperadrenocorticism
  - Exogenous corticosteroids
- Hypothyroidism
- Hypoadrenocorticism
- Hypokalemic polymyopathy (cat)
  - Increased urinary excretion
  - Decreased dietary intake
- Mitochondrial myopathies
- Lipid storage myopathies
- Glycogen storage disorders
- Malignant hyperthermia
- Hyperkalemic periodic paralysis (American Pit Bull Terrier)

**Inherited Myopathies**
- Muscular dystrophy
  - Hereditary Labrador Retriever muscular dystrophy
  - Also German Shorthaired Pointer, Rottweiler, others
  - Maine Coon, Siamese, Devon Rex, Sphynx, others
- Myotonia
  - Chow Chow, Staffordshire Bull Terrier, Labrador Retriever, Rhodesian Ridgeback, Great Dane, others
- Malignant hyperthermia
  - Hypermetabolic disorder of skeletal muscle
  - Genetic defect in intracellular calcium homeostasis
- Inherited myopathy of Great Danes
- Centronuclear myopathy
  - Labrador Retriever
- Episodic/Exercise-induced collapse
  - Labrador Retriever
- Exertional rhabdomyolysis

### Neurologic Examination

#### Components

**Mental State**
- Normal
- Depression
- Stupor
- Coma
- Agitation
- Delirium
Posture
- Normal, upright
- Head tilt
- Wide-based stance
- Recumbent
- Extensor posturing
- Opisthotonus
- Pleurothotonus

Gait
- Proprioceptive deficits
- Paresis
- Circling
- Ataxia
- Dysmetria
- Lameness

Postural Reactions
- Conscious proprioception
- Hopping
- Wheelbarrowing
- Hemiwalking
- Extensor postural thrust

Muscle Tone
- Atrophy
- Decreased muscle tone (lesions of lower motor neurons)
- Increased muscle tone (lesions of upper motor neurons)
- Schiff-Sherrington posture (increased muscle tone and hyperextension of thoracic limbs)

Spinal Reflexes
- Absent, depressed, normal, or exaggerated
- Thoracic limb withdrawal (sixth cervical [C6], C7, C8, first thoracic [T1])
- Biceps (C6-C8) and Triceps (C7-T2) reflexes
- Patellar (fourth lumbar [L4], L5, L6)
- Pelvic limb withdrawal (L6, L7, first sacral [S1])
- Sciatic (L6, L7, S1)
- Cranial tibial (L6, L7)
- Perineal (S1, S2, S3, pudendal nerve)
- Bulbourethral (S1, S2, S3, pudendal nerve)
- Panniculus (response absent caudal to spinal cord lesion, used at T3-L3)
- Crossed extensor reflex (indicative of UMN disease)
- Cutaneous trunci reflex
Sensation and Pain
Superficial pain
Deep pain
Hyperesthesia

Urinary Tract Function
Cranial Nerves

Paroxysmal Disorders Confused with Epileptic Seizures

Differential Diagnosis

Syncope (reduced cerebral blood flow)
Cardiac arrhythmias
Hypotension

Episodic Weakness
Hypoglycemia
Low blood cortisol
Electrolyte disturbances

Myasthenia Gravis

Acute Vestibular “Attacks”

Movement Disorders
Episodic falling
Scotty cramp
Head bobbing
Dyskinesias

Sleep Disorders
Narcolepsy
Cataplexy

Obsessive Compulsive Disorder

Peripheral Neuropathies
Clinical signs depend on the nerve affected and the severity of the lesion.

Differential Diagnosis

Focal Disease

Trauma
Mechanical blows
Fractures
Pressure
Stretching
Laceration
Injection of agents into nerves

**Peripheral Nerve Tumors**
- Schwannoma
- Neurofibroma
- Neurofibrosarcoma
- Lymphoma

**Facial Nerve Paralysis**
- Otitis media
- Trauma
- Neoplasia
- Foreign body (e.g., grass awn)
- Nasopharyngeal polyp in cats
- Hypothyroidism
- Idiopathic

**Trigeminal Nerve Paralysis**
- Bilateral, idiopathic disorder, often self-limiting
- Middle-aged to older dogs, rarely cats

**Idiopathic Peripheral Vestibular Disease**

**Hyperchylomicronemia**
- Leads to xanthomas in skin
- May compress peripheral nerves

**Ischemic Neuromyopathy**
- Caudal aortic thromboembolism

**Generalized Chronic Polyneuropathies**
- Idiopathic
- Metabolic disorders
  - Diabetes mellitus
  - Hypothyroidism
- Paraneoplastic syndromes
  - Insulinoma
  - Other tumors
- Systemic lupus erythematosus (SLE) or other immune-mediated disease
- Chronic organophosphate toxicity
- Ehrlichiosis

**Generalized Acute Neuropathies**
- Acute polyradiculoneuritis (“coonhound paralysis”)
- Neospora polyradiculoneuritis (puppies)
- Disorders of neuromuscular junction
  - Botulism
  - Tick paralysis
  - Myasthenia gravis
Protozoal polyradiculoneuritis
Dysautonomia

Developmental/Congenital Neuropathies
Loss of motor neurons—Cairn Terrier, German Shepherd, English Pointer, Rottweiler, Swedish Lapland, Brittany Spaniel
Loss of peripheral axons—German Shepherd, Alaskan Malamute, Birman cat, Rottweiler, Boxer, Dalmatian
Schwann cell dysfunction—Golden Retriever, Tibetan Mastiff
Loss of sensory neuron of axon and laryngeal nerves—Dachshund, English Pointer, Shorthaired Pointer, Bouvier des Flandres, Siberian Husky

Inborn errors of metabolism
- Hyperchylomicronemia (cat)
- Hyperoxaluria type 2 (shorthaired cat)
- α-1-Fucosidosis (English Springer Spaniel)
- Atypical GM2 gangliosidosis (cat)
- Globoid cell leukodystrophy
- Niemann-Pick disease (Siamese)
- Glycogen storage disease (Norwegian forest cat)

Spinal Cord Disease

Differential Diagnosis

Acute
- Trauma
- Hemorrhage/coagulopathy
- Infarction
- Type I intervertebral disk herniation
- Fibrocartilaginous embolism
- Atlantoaxial subluxation

Subacute/Progressive
- Discospondylitis
- Noninfectious inflammatory diseases
  - Corticosteroid-responsive meningitis/arteritis
  - Granulomatous meningoencephalitis
  - Feline polioencephalomyelitis
- Infectious inflammatory diseases
  - Bacterial, fungal, rickettsial, protothecal, protozoal, nematodiasis
  - Distemper myelitis
- Feline infectious peritonitis (FIP) meningitis/myelitis
**Chronic Progressive**
- Neoplasia
- Type II intervertebral disk protrusion
- Degenerative myelopathy
- Cauda equina syndrome
- Cervical vertebral malformation/malarticulation (wobbler syndrome)
- Lumbosacral vertebral canal stenosis
- Spondylosis deformans
- Hypervitaminosis A (cats)
- Dural ossification
- Diffuse idiopathic skeletal hyperostosis
- Synovial cyst

**Progressive in Young Animals**
- Neuronal abiotrophies and degenerations
- Metabolic storage diseases
- Atlantoaxial luxation
- Congenital vertebral anomalies

**Congenital (Constant)**
- Spinal bifida
- Congenital dysgenesis of Manx cats
- Spinal dysraphism
- Hereditary ataxia
- Pilonidal, epidermoid, and dermoid cysts
- Syringomyelia/hydromyelia

**Spinal Cord Lesions**

**Localization**

**Cranial Cervical Lesion (C1-C5)**
- Upper motor neuron (UMN) signs in rear limbs
- UMN signs in forelimbs

**Caudal Cervical Lesion (C6-T2)**
- UMN signs in rear limbs
- Lower motor neuron (LMN) signs in forelimbs

**Thoracolumbar Lesion (T3-L3)**
- UMN signs in rear limbs
- Normal forelimbs

**Lumbosacral Lesion (L4-S3)**
- LMN signs in rear limbs
- Loss of perineal sensation and reflexes
- Normal forelimbs
Sacral Lesion (S1-S3)
- Normal forelimbs
- Normal patellar reflexes
- Loss of sciatic function
- Loss of perineal sensation and reflexes

Systemic Disease

Neurologic Manifestations

Oxygen Deprivation

Vascular Disease
- Ischemia
  - Thromboembolic disease
  - Shock
  - Cardiac disease
- Hemorrhage (anemia)
  - Vessel rupture secondary to hypertension
  - Coagulopathy
  - Vasculitis

Anesthetic Accidents
- Hypotension
- Cardiac arrhythmia
- Extensive blood loss
- Hypercapnia
- Hypoxemia

Hypoxia
- Pulmonary disease
- Decreased oxygen transport
- Heart failure

Hypertension

Hypoglycemia

Decreased Output or Metabolism
- Primary liver disease
- Malnutrition
- Thiamine deficiency

Increased Uptake
- Hyperinsulinemia
  - Islet cell tumors
  - Insulin overdose
- Non–Islet Cell Neoplasia
  - Hepatoma
  - Leiomyoma
Excessive Metabolism
  Sepsis
  Breed or activity-related

_Increased Uptake of Amino Acids by Extrahepatic Tissues_

Water and Ionic Imbalances

**Water**
- Hypoosmolar States (Retention of Free Water)
  - Hyponatremia
- Hyperosmolar States (Loss of Free Water)
  - Hypernatremia (diabetes insipidus)
  - Hyperglycemia (diabetes mellitus)

**Ions (Excess or Deficiency)**
- Calcium
- Potassium

Endogenous Neurotoxins

_Renal Toxins_

_Hepatoencephalopathy_

Endocrine Disease

Adrenal
- Hyperadrenocorticism
- Hypoadrenocorticism

Adrenergic Dysregulation
- Pheochromocytoma

Thyroid
- Hypothyroidism
  - Myxedema
  - Neuromyopathy
- Thyrotoxicosis
  - Hyperthyroidism
  - Iatrogenic

Exogenous Neurotoxins

- Plant toxins
- Sedative depressant drugs (e.g., antiepileptic drugs)
- Heat stroke

Remote Neurologic Manifestations of Cancer

- Metastasis to the nervous system
- Vascular accidents and infection
- Adverse effects of therapy
- Paraneoplastic syndromes
Vestibular Disease

Clinical Findings

Central and Peripheral Vestibular Disease
- Head tilt to side of lesion
- Circling/falling/rolling to side of lesion
- Vomiting, salivation
- Incoordination
- Ventral strabismus on side of lesion (±)
- Nystagmus, fast phase away from lesion
- Nystagmus may intensify with changes in body position.

Peripheral Vestibular Disease
- Nystagmus is horizontal or rotatory.
- No change in nystagmus direction with changes in head position
- Postural reactions and proprioception normal
- Concurrent Horner syndrome, cranial nerve VII paralysis with middle/inner ear involvement; other cranial nerves normal

Central Vestibular Disease
- Nystagmus horizontal, rotatory, or vertical
- Nystagmus direction may change direction with change in head position.
- Abnormal postural reactions and proprioception may be seen on side of lesion.
- Multiple cranial nerve deficits may be seen.

Paradoxical Vestibular Syndrome (Cerebellar Lesion)
- Head tilt and circling away from side of lesion
- Fast phase nystagmus toward the lesion
- May exhibit vertical nystagmus
- Abnormal postural reactions on side of lesion
- ± Multiple cranial nerve deficits on side of lesion
- ± Hypermetria, truncal sway, and head tremor
Anisocoria

**Differential Diagnosis**

**Nonneurologic Causes of Anisocoria**

*Conditions That Cause Miosis*
- Anterior uveitis
- Corneal ulcers and lacerations (reflex miosis mediated by trigeminal nerve)

*Conditions That Cause Mydriasis*
- Iris atrophy
- Iris hypoplasia
- Glaucoma
- Iridal tumors (e.g., melanoma) that infiltrate iridal musculature
- Unilateral retinal disease (e.g., retinal detachment)
- Severe chorioretinitis that affects a larger area on one eye than the other
- Unilateral optic neuritis or optic nerve neoplasia
- Orbital neoplasia, retrobulbar abscess, cellulitis

**Pharmacologic Causes of Anisocoria**

Drugs That Cause Miosis (usually agents used for management of glaucoma)
- Pilocarpine
- Demecarium bromide
- Synthetic prostaglandins such as latanoprost

Drugs That Cause Mydriasis
- Tropicamide, atropine
Ocular contact with toxins like jimsonweed (*Datura stramonium*)

Ocular decongestants like phenylephrine

**Neurologic Causes of Anisocoria**

**Afferent Lesions**

Anisocoria is reduced or abolished in darkness as both pupils dilate. This is because the stimulus producing the anisocoria, light causing constriction of the normal pupil, is eliminated.

- Unilateral retinal or prechiasmal optic nerve lesion
- Unilateral optic tract lesion
- Optic chiasm lesion

**Efferent Lesions**

Parasympathetic efferent lesions (In dogs, preganglionic efferent nerves are purely parasympathetic and postganglionic nerves are mixed. In cats both nerves are purely parasympathetic.)

- Lesions of the nucleus of CN III, the preganglionic fibers, or the ganglion itself

Sympathetic efferent lesions (Loss of sympathetic tone to the eye is known as Horner syndrome, is always ipsilateral to lesion, and features miosis, ptosis, protrusion of the third eyelid, and enophthalmos.)

- Head, neck, or chest trauma
- Brachial plexus avulsion
- Intracranial, mediastinal, or intrathoracic neoplasia
- Otitis media/interna
- Injury to the ear during ear flushing
- Idiopathic (Golden Retriever and Collie may be predisposed.)

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**Blindness, Acute**

**Differential Diagnosis, Dogs and Cats**

**Cornea**

- Edema (glaucoma, trauma, endothelial dystrophy, immune-mediated keratitis, neurotropic keratitis, anterior uveitis)
- Melanin (entropion, ectropion, lagophthalmos, facial nerve paralysis, keratoconjunctivitis sicca, pannus)
- Cellular infiltrate (bacterial, viral, fungal)
- Vascular invasion (exposure keratitis)
- Fibrosis (scar formation)
Dystrophy (lipid, genetic)
Symblepharon (conjunctiva adhered to cornea)

**Aqueous Humor**
Fibrin (anterior uveitis: many etiologies)
Hyphema (trauma, coagulopathies, neoplasia, systemic hypertension, retinal detachment)
Hypopyon (immune-mediated, lymphoma, systemic fungal infection, toxoplasmosis, FIP, protothecosis, brucellosis, bacterial septicemia)
Lipemic (hyperlipidemia with concurrent blood-aqueous barrier disruption [uveitis])

**Lens**
Cataracts (genetic, diabetes, retinal degeneration, hypocalcemia, electric shock, chronic uveitis, lens luxation, metabolic, toxic, traumatic, nutritional)

**Vitreous**
Hemorrhage (trauma, systemic hypertension, retinal detachment, neoplasia, coagulopathy)
Hyalitis (numerous infectious agents, penetrating injury)

**Retina**
Retinopathy (glaucoma, sudden acquired retinal degeneration [SARD], progressive retinal atrophy, central progressive retinal atrophy, feline central retinal atrophy, toxicity, taurine deficiency in cats, vitamin E deficiency in dogs, enrofloxacin toxicity in cats)
Chorioretinitis (systemic mycoses, ehrlichiosis, RMSF, canine distemper, toxoplasmosis, FIP, protothecosis, brucellosis, bacterial septicemia, intraocular larval migrans, neoplasia)
Retinal detachment (neoplasia, retinal dysplasia, hereditary/congenital, exudative/transudative disorders such as systemic hypertension or infection-induced inflammatory disease)

**Lesions that Prevent Transmission of the Image (optic nerve disease)**
Viruses (canine distemper, feline infectious peritonitis [FIP])
Systemic diseases (neoplasia, traumatic avulsion of optic nerve, granulomatous meningoencephalitis, hydrocephalus, optic nerve hypoplasia, immune-mediated optic neuritis, systemic mycoses)

**Lesions that Prevent Interpretation of the Visual Message**
Canine distemper, FIP, toxoplasmosis, granulomatous meningoencephalitis, systemic mycoses, trauma, heat stroke, hypoxia, hydrocephalus, hepatoencephalopathy, neoplasia, storage diseases, postictal, meningitis
Corneal Color Changes

Diagnostic Tests

Red (blood vessels)
- Mechanism is chronic irritation
- Fluorescein stain, Schirmer tear test (STT), palpebral and corneal reflexes

“Fluffy” Blue (stromal edema)
- Mechanisms are endothelial or epithelial dysfunction
- Fluorescein stain, intraocular pressure (IOP), flare, check for lens luxation

“Wispy” Gray (stromal scar)
- Mechanism is previous (inactive) inflammation
- Fluorescein stain

“Sparkly” White (lipid/mineral accumulation)
- Mechanisms are dystrophy, degeneration, or hyperlipidemia
- Fluorescein stain, systemic lipid analysis

Black (pigmentation)
- Mechanism is chronic irritation
- Fluorescein stain, STT

“Punctate” Tan (keratinic precipitates or staphyloma)
- Mechanism is uveitis
- IOP, flare, systemic disease testing

Yellow-Green (inflammatory cell infiltration)
- Inflammation (usually septic)
- Fluorescein stain, cytology, culture and sensitivity testing, polymerase chain reaction (PCR)

Eyelids and Periocular Skin

Differential Diagnosis

Infectious Blepharitis

Bacterial Blepharitis
- Usually Staphylococcus spp.
- External hordeolum or stye— infection of the glands of Zeis or Moll
- Internal hordeolum— infection of the meibomian glands
- Chalazion— meibomian secretions thicken and obstruct the duct, leading to glandular rupture and lipogranuloma formation
**Fungal Blepharitis**
- Dermatophytes (*Microsporum canis, Microsporum gypseum, Trichophyton mentagrophytes*)
- *Malassezia pachydermatitis*—most dogs with *Malassezia* dermatitis have concurrent dermatoses, in cats *Malassezia* infection is linked to systemic disease like diabetes, retroviral infection, internal neoplasia

**Parasitic Blepharitis**
- Demodecosis
- Feline herpetic ulcerative dermatitis

**Allergic Blepharitis**
- Atopic dermatitis
- Cutaneous adverse food reaction (food allergy)

**Metabolic/Nutritional Blepharitis**
- Zinc-responsive dermatosis
- Superficial necrolytic dermatitis (hepatocutaneous disease)

**Immune-Mediated Blepharitis**
- Pemphigus foliaceus
- Pemphigus erythematosus
- Systemic lupus erythematosus
- Erythema multiforme

**Iatrogenic Blepharitis**
- Adverse reactions to topical medications

**Pigmentary Changes Involving the Eyelid**
- Lentigo simplex of orange cats (black macules, not pathogenic)
- Vitiligo (hypopigmentation)
- Uveodermatologic (Vogt-Koyanagi-Harada-like) syndrome (leukoderma)

**Neoplastic Blepharitis**
- Meibomian gland adenoma
- Papillomas
- Squamous cell carcinoma
- Lymphosarcoma
- Mast cell tumor

**Miscellaneous Eyelid Diseases**
- Juvenile sterile granulomatous dermatitis and lymphadenitis/juvenile cellulitis (puppy strangles)
- Canine reactive histiocytosis
Nonhealing Corneal Erosions (Ulcers) in Dogs

Causes

Establish underlying cause of impaired wound healing.
- Mechanical trauma from lid masses
- Entropion
- Foreign bodies
- Secondary infection
- Corneal exposure caused by lid paralysis
- Exophthalmos
- Buphthalmos
- Tear film abnormalities
- Conformational abnormalities resulting in lagophthalmos
- Corneal edema
- Distichiasis
- Facial fold irritation of cornea

Spontaneous Chronic Corneal Epithelial Defects (SCCEDs)—also called indolent erosions/ulcers or boxer erosions/ulcers
- Middle-aged dogs
- Boxers predisposed
- Likely instigated by superficial trauma
- Dogs with diabetes mellitus predisposed
- Rim of loose epithelium surrounds corneal defect
- No loss of stromal substance (stromal loss indicates more severe process, typically infection)
- Blepharospasm/epiphora
- Neovascularization may be delayed compared with healing corneal ulcers.

Bullous Keratopathy

Ocular Manifestations of Systemic Diseases

Surface Ocular Disease

Eyelids

Immunosuppressive disorders may predispose to meibomian gland infection with *Demodex* or *Staphylococcus* spp. Eyelids have mucocutaneous junction; affected by autoimmune disorders such as systemic lupus
erythematous (SLE) and pemphigoid diseases; also may be affected by uveodermatologic syndrome and vasculitis

Altered lid position, cranial nerve III or VII dysfunction

Horner syndrome: decreased sympathetic tone causing enophthalmos with third eyelid protrusion, ptosis, and miosis; often idiopathic; may be seen with disease of brain, spinal cord, brachial plexus, thorax, mediastinum, neck, temporal bone, tympanic bulla, or orbit

**Conjunctivitis**

- May reflect disease of deeper ocular structures
- Good location to detect pallor, cyanosis, icterus
- Feline herpesvirus type 1 (FHV-1) and *Chlamydophila felis* are primary pathogens of the conjunctiva.

**Cornea/Sclera**

- Creamy pink discoloration of cornea may be seen with lymphoma.
- Corneal lipidosis appears similar; it may be secondary to hyperlipidemia from hypothyroidism, hyperadrenocorticism, diabetes mellitus, and familial hypertriglyceridemia.

**Keratoconjunctivitis Sicca**

- Most cases are caused by lymphoplasmacytic dacryoadenitis.
- Rarely seen with xerostomia (Sjögren-like syndrome)
- Possible causes include drug therapy, atropine, sulfa drugs, etodolac, and anesthetic agents.
- Others causes include canine distemper, FHV-1, and dysautonomia.

**Uveal Tract, Lens, Fundus**

**Uveal Tract**

*Hyphema or Hemorrhage*

- Hypertension, rickettsial disease, trauma, coagulopathy, lymphoma, metastatic neoplasia

*Protein or Fibrin Deposition*

- Trauma, feline infectious peritonitis (FIP), uveodermatologic syndrome, lens capsule rupture, rickettsial disease

*Cellular (Hypopyon) or Granulomatous Infiltrates*

- Trauma, lymphoma, metastatic neoplasia, uveodermatologic syndrome, algae or yeast, lens capsule rupture, FIP, systemic mycoses, toxoplasmosis
Other infectious agents associated with uveal tract disease include feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), mycobacteria, FHV-1, Bartonella spp., Ehrlichia spp., Leishmania donovani, Rickettsia rickettsii, Brucella canis, Leptospira spp., and canine adenovirus.

**Iris Abnormalities (Papillary Changes)**
- Anisocoria with FeLV
- Miosis with Horner syndrome
- Mydriasis with dysautonomia

**Lens**

**Cataracts**
- Most common cause in dogs is hereditary.
- Cataracts are frequent complication of diabetes mellitus.
- Uveitis may also cause cataracts (most common cause in cats).
- Other causes include hypocalcemia (hypoparathyroidism), electric shock, lightning strike, altered nutrition (e.g., puppies fed milk replacer).

**Lens Luxation/Subluxation**
- Most often secondary to severe intraocular disease (uveitis)
- May be primary in terriers

**Fundus**
- Usually affected by diseases that extend from the uveal tract (see previous section) or from central nervous system (immune-mediated diseases such as granulomatous meningoencephalitis or neoplasia of CNS).

**Papilledema**
- Optic nerve edema without hemorrhage, exudates, or blindness
- Seen with increased intracranial pressure

**Taurine Deficiency**
- Retinal degeneration
- May also cause dilated cardiomyopathy

**Retinal Visualization**
- Allows assessment of systemic condition including anemia (attenuated, pale vessels), hyperlipidemia (creamy orange hue to vessels), hyperviscosity (increased vessel tortuosity)

**Systemic Hypertension**
- Causes extravasation of blood into retina, choroid, or subretinal space
**Ocular Neoplasia**

**Orbital Neoplasia (presents as exophthalmos, strabismus, protrusion of the third eyelid, epiphora, and exposure keratitis)**

- Osteosarcoma
- Multilobular osteosarcoma
- Fibrosarcoma
- Invasion of orbit by neoplasms of surrounding structures such as nose, sinuses, oral cavity, and orbital glands (nasal adenocarcinoma most commonly)
- Cats are more likely to have invasion of orbit from surrounding structures (fibrosarcoma, undifferentiated sarcoma, adenocarcinoma, lymphoma). Rarely see primary orbital neoplasia (squamous cell carcinoma, melanoma)

**Adnexal Neoplasia (eyelid neoplasia common in dogs and rare in cats)**

- 90% of eyelid tumors are benign (meibomian adenomas, melanomas, papillomas most commonly).
- Less common adnexal tumors include histiocytoma, malignant melanoma, adenocarcinoma, basal cell carcinoma, mast cell tumor, squamous cell carcinoma, hemangiosarcoma.
- Squamous cell carcinoma is the most common eyelid tumor in cats. Associated with sun exposure in cats that lack periocular pigmentation.

**Surface Ocular Neoplasia (tumors of the conjunctiva, third eyelid, cornea)**

- Dermoid
- Epibulbar or limbal melanocytoma
- Conjunctival neoplasia: hemangioma, hemangiosarcoma, mast cell tumor, lymphoma, squamous cell carcinoma, papilloma
- Third eyelid neoplasia: adenocarcinoma (most common), hemangiosarcoma, lobular adenoma, squamous cell carcinoma, melanoma

**Intraocular Neoplasia (present with glaucoma, hyphema, corneal edema, buphthalmos, dyscoria, uveitis, retinal detachment, blindness)**

- Anterior uveal melanoma (most common), 82% are benign in dogs, poorer prognosis in cats
- Other primary tumors of dogs include ciliary body adenocarcinoma and medulloepithelioma.
- Other primary tumors of cats include posttraumatic sarcoma and lymphoma.
Red Eye

Differential Diagnosis

**Erythema of Primarily Conjunctival Vessels**
- Corneal ulceration
- Eyelid abnormalities
- Dacryocystitis
- Cilia abnormalities
- Keratoconjunctivitis sicca
- Allergic conjunctivitis
- Bacterial or fungal keratitis
- Orbital disease

**Erythema of Primarily Episcleral Vessels**
- Anterior uveitis (low intraocular pressure)
- Glaucoma (high intraocular pressure)

**Focal Erythema**

*Masses*
- Prolapse of the gland of the third eyelid
- Neoplasia
- Episcleritis
- Nodular granulomatous episcleritis
- Granulation tissue

*Hemorrhage*
- Trauma
- Systemic disease (vasculitis, coagulopathy)

Retinal Detachment

Differential Diagnosis

*Three Main Mechanisms—exudative, associated with retinal tears (rhegmatogenous), or traction pulling on retina*
- Trauma—penetrating injuries such as animal bites, projectiles, or foreign bodies may result in retinal tears or induce intraocular hemorrhage, inflammation, or vitreous infection with subsequent traction retinal detachment. Typically unilateral, although strangulation can lead to bilateral retinal detachment
- Ocular anomalies such as severe retinal dysplasia, optic nerve colobomas, vitreous abnormalities, and retinal nonattachment (developmental failure of the two retinal layers to unite)
- Later-onset ocular anomalies such as cataracts and vitreous degeneration may lead to rhegmatogenous RD, especially
with rapid-forming or hypermature cataracts that lead to lens-induced uveitis.

- Hypertension is most often related to renal disease but may also be seen with hyperthyroidism and pheochromocytoma.
- Hyperviscosity—severe hyperlipidemia, hyperglobulinemia, polycythemia
- Neoplasia—most commonly due to multiple myeloma (hyperproteinemia and hyperviscosity) and lymphoma (infiltration of retina and choroid). Large intraocular tumors may induce traction retinal detachment.
- Chorioretinitis, retinochoroiditis
  - Bacteria (leptospirosis, brucellosis, Bartonellosis)
  - Rickettsia (ehrlichiosis, Rocky Mountain spotted fever)
  - Fungal (aspergillosis, blastomycosis, coccidioidomycosis, histoplasmosis, cryptococcosis)
  - Algae (geotrichosis, protothecosis)
  - Viral (canine distemper virus, FIP)
  - Secondary to retroviral infection (FeLV, FIV by predisposing to lymphosarcoma or an opportunistic infection like toxoplasmosis)
- Parasitic (causes smaller areas of detachment—larval migrans of strongyles, ascarids, or Baylisascaris larvae. Toxoplasmosis, leishmaniasis, neospora, babesiosis.
- Immune-mediated disease—causes vasculitis with or without chorioretinitis
  - Systemic lupus erythematosus
  - Uveodermatologic syndrome
  - Granulomatous meningoencephalitis
- Toxic—trimethoprim/sulfa or ethylene glycol in dogs, griseofulvin in cats
- Idiopathic

### Uveitis

#### Differential Diagnosis in the Dog(d) and Cat(c)

**Systemic Infection**

**Bacterial**

- Bacteremia or septicemia (d, c)
- Bartonellosis (d, c)
- Leptospirosis (d)
- Borreliosis (d)
- Brucellosis (d)

**Rickettsial**

- Ehrlichiosis (d, c)
- Rocky Mountain spotted fever (d)
Viral
• Canine adenovirus-1 (d)
• Feline leukemia virus (c)
• Feline immunodeficiency virus (c)
• Feline infectious peritonitis (c)

Mycotic
• Blastomycosis (d, c)
• Histoplasmosis (d, c)
• Coccidiomycosis (d, c)
• Cryptomycosis (d, c)
• Aspergillosis (d)

Algal
• Protothecosis

Parasitic
• Aberrant nematode larval migration
• *Toxocara* (ocular larval migrans) (d, c)
• *Dirofilaria* larvae (d)

Protozoan
• Toxoplasmosis (d, c)
• Leishmaniasis (d, c)

Immune-Mediated uveitis
• Idiopathic anterior uveitis (d, c)
• Lens-induced uveitis (d, c)
• Canine adenovirus vaccine reaction (d)
• Uveodermatologic syndrome (d) (primarily Akita and Arctic breeds)
• Pigmentary uveitis (d) (primarily Golden Retrievers)

Neoplasia
• Primary (d, c)
• Metastatic (most commonly lymphoma) (d, c)

Metabolic
• Diabetes mellitus (lens-induced uveitis) (d)
• Hyperlipidemia (d)

Trauma
• Blunt or sharp (d, c)

Miscellaneous Causes of Blood/Eye Barrier Disruption
• Hyperviscosity syndrome (d, c)
• Hypertension (d, c)
• Scleritis (d)
• Ulcerative keratitis (d, c)
### Chemical Toxicoses

#### Toxicants

**Kerosene, Gasoline, Mineral Seal Oil, Turpentine, Others**
Pulmonary, central nervous system (CNS), and gastrointestinal (GI) signs: may lead to hepatotoxicity, renal toxicity, and cardiac arrhythmias

**Naphthalene (Mothballs)**
Vomiting, lethargy, seizures, acute Heinz body hemolytic anemia, methemoglobinemia, hemoglobinuria, renal failure

**Ethanol, Methanol (Wood Alcohol)**
CNS depression, behavioral changes, ataxia, hypothermia, respiratory and cardiac arrest

**Ethylene Glycol**
Early intoxication: ataxia, progresses to oliguric renal failure with renomegaly, vomiting, hypothermia, coma, and death

**Soaps and Detergents**
GI irritants

**Household Corrosives**
Toilet bowl cleaners, calcium/lime/rust removers, drain cleaners, oven cleaners, bleaches

**Propylene Glycol**
Ataxia, CNS depression

**Phenol Products (Household Cleaners)**
Cats particularly sensitive; hepatic and renal damage, ataxia, weakness, tremors, coma, seizures, respiratory alkalosis

**Anticoagulant Rodenticides**
Petechiae, ecchymosis, weakness, pallor, respiratory distress, CNS depression, hematemesis, epistaxis, melena, ataxia, paresis, seizures, sudden death
Zinc Phosphate
Anorexia, lethargy, weakness, abdominal pain, vomiting early after ingestion, progresses to recumbency, tremors, seizures, cardiopulmonary collapse, death

Cholecalciferol (Vitamin D) Rodenticides and Medications
Anorexia, CNS depression, vomiting, muscle weakness, constipation, bloody diarrhea, polyuria/polydipsia

Bromethalin Rodenticides
High-dose exposure: muscle tremors, hyperexcitability, vocalization, seizures, hyperesthesia, vomiting, dyspnea

Pyrethrin and Pyrethroid Insecticides
CNS depression, hypersalivation, muscle tremors, vomiting, ataxia, dyspnea, anorexia, hypothermia, hyperthermia, seizures, rarely death

Organophosphate and Carbamate Insecticides
Muscarinic signs (salivation, lacrimation, bronchial secretion, vomiting, diarrhea) and nicotinic signs (muscle tremors, respiratory paralysis), mixed signs (CNS depression, seizures, miosis, hyperactivity)

2,4-Dichlorophenoxyacetic Acid
Vomiting, diarrhea; greater exposure may cause CNS depression, ataxia, and hindlimb myotonia.

Lead (Paints, Batteries, Linoleum, Solder, Plumbing Supplies, Fishing Weights)
High-level exposure: vomiting, abdominal pain, anorexia, diarrhea, megaesophagus
CNS signs, behavioral changes, hysteria, ataxia, tremors, opisthotonos, blindness, seizures

Zinc
Acute ingestion: vomiting, CNS depression, lethargy, diarrhea
Chronic exposure: anorexia, vomiting, diarrhea, CNS depression, pica, hemolysis, regenerative anemia, spherocytosis, inflammatory leukogram, icterus, renal failure

Iron
Vomiting, diarrhea, abdominal pain, hematemesis, melena; rarely, progresses to multisystemic failure
Plant Toxicoses

Plants That Cause Hemolysis

Onion

Plants That Affect the Cardiovascular System

Cardiac glycoside toxicity: bradycardia with first-, second-, or third-degree atrioventricular (AV) block, ventricular arrhythmias, asystole, and sudden death; also see gastrointestinal (GI) signs
  - Common oleander (Nerium oleander)
  - Yellow oleander (Thevetia peruviana)
  - Foxglove (Digitalis purpurea)
  - Lily of the valley (Convallaria majalis)
  - Kalanchoe (Bryophyllum spp.)
Azalea (Rhododendron spp.): weakness, hypotension, dyspnea, respiratory failure, GI signs
Yew (Taxus spp.): conduction disturbances, bradycardia, GI signs, weakness, seizures; poor prognosis once signs are seen

Plants Affecting the Gastrointestinal System

Oxalate-containing plants: gastric and ocular irritants
  - Dumbcane (Dieffenbachia spp.)
  - Philodendron (Philodendron spp.)
  - Peace lily (Spathiphyllum spp.)
  - Devil’s ivy (Epipremnum aureum)
  - Rhubarb leaves (Rheum spp.)
Philodendron may cause renal and central nervous system (CNS) signs in cats.
Chinaberry tree (Melia azedarach): vomiting, diarrhea, abdominal pain, hypersalivation, may progress to CNS signs and death
Cycad palms (Cycas spp.) or sago palms (Macrozamia spp.): vomiting, diarrhea, followed by lethargy, depression, liver failure, and death (dogs)
English ivy (Hedera helix): GI irritation, profuse salivation, abdominal pain, vomiting, diarrhea
Castor bean plant (Ricinus communis): ricin is among the most deadly poisons in the world; severe abdominal pain, vomiting, diarrhea, seizures, cerebral edema; prognosis for recovery is poor once clinical signs develop.
Holly (Ilex spp.), poinsettia (Euphorbia pulcherrima), mistletoe (Phoradendron flavescens): mild GI irritation, occasionally diarrhea, more serious effects with mistletoe
Amaryllis, jonquil, daffodil (family Amaryllidaceae), tulip (family Liliaceae), iris (family Iridaceae): ingestion of bulb associated with mild to moderate gastroenteritis
Autumn crocus (*Colchinum autumnale*), glory lily (*Gloriosa* spp.): colchicine, vomiting, diarrhea, abdominal pain, hypersalivation progressing to depression, multiple organ system collapse and death

Solanaceae family: tomato, eggplant, deadly or black nightshade, Jerusalem cherry-solanine, gastric irritant; may cause CNS depression and cardiac arrhythmias; nightshade can also contain belladonna.

Mushrooms: amanitine poisoning (*Amanita virosa, Amanita phalloides, Conocybe filaris*), orellanine poisoning (*Cortinarius orellanus, Cortinarius rainierensis*), monomethylhydrazine (*Gyromitra esculenta*)—severe hepatic disease; survivors of hepatic phase may succumb to renal tubular necrosis.

**Plants Affecting the Neurologic System**

Tobacco (*Nicotiana tabacum*): vomiting, CNS involvement, cardiac involvement

Hallucinogenic plants: psilocybins or “magic mushrooms,” marijuana (*Cannabis sativa*), jimsonweed (*Datura stramonium*), thorn apple (*Datura metaliodyl*), blue morning glory (*Ipomoea violacea*), nutmeg (*Myristica fragrans*), peyote (family Cactaceae)

Nettle toxicity (family Urticaceae): hunting dogs, toxins contained in needles (histamine, acetylcholine, serotonin, formic acid), salivation, vomiting, pawing at mouth, tremors, dyspnea, slow and irregular heartbeat

Macadamia nuts: locomotor disturbances, tremors, ataxia, weakness

Yesterday, today, tomorrow (*Brunfelsia* spp.)

**Plants Affecting the Renal System**

Easter lily (*Lilium longiflorum*) and daylily (*Hemerocallis* spp.), possibly other lilies: toxic to cats, vomiting, depression, anorexia, leading to acute renal failure, poor prognosis without early treatment

Raisins/grapes: acute renal failure

**Plants Causing Sudden Death**

Seeds of many fruit trees (apple, apricot, cherry, peach, plum), contain cyanogenic glycosides

**Venomous Bites and Stings**

**Snakes, Spiders, Others**

*Crotalids (Pit Vipers, Rattlesnakes, Copperheads, Water Moccasins)*

Enzymatic and nonenzymatic proteins, local tissue damage: localized pain, salivation, weakness, fasciculations,
hypotension, alterations in respiratory pattern, regional lymphadenopathy, mucosal bleeding, obtundation, convulsions, anemia, echinocytosis, stress leukogram

**Elapids (Coral Snakes)**
Rare envenomation, signs delayed 10-18 hours, emesis, salivation, agitation, central depression, quadriplegia, hyporeflexia, intravascular hemolysis, respiratory paralysis

**Latrodectus spp. (Widow Spiders)**
Hyperesthesia, muscle fasciculations, cramping, somatic abdominal pain (characteristic sign), respiratory compromise, hypertension, tachycardia, seizures, agitation, ataxia, cardiopulmonary collapse

**Loxoscelidae (Recluse or Brown Spiders)**
Cutaneous form: bull’s-eye lesion, pale center with localized thrombosis, surrounded by erythema, develops into a hemorrhagic bulla with underlying eschar
Viscerocutaneous form: Coombs-negative hemolytic anemia, thrombocytopenia, disseminated intravascular coagulation (DIC)

**Tick Paralysis**
*Dermacentor* and *Haemaphysalis* ticks, ascending paralysis, lower motor neuron signs, megaesophagus and aspiration pneumonia in severe cases, spontaneous recovery a few days after tick removal

**Hymenopteran Stings**
Bites and stings of winged insects and fire ants
Toxic and allergic reactions (localized angioedema, urticaria, emesis, diarrhea, hematochezia, respiratory depression, death)

**Helodermatidae Lizard (Gila Monster)**
Salivation, lacrimation, emesis, tachypnea, respiratory distress, tachycardia, hypotension, shock
Urogenital Disorders

Differentiating between Urine Marking and Inappropriate Elimination in Cats

Glomerular Disease
Indications for Cystoscopy
Mammary Masses
Prostatic Disease
Proteinuria in Dogs and Cats
Pyelonephritis, Bacterial
Renal Disease
Reproductive Disorders
Ureteral Diseases
Urinary Tract Infection (UTI)
Uroliths, Canine
Vaginal Discharge

Differentiating between Urine Marking and Inappropriate Elimination in Cats

Urine Marking

- Generally vertical surfaces (can be horizontal)
- Marking behavior (may be territorial signaling or an anxiety-or conflict-induced response)
- Most common in intact males, females in estrous
- Adults
- Urine (rarely stool)
- Doors, windows, new objects, owner’s possessions, frequently used furniture

Inappropriate Elimination

- Horizontal surfaces (rarely vertical)
- Elimination behavior
- Males or females, intact or neutered
- Any age
- Urine and/or stool
- Elimination in a variety of areas

Glomerular Disease

Types, Dogs and Cats

Glomerulonephritis
  Membranoproliferative form
• Type I (mesangiocapillary)
• Type II (dense deposit disease)
  Proliferative glomerulonephritis (mesangial and endocapillary)
  Crescentic type (rare)
Amyloidosis
Glomerulosclerosis
Focal segmental glomerulosclerosis
Hereditary nephritis
Immunoglobulin A (IgA) nephropathy
Lupus nephritis
Membranous glomerulopathy (most common in cats)
Minimal change glomerulopathy

Differential Diagnosis for Diseases Associated with Glomerular Disease, Dogs

Infection
  **Bacterial**
  Pyelonephritis
  Pyoderma
  Pyometra
  Endocarditis
  Bartonellosis
  Brucellosis
  Borreliosis
  Other chronic bacterial infections

  **Parasitic**
  Dirofilariasis

  **Rickettsial**
  Ehrlichiosis

  **Fungal**
  Blastomycosis
  Coccidioidomycosis

  **Protozoal**
  Babesiosis
  Hepatozoonosis
  Leishmaniasis
  Trypanosomiasis

  **Viral**
  Canine adenovirus (type I) infection

Inflammation
  Periodontal disease
  Chronic dermatitis
Pancreatitis
Inflammatory bowel disease
Polyarthritis
Systemic lupus erythematosus (SLE)
Other immune-mediated diseases

**Neoplasia**
- Lymphosarcoma
- Mastocytosis
- Leukemia
- Systemic histiocytosis
- Primary erythrocytosis
- Other neoplasms

**Miscellaneous**
- Corticosteroid excess
- Trimethoprim-sulfa therapy
- Hyperlipidemia
- Chronic insulin infusion
- Congenital C3 deficiency
- Cyclic hematopoiesis in gray Collies

**Familial**
- Amyloidosis (Beagle, English Foxhound)
- Hereditary nephritis (Bull Terrier, English Cocker Spaniel, Dalmatian, Samoyed)
- Glomerulosclerosis (Doberman Pinscher, Newfoundland)
- Glomerular vasculopathy and necrosis (Greyhound)
- Mesangiocapillary glomerulonephritis (Bernese Mountain Dog)
- Atrophic glomerulopathy (Rottweiler)
- Proliferative and sclerosing glomerulonephritis (Soft-Coated Wheaten Terrier)

**Idiopathic**

### Differential Diagnosis for Diseases Associated with Glomerular Disease, Cats

**Infection**

**Bacterial**
- Pyelonephritis
- Chronic bacterial infections
- Mycoplasmal polyarthritis

**Viral**
- Feline immunodeficiency virus (FIV)
- Feline infectious peritonitis (FIP)
- Feline leukemia virus (FeLV)
Inflammation
- Pancreatitis
- Cholangiohepatitis
- Chronic progressive polyarthritis
- SLE
- Other immune-mediated diseases

Neoplasia
- Lymphosarcoma
- Leukemia
- Mastocytosis
- Other neoplasms

Miscellaneous
- Acromegaly
- Mercury toxicity

Familial

Idiopathic

Indications for Cystoscopy
- Localization of source of hematuria
- Urinary tract neoplasia
  - Determine extent and location of tumors
  - Obtain samples for cytology or histopathology
- Recurrent urinary tract infections
  - Examine for anatomic abnormalities or uroliths
  - Obtain samples for cytology, histopathology, or culture
- Urinary tract trauma
  - Examine for perforations, ruptures, and patency of urinary tract
- Urinary incontinence
  - Examine for ectopic ureters and/or urethral anomalies
  - Laser ablation of intramural ectopic ureters
  - Periurethral collagen injections for treatment of refractory urethral incompetence
- Urolithiasis
  - Confirm and remove small uroliths from bladder or urethra
  - Obtain uroliths for quantitative analysis and culture
  - Retrieve uroliths from bladder or urethra using stone forceps or stone basket
  - Fragment uroliths with laser lithotripsy
  - Fill bladder before and after voiding urohydropropulsion to remove small uroliths
Mammary Masses

Differential Diagnosis

- Benign mammary tumors
  - Mixed tumors (fibroadenomas)
  - Adenomas
  - Mesenchymal tumors
- Malignant mammary tumors
  - Solid carcinomas
  - Tubular adenocarcinomas
  - Papillary adenocarcinomas
  - Anaplastic carcinomas
  - Sarcomas (rare)
  - Most feline mammary tumors are adenocarcinomas
- Mammary hyperplasia
- Mastitis
- Granulomas
- Duct ectasia
- Skin tumors
- Lipomas
- Foreign bodies (e.g., BB pellets or shot may be confused with small mammary masses)

Prostatic Disease

Differential Diagnosis

Benign prostatic hyperplasia
Acute prostatitis
Chronic prostatitis
Abscess
Cyst
Prostatic neoplasia
  - Adenocarcinoma most common
  - Transitional cell carcinoma second most common
  - Sarcomatoid carcinoma
  - Primary and metastatic hemangiosarcoma
  - Lymphoma

Diagnostic Evaluation

- History of lower urinary tract signs, penile discharge, hematuria, dysuria, tenesmus, obstipation, ribbon stools, stiff gait. Severe systemic signs suggest sepsis or systemic inflammation raises suspicion of acute prostatitis. Intact males are more predisposed to BPH and prostatitis.
- Digital rectal examination along with caudal abdominal palpation is a noninvasive initial screening test. The
rectum should be bilaterally symmetric, have a smooth and regular surface, have soft parenchyma, and not be painful to touch.

- Radiography of limited value for providing an actual diagnosis but may provide information about size, shape, contour, and location of the prostate. Prostatomegaly may cause dorsal displacement of the colon and cranial displacement of the urinary bladder. Mineralization with neoplasia, bacterial prostatitis, and abscessation may be apparent.
- Prostatic ultrasound is the most useful and practical imaging method. Normal prostate should have smooth borders and homogenous parenchymal pattern of moderate echogenicity. Ultrasound also offers the opportunity for guided aspirates and core biopsy sampling for culture, cytology, and histopathology.
- CT and MRI can evaluate size, shape, homogeneity of prostate and allow evaluation of intrapelvic lesions, metastatic spread, and ureteral obstruction.
- Definitive diagnosis requires cytologic, histologic, or bacteriologic evaluation of a prostate sample. Samples can be obtained using procedures such as semen collection, prostatic massage and wash, brush technique, fine needle aspiration, and biopsy.

Proteinuria in Dogs and Cats

Diagnostic Approach

- Stop use of nephrotoxic drugs.
- If proteinuria is insignificant (trace to 1+ dipstick reading and urine specific gravity > 1.035), there is no need for further workup.
- Perform urinalysis to exclude hemorrhage, infection, or inflammation as cause of proteinuria. If these conditions present, do urine culture. If these conditions are not present, do urine protein/creatinine ratio.
- Perform serum chemistry and CBC. Evaluate serum albumin and globulin.
  - Marked proteinuria ratio (UP/UC > 3) with quiet sediment and normal globulins or a polyclonal gammopathy is consistent with renal glomerular disease (glomerulonephritis, amyloidosis). Rule out causes of glomerulonephropathy such as heartworm disease, hepatozoonosis, immune-mediated diseases such as SLE, chronic infectious diseases such as borreliosis, feline leukemia virus, feline immunodeficiency virus, ehrlichiosis, other chronic inflammatory diseases, neoplasia, and hyperadrenocorticism).
• If no underlying disease found, may need renal biopsy to assess for glomerulonephritis or amyloidosis.
• Proteinuria detected by precipitation testing but not dipstick or proteinuria associated with a monoclonal gammopathy may be caused by Bence Jones proteins. This requires a search for osteolytic or lymphoproliferative lesions. Ehrlichiosis may mimic myeloma. If Ehrlichia negative, protein electrophoresis in indicated. A monoclonal gammopathy suggests myeloma.

**Pyelonephritis, Bacterial**

### Clinical Findings, Dogs and Cats

- Fever
- Renal pain
- Leukocytosis
- Anorexia
- Lethargy
- Cellular casts in urine sediment
- Azotemia
- Inability to concentrate urine
- Polyuria/polydipsia
- Ultrasonographic or excretory urographic abnormalities
  • Renal pelvis dilatation
  • Asymmetric filling of diverticula
  • Dilated ureters
- Bacteria in inflammatory lesions on histopathologic examination
- Positive culture of ureteral urine collected by cystoscopy
- Positive culture of urine obtained after rinsing bladder with sterile saline
- Positive culture of urine obtained by ultrasound-guided pyelocentesis

### Renal Disease

*See Glomerular Disease.*

#### Familial—Dogs And Cats

- Amyloidosis—Beagle, English Foxhound, Shar-Pei, Abyssinian cat, Oriental shorthaired cat, Siamese cat
- Renal Dysplasia—Lhasa Apso, Shih Tzu, Standard Poodle, Soft Coated Wheaten Terrier, Chow Chow, Alaskan Malamute, Miniature Schnauzer, Dutch Kooiker (Dutch decoy dog)
- Fanconi syndrome (tubular dysfunction)—Basenji
Tubular dysfunction (renal glucosuria)—Norwegian Elkhound
Basement membrane disorder—Bull Terrier, Doberman Pinscher, English Cocker Spaniel, Samoyed
Membranoproliferative glomerulonephritis—Bernese Mountain Dog, Brittany Spaniel, Soft-Coated Wheaten Terrier
Primary glomerular disease—Rottweiler, Beagle, Pembroke Welsh Corgi, Newfoundland, Bullmastiff, Doberman Pinscher, Dalmatian, Bull Terrier, English Cocker Spaniel, Samoyed
Periglomerular fibrosis—Norwegian Elkhound
Polycystic kidney disease—Cairn Terrier, West Highland White Terrier, Bull Terrier, Persian cat
Multifocal cystadenocarcinoma—German Shepherd

**Differential Diagnosis, Renal Tubular Disease**

**Cystinuria**
- Inherited proximal tubular defect
- Many breeds of dogs including mixed breeds
- Often leads to cystine calculi formation

**Carnitinuria**
- Reported in dogs with cystinuria
- May lead to carnitine deficiency and cardiomyopathy

**Hyperuricosuria**
- Abnormal purine metabolism
  - Dalmatian
  - Dogs with primary hepatic disease
- May lead to urate urolithiasis

**Hyperxanthinuria (rare)**
- Seen in dogs receiving allopurinol to prevent urate uroliths
- Congenital hyperxanthinuria seen in a family of Cavalier King Charles Spaniels

**Renal Glucosuria**
- Primary renal glucouria (rare)
  - Scottish Terrier, Basenji, Norwegian Elkhound, mixed breeds

**Fanconi Syndrome**
- Inherited proximal tubular defect
- Basenji most common
- May lead to renal failure
Renal Tubular Acidosis
Rare tubular disorders that lead to hyperchloremic metabolic acidosis
- Proximal renal tubular acidosis
- Distal renal tubular acidosis

Nephrogenic Diabetes Insipidus
Any renal disorder that suppresses the kidneys’ response to antidiuretic hormone (ADH)
Congenital (rare)
Acquired
- Toxic (*Escherichia coli* endotoxin)
- Drugs (glucocorticoids, chemotherapeutics)
- Metabolic disease (hypokalemia, hypercalcemia)
- Tubular injury or loss (polycystic renal disease, bacterial pyelonephritis)
- Medullary washout

**Differentiating Acute from Chronic Renal Failure**

**Acute Renal Failure**
- History of ischemia
- History of exposure to toxin
- Active urine sediment
- Good body condition
- Hyperkalemia (if oliguric)
- Normal to increased hematocrit
- Enlarged kidneys
- Potentially severe metabolic acidosis
- Severe clinical signs for level of dysfunction

**Chronic Renal Failure**
- History of previous renal disease
- History of polyuria/polydipsia
- Small irregular kidneys
- Nonregenerative anemia
- Normal to hypokalemia
- Normal to mild metabolic acidosis
- Inactive urine sediment
- Weight loss/cachexia
- Mild clinical signs for level of dysfunction

**Renal Toxins in Dogs and Cats**

**Therapeutic Agents**

*Antibacterial Agents*
- Aminoglycosides
- Sulfonamides
Nafcillin
Penicillins
Cephalosporins
Fluoroquinolones
Carbapenems
Rifampin
Tetracyclines
Vancomycin

**Antifungal Agents**
Amphotericin B

**Antiviral Agents**
Acyclovir
Foscarnet

**Antiprotozoal Agents**
Pentamidine
Sulfadiazine
Trimethoprim-sulfamethoxazole
Dapsone

**Anthelmintics**
Thiacetarsamide

**Cancer Chemotherapeutics**
Cisplatin/carboplatin
Methotrexate
Doxorubicin
Azathioprine

**Immunosuppressive Drugs**
Cyclosporine
Interleukin-2

**Nonsteroidal Antiinflammatory Drugs (NSAIDs)**

**Angiotensin-Converting Enzyme (ACE) Inhibitors**

**Diuretics**

**Miscellaneous Agents**
Dextran 40
Allopurinol
Cimetidine
Apomorphine
Deferoxamine
Streptokinase
Methoxyflurane
Penicillamine
Acetaminophen
Tricyclic antidepressants
Radiocontrast Agents

Nontherapeutic Agents

Heavy Metals
- Lead
- Mercury
- Cadmium
- Chromium

Organic Compounds
- Ethylene glycol
- Carbon tetrachloride
- Chloroform
- Pesticides
- Herbicides
- Solvents

Miscellaneous Agents
- Mushrooms
- Snake venom
- Grapes/raisins
- Bee venom
- Lily

Pigments
- Hemoglobin/myoglobin

Hypercalcemia

Causes of Acute Renal Failure in Dogs and Cats

Primary Renal Disease

Infection
- Pyelonephritis
- Leptospirosis
- Infectious canine hepatitis

Immune-Mediated Disease
- Acute glomerulonephritis
- Systemic lupus erythematosus (SLE)
- Renal transplant rejection

Renal Neoplasia
- Lymphoma

Nephrotoxicity
- Exogenous toxins
- Endogenous toxins
- Drugs
Renal Ischemia

Prerenal Azotemia
- Dehydration/hypovolemia
- Deep anesthesia
- Sepsis
- Shock/vasodilation
- Decreased oncotic pressure
- Hyperthermia
- Hypothermia
- Hemorrhage
- Burns
- Transfusion reaction

Renal Vascular Disease
- Avulsion
- Thrombosis
- Stenosis

Systemic Diseases with Renal Manifestations
Infection
- Bacterial endocarditis
- Feline infectious peritonitis (FIP)
- Borreliosis
- Babesiosis
- Leishmaniasis
Pancreatitis
Diabetes mellitus
Hyperadrenocorticism
Hypoadrenocorticism
Hypocalcemia
Hypokalemia
Hypomagnesemia
Hyponatremia
Systemic inflammatory response syndrome (SIRS)
Sepsis
Multiple organ failure
Disseminated intravascular coagulation (DIC)
Heart failure
SLE
Hepatorenal syndrome
Malignant hypertension
Hyperviscosity syndrome
- Polycythemia
- Multiple myeloma
Urinary outflow obstruction
Envenomation
Causes of Chronic Renal Failure in Dogs and Cats

Inflammatory/infectious
- Pyelonephritis
- Leptospirosis
- Blastomycosis
- Leishmaniasis
- FIP

Familial/congenital (see p. 265)

Amyloidosis

Neoplasia
- Lymphosarcoma
- Renal cell carcinoma
- Nephroblastoma
- Tumor lysis syndrome
- Others

Nephrotoxicants (see p. 267)

Renal ischemia

Sequela of acute renal failure

Glomerulopathies (see p. 259)

Nephrolithiasis

Bilateral hydronephrosis
- Spay granulomas
- Transitional cell carcinoma at trigone obstructing both ureters
- Nephrolithiasis

Polycystic kidney disease

Urinary outflow obstruction

Idiopathic

Reproductive Disorders

Infertility—Differential Diagnosis, Canine Female

Normal Cycles
- Improper breeding management
- Failure to determine optimal breeding time
- Female behavior
- Infertile male
- Elevated diestrual progesterone
  - Early embryonic death
  - Lesions in tubular system (vagina, uterus, uterine tubes)
  - Placental lesions (brucellosis, herpes)
- Normal diestrual progesterone
  - Cystic follicles (ovulation failure)
Abnormal Cycles

*Abnormal Estrus*

Will Not Copulate
- Not in estrus
- Inexperience
- Partner preference
- Vaginal anomaly
- Hypothyroidism (possibly)

Prolonged Estrus
- Cystic follicles
- Ovarian neoplasia
- Exogenous estrogens
- Prolonged proestrus

Short Estrus
- Observation error
- Geriatric
- Ovulation failure
- Split estrus

*Abnormal Interestrual Interval*

Prolonged Interval
- Photoperiod (queen)
- Pseudopregnant/pregnant (queen)
- Normal breed variation
- Glucocorticoids (bitch)
- Old age
- Luteal cysts

Short Interval
- Normal (especially queen)
- Ovulation failure (especially queen)
- Corpus luteum failure
- “Split heat” (bitch)
- Exogenous drugs

*Not Cycling*

Prepubertal
- Ovariohysterectomy
- Estrus suppressants
- Silent heat
- Unobserved heat
- Photoperiod (queen)
- Intersex (bitch)
- Ovarian dysgenesis
- Hypothyroidism (possibly)
- Glucocorticoid excess
- Hypothalamic-pituitary disorder
- Geriatric
Infertility—Differential Diagnosis, Canine Male

Inflammatory Ejaculate
- Prostatitis
- Orchitis
- Epididymitis

Azoospermia
- Sperm-rich fraction not collected
- Sperm not ejaculated
  - Incomplete ejaculation
  - Obstruction
  - Prostate swelling
- Sperm not produced
  - Endocrine
  - Testicular
  - Metabolic disorders

Abnormal Motility/Abnormal Morphology
- Iatrogenic
- Prepubertal
- Poor ejaculation
- Long abstinence

Abnormal Libido
- Female not in estrus
- Behavioral
- Pain
- Geriatric

Normal Libido
- Improper stud management
- Infertile female

Normal Libido/Abnormal Mating Ability
- Orthopedic
- Neurologic
- Prostatic disease
- Penile problem
- Prepuce problem

Penis, Prepuce, and Testes Disorders—Differential Diagnosis

Acquired Penile Disorders
- Penile trauma
  - Hematoma
  - Laceration
  - Fracture of os penis
- Priapism (abnormal, persistent erection)
- Neoplasia
- Vesicles
Warts
Ulcers

**Congenital Penile Disorders**
- Persistent penile frenulum
- Penile hypoplasia
- Hypospadias (defect in closure of urethra)
- Diphallia (duplication of penis)

**Preputial Disorders**
- Balanoposthitis
  - Bacteria infection
  - Blastomycosis
  - Canine herpesvirus
- Phimosis
- Paraphimosis

**Testicular Disorders**
- Cryptorchidism
- Orchitis/epididymitis
  - *Mycoplasma* spp.
  - *Brucella canis*
  - *Blastomyces* spp.
  - *Ehrlichia* spp.
  - Rocky Mountain spotted fever
  - Feline infectious peritonitis (FIP)
- Testicular torsion
- Testicular neoplasia
  - Sertoli cell tumor
  - Leydig cell tumor
  - Seminoma

**Drugs and Metabolic Disorders Affecting Male Reproduction**
- Glucocorticoids (hyperadrenocorticism, exogenous glucocorticoids)
  - Decreased luteinizing hormone (LH), testosterone, sperm output, seminal volume, and libido; increased sperm abnormalities
- Estrogens, androgens, anabolic steroids
  - Decreased LH, testosterone, and spermatogenesis
- Cimetidine
  - Decreased testosterone, libido, and sperm count
- Spironolactone, anticholinergics, propranolol, digoxin, verapamil, thiazide diuretics, chlorpromazine, barbiturates, diazepam, phenytoin, primidone
  - Decreased testosterone and libido
- Progestagens, ketoconazole
  - Decreased testosterone
Amphoterin B, many anticancer drugs
Decreased spermatogenesis
Diabetes mellitus
  Decreased libido and sperm count, abnormal semen
Renal failure, stress
  Decreased libido and sperm count

Ureteral Diseases

Differential Diagnosis

Vesicoureteral Reflux
  Primary: 7-12 weeks old—intrinsic maldevelopment of ureterovesical junction, self-limiting
  Secondary to lower urinary tract obstruction, urinary tract infection, surgical damage, neurologic disease of bladder, ectopic ureters

Congenital Anomalies
  Ectopic ureters
  Ureterocele
  Ureter agenesis
  Ureter duplication

Acquired Ureteral Disease
  Ureteral trauma
  • Blunt trauma
  • Penetrating trauma
  • Iatrogenic damage during surgery
  Inadvertent ligation and transection during ovariohysterectomy
  Urinoma (paraureteral pseudocyst)
  Ureteral obstruction
  • Intraluminal (blood clot, calculus)
  • Intramural (fibrosis, stricture, neoplasia)
  • Extramural (retroperitoneal mass, bladder neoplasia, inadvertent ligature)
  Calculi (nephroliths or nephrolith fragments that have migrated into the ureter)
  • Calcium oxalate (most common in cat)
  • Struvite (both struvite and calcium oxalate are most common in dog)
  Neoplasia
  • Transitional cell carcinoma
  • Leiomyoma
  • Leiomyosarcoma
  • Sarcoma
  • Mast cell tumor
• Fibroepithelial polyp
• Benign papilloma
• Metastatic neoplasia

**Urinary Tract Infection (UTI)**

**Clinical Findings**

**Lower UTI**
- Dysuria
- Pollakiuria
- Urges incontinence
- Gross hematuria at end of micturition
- Cloudy urine
- Foul odor to urine
- Small, painful, thickened bladder
- Palpable urocystoliths
- Pyuria
- Hematuria
- Proteinuria
- Bacteruria
- Normal CBC

**Upper UTI**
- Polyuria/polydipsia
- Signs of systemic illness or infection
- Possible renal failure
- Fever
- Abdominal pain
- Kidneys normal to enlarged
- Leukocytosis
- Pyuria
- Hematuria
- Proteinuria
- Bacteruria
- Cellular or granular casts
- Decreased urine specific gravity

**Acute Prostatitis or Prostatic Abscess**
- Urethral discharge independent of micturition
- Signs of systemic illness/infection
- Fever
- Painful prostate or abdomen
- Prostatomegaly/asymmetry
- Leukocytosis (±)
- Pyuria
- Hematuria
Proteinuria
Bacteruria
Inflammatory prostatic cytology

**Chronic Prostatitis**
- Recurrent UTIs
- Urethral discharge independent of urination
- Possible dysuria
- Normal complete blood count (CBC)
- Pyuria
- Hematuria
- Proteinuria
- Bacteruria
- Prostatomegaly/asymmetry

**Canine Lower Urinary Tract Disease—Differential Diagnosis**

**Urocystoliths**
- Struvite (magnesium ammonium phosphate)
- Calcium oxalate
- Purine (urate/xanthine)
- Cystine
- Calcium phosphate
- Silica
- Compound uroliths

**Urethral Obstruction**
- Urethroliths (see Urocystoliths)
- Blood clots
- Urethral stricture
- Neoplasia
  - Transitional cell carcinoma
  - Prostatic adenocarcinoma
  - Leiomyoma
  - Leiomyosarcoma
  - Prostatic adenocarcinoma
  - Squamous cell carcinoma
  - Myxosarcoma
  - Lymphoma
  - Mast cell tumor
- Proliferative urethritis
- Urinary bladder entrapment in perineal hernia
- Trauma
  - Penile fracture

**Urinary Tract Trauma**
- Contusion (bladder or urethra)
- Urethral tears
Rupture of bladder (blunt trauma, secondary to pelvic fracture, penetrating wound)
Avulsion of bladder or urethra
Penile fracture

**Inflammation (Bladder or Urethra)**
- Bacterial UTI
- Fungal UTI
- Polypoid cystitis
- Emphysematous cystitis
- Cyclophosphamide-induced cystitis
- Parasitic cystitis (*Capillaria plica*)

**Feline Lower Urinary Tract Disease—Differential Diagnosis**
- Feline idiopathic cystitis
- Urethral plug (obstructive feline idiopathic cystitis)
- Urolithiasis
  - Struvite
  - Calcium oxalate
  - Urate
  - Cystine
- Bacterial cystitis (less common in cats than in dogs)
- Stricture
- Neoplasia

**Uroliths, Canine**

**Characteristics**

**Calcium Oxalate Monohydrate or Dihydrate**
- Radiopaque
- Acidic to neutral pH
- Sharp projections or smooth uroliths; calcium oxalate dihydrate uroliths may be jackstone shaped
- Not associated with urinary tract infection
- Calcium oxalate dihydrate crystals: square envelope shape
- Calcium oxalate monohydrate crystals: dumbbell shaped

**Struvite (Magnesium-Ammonium-Phosphate)**
- Radiopaque
- Alkaline pH
- Smooth to speculated if single; smooth and pyramidal in shape if multiple
- Associated with infection with urease-producing bacteria (*Staphylococcus*, *Proteus*, *Ureaplasma* spp., *Klebsiella*, *Corynebacterium*)
- “Coffin lid”—shaped crystals
Urate/Xanthine
Radiolucent to faintly radiopaque
Acidic pH
Smooth uroliths
Not associated with infection
Yellow-brown “thorn apple” (spherical) or amorphous crystals

Cystine
Faintly to moderately radiopaque
Acidic pH
Smooth, round uroliths; staghorn-shaped uroliths if nephroliths present
Not associated with infection
Hexagonal-shaped crystals

Calcium Phosphate
Radiopaque
Alkaline to normal pH for hydroxyapatite, acidic for brushite
Small, variably shaped uroliths for hydroxyapatite
Smooth, round or pyramidal for brushite
Not associated with infection
Amorphous phosphate crystals or thin prisms (calcium phosphate)

Silica
Radiopaque
Acidic to neutral pH
Jackstone-shaped uroliths
Not associated with infection
No crystals

Vaginal Discharge

Differential Diagnosis

Cornified Epithelial Cells
Normal proestrus
Normal estrus
Contamination of skin or epithelium
Ovarian remnant syndrome
Abnormal source of estrogen
• Exogenous
• Ovarian follicular cyst
• Ovarian neoplasia
Contamination of squamous epithelium
**Mucus**
- Normal late diestrus or late pregnancy
- Normal lochia
- Mucometra
- Androgenic stimulation

**Neutrophils**

*Nonseptic (no microorganisms seen)*
- Vaginitis
- Normal first day of diestrus
- Metritis or pyometra

*Septic*
- Vaginitis
- Metritis
- Pyometra
- Abortion

**Peripheral Blood**
- Subinvolution of placental sites
- Uterine or vaginal neoplasia
- Trauma to reproductive tract
- Uterine torsion
- Coagulopathies

**Cellular Debris**
- Normal lochia
- Abortion
Pain Diagnosis

Acute Pain Assessment
Acute Pain Preemptive Scoring System (examples in each category)
Chronic Pain Assessment

Acute Pain Assessment

Subjective evaluation of pain in animals relies on observation and interpretation of animal behavior. Pain may be indicated by loss of normal behaviors or appearance of abnormal behaviors.

Dogs

- Restless, agitated, delirious
- Lethargic, withdrawn, dull, obtunded
- May ignore environmental stimuli
- Abnormal sleep-wake cycle, inability to sleep
- May bite, lick, or chew painful area
- Adopt abnormal body positions to cope with pain
- Ears held back, eyes wide open with dilated pupils or closed with a dull appearance
- Disuse or guarding of painful area
- Vocalization (whimper, yelp, whine, groan, yowl)
- May become more aggressive and resist handling or palpation or may become more timid and seek increased contact with caregivers

Cats

- Hide, stay to back of cage
- Behavior may be mistaken for fear or anxiety
- May sit very quietly and pain may be missed by those looking for more active signs of pain
- May continue to purr while in pain
- May growl with ears flattened
- May attempt escape
- Lack of grooming
- Hunched posture, statue-like appearance
- Reduced or absent appetite
- Tail flicking
### Acute Pain Preemptive Scoring System
*(examples in each category)*

#### Minor Procedures: No Pain
- Physical examination, restraint
- Radiography
- Suture removal, cast application, bandage change
- Grooming
- Nail trim

#### Minor Surgeries: Minor Pain
- Suturing, debridement
- Urinary catheterization
- Dental cleaning
- Ear examination and cleaning
- Abscess lancing
- Removing cutaneous foreign bodies

#### Moderate Surgeries: Moderate Pain
- Ovariohysterectomy, castration, caesarean section
- Feline onychectomy
- Cystotomy
- Anal sacculectomy
- Dental extraction
- Cutaneous mass removal
- Severe laceration repair

#### Major Surgeries: Severe Pain
- Fracture repair, cruciate ligament repair
- Thoracotomy, laminectomy, exploratory laparotomy
- Limb amputation
- Ear canal ablation

### Chronic Pain Assessment
- Clinical signs of chronic pain depend on underlying cause and pathologic state.
- Range from subtle to obvious
- May see acute flareups that require changes in treatment (e.g., osteoarthritic dog that experiences acute pain after excessive strenuous activity)
- Decreased activity
- Reluctance to rise or play
- Changes in sleep patterns
- Changes in appetite
- Changes in social interaction and grooming habits
- Withdrawal, aggression
- Owner observations are extremely important
Laboratory Values and Interpretation of Results
PART THREE Laboratory Values and Interpretation of Results

**Acetylcholine Receptor Antibody**

**Normal range:**
- Feline: <0.3 nmol/L
- Canine: <0.6 nmol/L

**Elevated in:** myasthenia gravis

**Note:** A positive titer is diagnostic for myasthenia gravis. Negative titers occur in 10% to 20% of positive cases; therefore a negative titer does not exclude myasthenia gravis.

**Activated Coagulation Time (ACT)**

**Normal range:**
- Feline: 50-75 seconds
- Canine: 60-110 seconds

Screening test for intrinsic and common coagulation pathways (factors II, V, VII, IX, X, XI, XII); may also be prolonged with severe thrombocytopenia and decreased fibrinogen.

**Activated Partial Thromboplastin Time (APTT)**

**Normal range:**
- Feline: 10-25 seconds
- Canine: 10-25 seconds

Determines abnormalities in the intrinsic coagulation pathway. Prolonged with deficiencies in factors VIII, IX, XI, and XII and fibrinogen; also prolonged with disseminated intravascular coagulation (DIC). Prolonged with von Willibrand disease, acquired vitamin K deficiency, coumarin poisoning, bile insufficiency, liver failure. Severely prolonged with hemophilia A (factor VIII deficiency) and hemophilia B (factor IX).
**Adrenocorticotropic Hormone (ACTH), Endogenous**

**Normal range:**
Feline: not reported  
Canine: 10-70 pg/mL

**Elevated in:** pituitary-dependent hyperadrenocorticism

**Decreased in:** iatrogenic Cushing syndrome and adrenal tumors

**Adrenocorticotropic Hormone (ACTH) Stimulation Test**

**Normal range:**

**Pre-ACTH injection:**
Feline: 1.0-4.5 μg/dL  
Canine: 1.0-4.5 μg/dL

**Post-ACTH injection:**
Feline: 4.5-15.0 μg/dL (13-16 μg/dL: suggestive of hyperadrenocorticism, >16 μg/dL strongly suggestive)  
Canine: 5.5-20.0 μg/dL (18-24 μg/dL: suggestive of hyperadrenocorticism, >24 μg/dL strongly suggestive)  
From 15% to 20% are false-negative results; false-positive results may be seen with stress or nonadrenal illness.  
Pre-ACTH cortisol is in normal range, and post-ACTH cortisol shows little to no change with iatrogenic Cushing syndrome.  
Pre-ACTH cortisol is below normal, and post-ACTH cortisol shows little change with hypoadrenocorticism.  
Pre-ACTH and post-ACTH cortisol levels should be between 1 and 5 μg/dL with successful Lysodren induction or while on maintenance Lysodren therapy.  
Trilostane induction: <1.45 μg/dL, stop treatment. Restart on a lower dose.  
1.45-5.4 μg/dL, continue on same dose.  
5.4-9.1 μg/dL, continue on current dose if clinical signs well controlled or increase dose if clinical signs of hyperadrenocorticism still evident.  
>9.1 μg/dL, increase initial dose.

**Note:** ACTH stimulation does not differentiate pituitary-dependent hyperadrenocorticism from adrenal tumors. The low-dose dexamethasone test is more diagnostic for canine Cushing syndrome.
Alanine Aminotransferase (ALT, Formerly SGPT)

**Normal range:**
Feline: 10-100 IU/L  
Canine: 12-118 IU/L

**Elevated in:** hepatocellular membrane damage and leakage  
**Inflammation:** chronic active hepatitis, lymphocytic/plasmacytic hepatitis (cats), enteritis, pancreatitis, peritonitis, cholangitis, cholangiohepatitis  
**Infection:** bacterial hepatitis, leptospirosis, feline infectious peritonitis (FIP), infectious canine hepatitis  
**Toxicity:** chemical, heavy metals, mycotoxins  
**Neoplasia:** primary, metastatic  
**Drugs**  
**Endocrine:** diabetes mellitus, hyperadrenocorticism, hyperthyroidism  
**Trauma**  
**Hypoxia:** cardiopulmonary disease, thromboembolic disease  
**Metabolism:** feline hepatic lipidosis, storage diseases (e.g., copper)  
**Liver lobe torsion**  
**Hepatocellular regeneration**  
**Cirrhosis**

**Decreased in:** end-stage liver disease, but in most cases decreased ALT is not significant

Albumin

**Normal range:**
Feline: 2.5-3.9 g/dL  
Canine: 2.7-4.4 g/dL

**Elevated in:** dehydration (globulin and total protein should also be increased), spurious (e.g., hemolysis, lipemia, laboratory error), higher in adults than in juveniles

**Decreased in:** protein-losing nephropathy (amyloidosis, glomerulonephritis, glomerulosclerosis), gastroenteropathy (malabsorption, maldigestion, protein-losing enteropathy), liver failure, malnutrition (dietary, parasitism), exudative skin disease (vasculitis, burns, abrasions, degloving injury), neonates, external blood loss, compensatory (chronic effusions, hyperglobulinemia, multiple myeloma)
Alkaline Phosphatase, Serum (SAP or ALP)

**Normal range:**
Feline: 6-102 IU/L  
Canine: 5-131 IU/L

**Elevated in:** biliary tract abnormalities (pancreatitis, bile duct neoplasia, cholelithiasis, cholecystitis, ruptured gallbladder); hepatic parenchymal disease (cholangitis/cholangiohepatitis, chronic hepatitis, nodular hypoplasia, copper storage disease, hepatic lipodosis [cats], cirrhosis, hepatic neoplasia, lymphoma, hemangiosarcoma, hepatocellular carcinoma, metastatic carcinoma), toxic hepatitis, feline infectious peritonitis [cats]); corticosteroids; anti-convulsants (phenobarbital, primidone); endocrine disorders (diabetes mellitus, hyperadrenocorticism [dogs], hyperthyroidism [cats]); enteritis; bone isoenzyme; young dog with bone growth; osteosarcoma; osteomyelitis; ehrlichiosis; diaphragmatic hernia; passive congestion due to right heart failure; iatrogenic

**Note:** Almost any disorder that affects the liver can cause elevations in SAP levels.

Ammonia

**Normal range:**
Feline: 30-100 μg/dL  
Canine: 45-120 μg/dL

**Elevated in:** hepatic failure (portosystemic shunt, cirrhosis); spurious (e.g., hemolysis, lipemia, laboratory error)

**Note:** Due to instability of samples, this test has been mostly been replaced by serum bile acids.

Amylase, Serum

**Normal range:**
Feline: 100-1200 U/L  
Canine: 290-1125 U/L

**Elevated in:** pancreatitis, pancreatic neoplasia, pancreatic duct obstruction, pancreatic necrosis, enteritis, renal disease (decreased filtration of amylase)

**Note:** Serum amylase levels may not correlate with severity of disease. Not very sensitive or specific, especially in cats
Part Three
Laboratory Values and Interpretation of Results

Anion Gap

Normal range:
Feline: 12-24
Canine: 16.3-28.6

Laboratory calculation:
\[ [\text{Na} + \text{K}] - [\text{Cl} + \text{HCO}_3^-] = \text{Anion gap} \]

Elevated in: Metabolic acidosis from acids that do not contain chloride. Metabolic acidosis with normal anion gap has an increased plasma chloride concentration and is called **hyperchloremic acidosis**.

Decreased in: hypoalbuminemia, IgG multiple myeloma

Antinuclear Antibody (ANA)

Normal range:
Reported as a titer, very laboratory dependent. Refer to your laboratory for normal ranges.

High positive titer, with associated clinical and clinicopathologic signs, supports a diagnosis of systemic lupus erythematosus (SLE). Many immune-mediated, inflammatory, and infectious diseases and neoplasms can result in low positive titers. Results may be false negative with chronic glucocorticoid use.

Arterial Blood Gases

Normal range:

<table>
<thead>
<tr>
<th></th>
<th>Canine</th>
<th>Feline</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.35-7.45</td>
<td>7.36-7.44</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>36-44</td>
<td>28-32</td>
</tr>
<tr>
<td>PaO₂</td>
<td>90-100</td>
<td>90-100</td>
</tr>
<tr>
<td>TCO₂</td>
<td>25-27</td>
<td>21-23</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>24-26</td>
<td>20-22</td>
</tr>
</tbody>
</table>

Blood gas interpretation:

Evaluate PaO₂
Hypoxemia: arterial oxygen tension/partial pressure (PaO₂) of less than 85 mm Hg
Emergency treatment for hypoxemia needed when PaO₂ is less than 60 mm Hg. Cyanosis may be seen when PaO₂ is 50 mm Hg or lower, depending on hemoglobin concentration.

**Potential causes of hypoxemia**
- Right-left shunts (patent ductus arteriosus, ventricular septal defects, intrapulmonary shunts)
- Ventilation/perfusion mismatch (various pulmonary diseases)
- Diffusion impairment
- Hypoventilation (anesthesia, neuromuscular disease, airway obstruction, central nervous system disease, pleural space or chest wall abnormality)
- Decrease in fraction of inspired oxygen (hooked up to empty oxygen tank)

**Evaluate pH**
- Increase in pH: alkalemia (metabolic alkalosis or respiratory alkalosis)
- Decrease in pH: acidemia (metabolic acidosis or respiratory acidosis)

**Assess acid-base status**

**If acidemic:**
- Arterial carbon dioxide tension (PaCO₂) elevated: respiratory acidosis
- PaCO₂ decreased: compensatory respiratory alkalosis
- Bicarbonate (HCO₃⁻) decreased: metabolic acidosis
- HCO₃⁻ elevated: compensatory metabolic alkalosis

**If alkalotic:**
- PaCO₂ decreased: respiratory alkalosis
- PaCO₂ elevated: compensatory respiratory acidosis
- HCO₃⁻ elevated: metabolic alkalosis
- HCO₃⁻ decreased: compensatory metabolic acidosis

**Aspartate Aminotransferase (AST, Formerly SGOT)**

Not considered clinically significant in the dog or cat. Very sensitive but not very specific; significant amounts of AST found also in muscle.

**Basophil Count**

**Normal range:**
- Feline: 0-150 cells/µL
- Canine: 0-150 cells/µL
Elevated (basophilia) in: disorders associated with IgE production/binding (heartworm disease, atopy), inflammatory disease (gastrointestinal tract disease, respiratory tract disease), neoplasia (mast cell neoplasia, basophilic leukemia, lymphomatoid granulomatosis), associated with hyperlipoproteinemia and possibly hypothyroidism

Bicarbonate (HCO₃⁻)

**Normal range:**
- Feline: 20-22 mmol/L
- Canine: 24-26 mmol/L

If acidemic:
- Elevated in: metabolic alkalosis (with compensatory acidosis)
- Decreased in: metabolic acidosis

If alkalotic:
- Elevated in: metabolic alkalosis
- Decreased in: metabolic acidosis (with compensatory alkalosis)

Bile Acids

**Normal range:**

- **Preprandial:**
  - Feline and canine: 0-5.0 µmol/L
- **Postprandial:**
  - Feline: 1-20.0 µmol/L
  - Canine: 5.0-25.0 µmol/L

Elevated in: hepatocellular disease, cholestatic disease, portosystemic shunt

Decreased in: delayed gastric emptying, malabsorption disorders, rapid intestinal transport, ileal resection

Patient must be fasted and cannot be icteric. Typically measure preprandial and 2-hour postprandial serum samples. May also measure urine bile acids, although patients with portosystemic shunts tend to have lower urine bile acids than patients with hepatocellular disease.
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Bilirubin

*Normal range:*
Feline: 0.1-0.4 mg/dL  
Canine: 0.1-0.3 mg/dL

*Elevated in:* prehepatic, hemolytic anemia, cholestasis (extrahepatic [pancreatitis, cholangitis, cholecystitis, cholelithiasis, biliary neoplasia], intrahepatic [nodular hyperplasia, feline hepatic lipidosis, cholangitis/cholangiohepatitis, cirrhosis, hepatic lymphoma, acute hepatic necrosis]), duodenal perforation, ruptured gallbladder

Blood Urea Nitrogen (BUN)

*Normal range:*
Feline: 14-36 mg/dL  
Canine: 6-25 mg/dL

*Elevated in:* prerenal azotemia (dehydration, hypoadrenocorticism, heart failure, shock, gastrointestinal hemorrhage, high-protein diet); increased catabolism (fever, drugs, [e.g., tetracycline]); renal failure; pyelonephritis; postrenal azotemia (urethral [obstruction, urolith, urethral tear, plant awn]; bladder [obstruction, urolith, blood clot, polyp, neoplasia, rupture])

*Decreased in:* diuresis (polydipsia, hyperadrenocorticism, overzealous fluid therapy, drugs [e.g., glucocorticoids], diabetes insipidus); liver failure (portosystemic shunt, cirrhosis, urea cycle enzyme deficiency); low-protein diet; malnutrition; neonates

Buccal Mucosal Bleeding Time (BMBT)

*Normal range:*
Feline and canine: <3 minutes

Prolonged bleeding time is a sensitive and specific indicator of diminished platelet function (e.g., severe thrombocytopenia, von Willebrand disease and uremia).

Calcium (Ca)

*Normal range:*
Feline: 8.2-10.8 mg/dL  
Canine: 8.9-11.4 mg/dL
Elevated in: primary hyperparathyroidism; renal failure; hypoadrenocorticism; hypercalcemia of malignancy (lymphosarcoma, apocrine gland adenocarcinoma, carcinomas [nasal, mammary gland, gastric, thyroid, pancreatic, pulmonary]; osteolytic [multiple myeloma, lymphosarcoma, squamous cell carcinoma, osteosarcoma, fibrosarcoma]); hypervitaminosis D (cholecalciferol rodenticides, plants, excessive supplementation); dehydration; granulomatous disease (systemic mycosis [blastomycosis], schistosomiasis, feline infectious peritonitis [FIP]); nonmalignant skeletal disorder (osteomyelitis, hypertrophic osteodystrophy [HOD]); iatrogenic disorder (excessive calcium supplementation, excessive oral phosphate binders); factitious disorders (serum lipemia, postprandial measurement, young animal); laboratory error; idiopathic (cats)

Decreased in: renal failure (acute and chronic); acute pancreatitis; intestinal malabsorption; primary hypoparathyroidism (idiopathic, post-thyroidectomy); puerperal tetany (eclampsia); ethylene glycol toxicity; hypoprothrombinemia/hypoalbuminemia; hypomagnesemia; nutritional secondary hyperparathyroidism; tumor lysis syndrome; phosphate-containing enemas; anticonvulsant medications; sodium bicarbonate administration; laboratory error

Cerebrospinal Fluid (CSF)

Normal range: Normal CSF is colorless and clear. Discoloration usually means RBCs or neutrophils are present.

<table>
<thead>
<tr>
<th>Value</th>
<th>Canine</th>
<th>Feline</th>
<th>Cytology (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBCs (×10³/L)</td>
<td>≤3</td>
<td>≤2</td>
<td>Monocytes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>87  69-100</td>
</tr>
<tr>
<td>RBCs (×10⁶/L)</td>
<td>≤30</td>
<td>≤30</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4  0-27</td>
</tr>
<tr>
<td>Protein (mg/dL)</td>
<td>≤33</td>
<td>≤36</td>
<td>Neutrophils</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3  0-9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Eosinophils</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0  0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Macrophages</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6  0-3</td>
</tr>
</tbody>
</table>

Infectious central nervous system (CNS) disease: increased white blood cells (WBCs) and protein content
Inflammatory CNS disease: increased WBCs and protein content
Brain neoplasia: normal to mild elevation of WBCs, mild elevation of protein content
Hydrocephalus, lissencephaly: normal WBCs and protein content
Degenerative myelopathy, intervertebral disk disease, polyradiculoneuritis: normal WBCs and normal to mildly increased protein content
Most common cause of RBCs in CSF is contamination during collection.
Chloride (Cl)

**Normal range:**
Feline: 104-128 mEq/L
Canine: 102-120 mEq/L
Often changes proportionally with sodium. In those cases it is usually easier to search for the cause of the sodium change.

**Corrected Hyperchloremia (elevation of chloride disproportionate to elevation of sodium):**

**Excessive Loss of Sodium Relative to Chloride**
Small Bowel Diarrhea (common and important)

**Pseudohyperchloremia**
Lipemic Samples Using Colorimetric Methods
Potassium Chloride Therapy (common and important)

**Excessive Gain of Chloride Relative to Sodium**
Therapy with Chloride Salts (NH₄Cl, KCl)
Total Parenteral Nutrition
Fluid Therapy (0.9% NaCl, hypertonic saline, KCl-supplemented fluids)
Salt Poisoning
Renal Chloride Retention (renal failure, renal tubular acidosis, hypoadrenocorticism, diabetes mellitus, chronic respiratory alkalosis, drug-induced [acetazolamide, spironolactone])
Exercise (endurance exercise in sled dogs, short, submaximal exercise [agility])

**Corrected Hypochloremia (loss of chloride relative to sodium)**

**Gastrointestinal Loss**
Vomiting of Stomach Contents
Selected GI diseases associated with hyperkalemia and hyponatremia in dogs without hypoadrenocorticism (trichuriasia, salmonellosis, perforated duodenal ulcer)

**Renal Loss**
Therapy with Thiazide or Loop Diuretics
Chronic Respiratory Acidosis
Hyperadrenocorticism
Glucocorticoid Administration
Therapy with Solutions with High Sodium Concentration Relative to Chloride

Sodium Bicarbonate
Exercise in Racing Greyhounds

Cholesterol (CH)

**Normal range:**
Feline: 75-220 mg/dL
Canine: 92-324 mg/dL

**Elevated in:** postprandial, primary hyperlipidemia, endocrine disorders (hypothyroidism, hyperadrenocorticism, diabetes mellitus), cholestasis, dietary (high cholesterol diet), nephrotic syndrome, protein-losing nephropathy, idiopathic (Doberman Pinscher, Rottweiler)

**Decreased in:** liver failure, malabsorption, maldigestion, protein-losing enteropathy, portosystemic shunt, lymphangiectasia, starvation, hypoadrenocorticism

Cholinesterase

**Normal range:**
Feline: 500-4000 U/L
Canine: 800-4000 U/L

**Decreased in:** organophosphate toxicity, carbamate toxicity

Cobalamin

**Normal range:**
Feline: 290-1499 pg/mL
Canine: 251-908 pg/mL

**Decreased in:** exocrine pancreatic insufficiency, distal small intestinal disease, diffuse small intestinal disease, small intestinal bacterial overgrowth (usually combined with an increased serum folate level), hepatic disease in cats

Complete Blood Count (CBC)

**Normal range:**

**Total white blood cell (WBC) count:**
Feline: 3.5-16.0 $10^3/\mu$L
Canine: 4.0-15.5 $10^3/\mu$L
Total red blood cell (RBC) count:
Feline: 5.92-9.93 \times 10^6/\mu L
Canine: 4.8-9.3 \times 10^6/\mu L

Hemoglobin:
Feline: 9.3-15.9 g/dL
Canine: 12.1-20.3 g/dL

Hematocrit (packed cell volume):
Feline: 29-48%
Canine: 36-60%

Reticulocyte count:
Feline: 0-10.5% punctate or 0-1.0% aggregate
Canine: 0-1.0% aggregate

Mean corpuscular volume (MCV):
Feline: 37-61 fl
Canine: 58-79 fl

Mean corpuscular hemoglobin (MCH):
Feline: 11-21 pg
Canine: 19-28 pg

Mean corpuscular hemoglobin concentration (MCHC):
Feline: 30-38 g/dL
Canine: 30-38 g/dL

Platelet count:
Feline: 200-500 \times 10^3/\mu L
Canine: 170-400 \times 10^3/\mu L

Total solids:
Feline: 5.2-8.8 g/dL
Canine: 5.0-7.4 g/dL

Coombs Test
Indicates presence of antibody and/or complement on the surface of erythrocytes; supports the diagnosis of immune-mediated hemolytic anemia

Cortisol
Normal range:
Feline and canine: 1.0-4.5 \mu g/dL
Not a reliable indicator of disease; considerable overlap between normal patients and those with adrenal disease.
**Elevated in:** stress (environmental, illness), drugs (prednisone and prednisolone [may cross-react in assay], anticonvulsants), pituitary- and adrenal-dependent hyperadrenocorticism

**Decreased in:** drugs (suppression of adrenal function), hypoadrenocorticism

**Creatine Kinase (CK, formerly CPK)**

**Normal range:**
Feline: 56-529 U/L
Canine: 59-895 U/L

**Elevated in:** trauma, myositis (immune mediated, eosinophilic myositis, masticatory muscle myositis, infectious [toxoplasmosis, neosporosis], endocarditis), exertional myositis, nutritional (hypokalemia [polymyopathy], taurine deficiency), prolonged recumbency, intramuscular injections, pyrexia, hypothermia, postinfarct ischemia (cardiomyopathy, disseminated intravascular coagulation [DIC]), muscle ischemia secondary to status epilepticus

**Creatinine**

**Normal range:**
Feline: 0.6-2.4 mg/dL
Canine: 0.5-1.6 mg/dL

**Elevated in:** azotemia (prerenal, renal, postrenal, rhabdomyolysis)

**Decreased in:** any condition that causes decreased muscle mass

**Cytologic Criteria of Malignancy**

**General Criteria**

- Anisocytosis and macrocytosis—variation in cell size
- Hypercellularity—increased cell exfoliation due to decreased cell adherence
- Pleomorphism—variable size and shape of cells of the same type

**Nuclear Criteria**

- Macrokaryosis—increased nuclear size. Nuclei larger than 20 μ suggestive of neoplasia
- Increased nucleus-to-cytoplasm ratio (N:C)—normal nonlymphoid cells have usually have a N:C of 1.3:1.8. Ratios of 1.2 or less suggestive of malignancy
• Anisokaryosis—variation in nuclear size. Especially important if the nuclei of multinucleated cells vary in size
• Multinucleation—especially important if the nuclei vary in size
• Increased mitotic figures—mitosis is rare in normal tissues
• Abnormal mitosis—improper alignment of chromosomes
• Coarse chromatin pattern—may appear ropy or cord-like
• Nuclear molding—deformation of nuclei by other nuclei within the same cell or adjacent cells
• Macronucleoli—nucleoli are increased in size (>5 μ suggestive of malignancy, for reference, RBCs are 5-6 μ in the cat and 7-8 μ in the dog
• Angular nucleoli—fusiform or have other angular shapes instead of their normal round to slightly oval shape
• Anisonucleoliosis—variation in nucleolar shape or size (especially important if the variation is within the same nucleus)

Cytologic Features of Discrete Cell (Round Cell) Tumors

Discrete Cells (Round Cells)
• Present individually in tissues, not adhered to other cells for connective tissue matrix
• Most discrete cells are of hematogenous origin.
• Aspirates of normal lymphoid tissues like spleen and lymph nodes yield discrete cells.
• Discrete cell patterns in other tissues indicate the presence of a discrete cell tumor (round cell tumor).
• Cells tend to be small to medium sized and round.

Specific Discrete Cell Tumors

Mast Cell Tumor
Highly cellular smears of predominately mast cells
• Small, red-purple intracytoplasmic granules
• Number of granules seen vary from few to so many the cytoplasm is packed with granules. Some mast cells may degranulate during aspiration. More granules in background, fewer in cells
• Anaplastic mast cell tumors may be virtually devoid of granules.

Lymphoma
Most cases of lymphoma in dogs and cats are high-grade tumors composed mostly of large blastic lymphoid cells. Cytology typically shows greater than 50% of cells are
large, blastic lymphocytes. Lymphoblasts have a high nuclear-to-cytoplasmic ratio and intensely basophilic cytoplasm.

- Low grade, well-differentiated lymphoma may yield predominately small lymphocytes. Such tumors are difficult to differentiate from normal or reactive lymphoid tissue and require biopsy and histopathology.

**Canine Cutaneous Histiocytoma**
Benign tumors of dendritic cell origin, common in young dogs

- Medium sized cells, round to oval nuclei that may be indented. Finely stippled chromatin with indistinct nucleoli. Moderate amount of light blue-gray cytoplasm
- Most histiocytomas regress spontaneously. The presence of small lymphocytes with these tumor cells may be seen in tumors that are regressing.

**Malignant Histiocytosis/Histiocytic Sarcoma/Systemic Histiocytosis**
Cytologic appearance varies from benign looking cells to populations of histiocytic cells with marked atypia.

- Common features include large discrete cells with abundant vacuolated cytoplasm, prominent cytophagia, and multinucleation. May demonstrate marked anisocytosis, anisokaryosis, and variation of nuclear:cytoplasmic ratio. Macrocytosis, karyomegaly, and large multinucleated cells are common.
- Definitive diagnosis may not be possible based on cytology alone.

**Plasmacytoma**
Tumors of plasma cell origin include multiple myeloma (arising primarily from bone marrow) and extramedullary plasmacytomas (usually cutaneous but may be in other sites such as GI).

- Cutaneous plasmacytomas are usually benign. GI tumors are more likely to be malignant.
- Well-differentiated plasmacytomas yield cells that resemble normal plasma cells. Small, round nuclei with deeply basophilic cytoplasm exist with or without the characteristic paranuclear clear zone. Poorly differentiated plasmacytoma cells are less distinct and demonstrate significant criteria of malignancy. Binucleate and multinucleate cells are common in both well and poorly differentiated plasmacytomas.
This and a lack of lymphoglandular bodies help differentiate these tumors from lymphosarcoma.

**Transmissible Venereal Tumor**

TVT cells are typically more pleomorphic than other discrete cell tumors.
- Moderate smoky to light blue cytoplasm, numerous cytoplasmic vacuoles that may also be found extracellularly. Nuclei show moderate to marked anisokaryosis and have coarse nuclear chromatin. Nucleoli may be prominent and mitotic figures are common.

**Melanoma**

Great imitators, cells show features of discrete cells, epithelial cells, or mesenchymal cells. Usually easily recognized due to their pigment. Individual melanin granules are rod-shaped and stain dark green to black. Cells may be heavily to sparsely pigmented.
- Poorly differentiated melanomas may have sparse pigmentation and show marked criteria of malignancy.

### Cytologic Features of Mesenchymal Cells

- Mesenchymal cells are cells that form connective tissue, blood vessels, and lymphatics.
- Hematopoietic cells are classified as mesenchymal cells, but because their appearance is so distinct, they are typically considered as a separate classification. Usually, discussion of mesenchymal cells implies stromal connective tissue cells.
- Cytoplasmic borders are often indistinct.
- Most connective tissues exfoliate no cells when sampled by fine needle aspiration. May see fibroblasts or fibrocytes on occasion. Reactive fibroblast may be seen in aspirates of inflamed tissue or tissues undergoing tissue repair. Reactive fibroblasts may show many criteria of malignancy, but reactive fibroblasts should be suspected when seen within a population of inflammatory cells.
- Highly cellular smears that contain predominately a pure population of mesenchymal cells are likely to indicate a mesenchymal neoplasm (sarcoma).
- Mesenchymal cells are often elongated with cytoplasm that tapers in one or more directions (referred to as *spindle cells*).
- May see elongated cells with rod-shaped nuclei to plump, minimally tapered cells with round nuclei. Neoplastic mesenchymal cell tumors may show features more consistent with epithelial or discrete cells.
PART THREE  Laboratory Values and Interpretation of Results

Cytologic Features of Normal Epithelial Cells

- Cell-to-cell adhesion
- Although normal epithelial cells can be small to large, they can be very large and have abundant cytoplasm.
- Round to columnar to caudate in shape and have sharply defined cytoplasmic borders.
- Nuclei generally are round to oval.
- Squamous epithelial cells tend to be more individually oriented when collected by surface swabs or scrapings. As they mature, their nuclei become small and pyknotic and eventually the cell becomes anucleate.
- Respiratory and gastrointestinal cells are distinctly columnar. May show long rows of cells with nuclei lined up at the basal end. Cilia may be seen at the apical end of respiratory epithelial cells.
- Glandular epithelial cells may show evidence of tubular or acinar formation.
- Tumors of epithelial cell origin may retain characteristic features.

Cytology of Ear Canal Swabs

Bacteria

- Ear canals normally contain small amounts of bacteria.
- With bacterial otitis, large numbers of bacteria are seen free in the smear.
- Neutrophilic inflammation is sometimes seen, especially with concurrent otitis media.
- Visualization of cocci on the smear often represents *Staphylococcus* but may also be *Enterococcus* or *Streptococcus*.
- Rods most commonly indicate *Pseudomonas* followed by *Proteus* and *Escherichia coli*.

Fungi

- *Malassezia pachydermatis* is by far the most common yeast seen on ear cytologies but may be found in smaller numbers in normal ears.
- May see concurrent bacteria and yeast infection
- Yeasts overgrow when the environment is favorable.
- Rarely see *Candida* and *Microsporum*

Mites

- *Otodectes cyanotis* common primary cause of otitis (50% of cats, 5% of dogs)
- *Demodex canis* and *D. cati*, *Sarcoptes scabiei*, and *Notoedres cati* are infrequently seen in ear canals.
• Mites tend to wash off slides during staining. Unstained slides of ear secretions or swabs rolled in mineral oil may be better for finding mites in the ear canal. Skin scrapings of the ear pinna are best for finding Demodex, Sarcoptes, or Notoedres.

Neoplasia

• The most common benign tumors are seen in ear canal are polyps, papillomas, basal cell tumors, and ceruminous gland adenomas.
• The most common malignant tumors are ceruminous gland adenocarcinomas, squamous cell carcinomas, and other carcinomas.
• Unfortunately, neoplastic cells are rarely seen on ear cytologies.
• May only see cytologic evidence of inflammation
• Fine-needle aspiration or biopsy of otic masses is usually necessary to establish a diagnosis.

Miscellaneous

• Ceruminous otitis externa is associated with seborrheic conditions.
• Oily, yellow discharge may resemble purulent exudate, but cytology is relatively devoid of inflammatory cells.

Cytology of Nasal Swabs or Flush Specimens

Normal Findings

• Simonsiella spp.—large, stacked, rod-shaped bacteria, normal inhabitants of the oral cavity
• Nonkeratinized squamous epithelial cells, often with adherent bacteria, are obtained from the external nares and oropharynx.
• Ciliated pseudostratified columnar epithelial cells and mucus from nasal turbinates
• Basal epithelial cells are smaller and rounded and have dark blue cytoplasm.
• May see red blood cells from hemorrhage secondary to sampling

Infectious Agents

• Neutrophils predominate with bacterial, viral, or fungal infections.
• May also see macrophages, lymphocytes, and plasma cells
• Bacterial infection suspected when bacteria seen within neutrophils
• Because bacteria from the oral cavity are usually a pleomorphic population, monomorphic populations suggest infection.
• Bacterial infection of the nasal cavity usually is secondary to trauma, foreign bodies, viral or fungal infection, neoplasia, or oronasal fistulas.
• Intranuclear viral inclusions may be seen in epithelial nuclei with herpes infections in cats.
• Fungal hyphae may be present, may need special stains to identify. Nasal cavity fungi include Aspergillus spp., Penicillium spp., Cryptococcus neoformans, Rhinosporidium spp.
• Nasal mites (Pneumonyssus caninum, Linguatula serrata). Capillaria aerophila may be found in nasal sinuses.

Noninfectious Conditions
• Foreign bodies often consist of inhaled plant material (grass awns or foxtails).
• May lead to chronic rhinitis
• Exudates with eosinophils may be seen with inhaled allergens.
• Neoplasia of the nasal cavity is usually seen in older patients.
• Epithelial, mesenchymal tumors of nasal cavity cells, extension of oral neoplasms, or transplanted from other sites (e.g., transmissible venereal tumor)
• Most nasal tumors are epithelial in origin. Adenocarcinomas most common, followed by squamous cell carcinomas and undifferentiated carcinomas
• Mesenchymal tumors of the nasal cavity include fibrosarcomas, chondrosarcomas, osteosarcomas, hemangiosarcomas, and undifferentiated sarcomas. Do not exfoliate readily
• Round cell tumors of the nasal cavity include transmissible venereal tumors, lymphosarcomas, and mast cell tumors.

Dexamethasone Suppression Tests

Low-Dose Dexamethasone Suppression Test (LDDST)

Normal: 4-hour cortisol level suppresses to less than 50% of baseline cortisol (usually < 1.4 μg/dL), and then 8-hour cortisol remains at or near that level.

Pituitary-dependent hyperadrenocorticism (PDH): 4-hour cortisol level is suppressed to less than 50% of baseline (60% of dogs) or less than 1.4 μg/dL (25% of dogs) and an 8-hour cortisol level of less than 50% of baseline but 1.4 μg/dL or greater (25% of dogs).
Dexamethasone resistance, in which none of the above criteria is met, occurs in 40% of PDH cases.

**Functional adrenal tumor (FAT):**
Dexamethasone administration has no effect on cortisol levels.

**High-Dose Dexamethasone Suppression Test**
Differentiates PDH from FAT in cases where none of the criteria for PDH is met with the LDDST.

**FAT:**
8-hour cortisol level—no suppression of cortisol levels with dexamethasone administration.

**PDH:**
8-hour cortisol level is less than 50% of baseline cortisol or less than 1.4 μg/dL.

**Disseminated Intravascular Coagulation (DIC), Diagnostic Tests**

**Fibrinogen:** increased

**Activated partial thromboplastin time (APTT):** prolonged

**Prothrombin time (PT):** prolonged

**Platelet count:** decreased

**Fibrin degradation products (assays for breakdown of fibrin clots):** increased

**D-Dimer (assays for proteolytic fragment of fibrinogen degradation):** increased

*Note:* D-Dimer has a high negative predictive value. A negative test reliably rules out DIC.

**Eosinophil Count**

**Normal range:**
Feline: 0-1000 cells/μL
Canine: 0-1200 cells/μL

**Eosinophils:**

**Elevated (eosinophilia) in:** parasitic disorders (hookworm, dirofilariasis, dipetalonemiasis, fleas, filaroides, aelurostrongyllosis, roundworms, paragonimiasis, *Cuterebra*); hypersensitivity (flea allergy dermatitis, atopy, food allergy); eosinophilic
infiltrative disease (eosinophilic granuloma complex, feline bronchial asthma, eosinophilic gastroenteritis/colitis, pulmonary infiltrates with eosinophils [dogs], hypereosinophilic syndrome); infectious diseases (toxoplasmosis, suppurative processes); neoplasia (eosinophilic leukemia, mast cell neoplasia, lymphoma, myeloproliferative disorders, solid tumors), hypoadrenocorticism, pregnancy

Decreased (eosinopenia) in: stress, hyperadrenocorticism, glucocorticoid therapy

**Erythrocyte Count (Red Blood Cell [RBC] Count)**

**Normal range:**
- Feline: 5.92-9.93 $\times 10^6/\mu L$
- Canine: 4.8-9.3 $\times 10^6/\mu L$

**Elevated in:** dehydration, splenic contraction, polycythemia

**Decreased in:**
- Regenerative anemias
  - Acute and chronic hemorrhage
  - Gastrointestinal hemorrhage
  - Ulcer disease
  - Neoplasia
- Trauma
- Coagulopathies
- Ectoparasites (fleas, ticks)
- Endoparasites (hookworms, coccidia)
- Hematuria
- Hemolytic anemia
- Immune mediated
- Cold hemagglutinin disease
- Oxidant injury (onion, kale, phenothiazines, methylene blue)
- Parasitic
  - Babesiosis
  - *Haemobartonella felis* (*Mycoplasma haemofelis*)
  - *Haemobartonella canis* (*Mycoplasma haemocanis*)
  - *Cytauxzoon felis*
  - Infectious
    - Leptospirosis
    - *Escherichia coli*
- Microangiopathic
  - Dirofilariasis
  - Vascular neoplasia
  - Vasculitis
  - Disseminated intravascular coagulation (DIC)
Zinc or copper toxicosis
Hypophosphatemia
Pyruvate kinase deficiency
Phosphofructokinase deficiency
Nonregenerative anemias
Renal failure
Anemia of chronic disease
Inflammatory disease
Infectious disease
Neoplasia
Drugs
Chemotherapeutics
Chloramphenicol
Sulfadiazine
Phenylbutazone
Iron deficiency
Chronic blood loss
Nutritional
Endocrine disease
Hypothyroidism
Hypoadrenocorticism
Hyperestrogenism
Diethylstilbestrol
Estradiol
Sertoli cell tumor
Infectious
Feline leukemia virus (FeLV)
Feline immunodeficiency virus (FIV)
Ehrlichiosis
Feline panleukopenia virus (FPV)
Idiopathic aplastic anemia
Red cell aplasia
Myeloproliferative disease
Myelophthisis
Hypersplenism
Lead poisoning
Leukemias

Folate

**Normal range:**
Feline: 9.7-21.6 ng/mL
Canine: 7.7-24.4 ng/mL
Usually performed in conjunction with serum cobalamin and trypsin-like immunoreactivity
Elevated in: exocrine pancreatic insufficiency, small intestinal bacterial overgrowth, dietary supplementation

Decreased in: small intestinal mucosal disease

Fructosamine

Normal range:
Feline and canine: 175-400 μmol/L

Single sample test that assays mean blood glucose over the previous 1-3 weeks

Elevated: >500 μmol/L: indicates poor glycemic control (hyperglycemia)

Declining or within normal range: indicates improving or adequate glycemic control

Decreased to below lower end of reference range (<300 μmol/L): suggests that patient has experienced significant periods of hypoglycemia over past 1-3 weeks

Values within normal range with PU/PD and polyphagia: suggestive of Somogyi phenomenon

Note: Fructosamine values should not be used to make specific adjustments in insulin dosage.

Gamma Glutamyltransferase (GGT)

Normal range:
Feline: 1-10 U/L
Canine: 1-12 U/L

Elevated: cholestasis—GGT mirrors alkaline phosphatase (intrahepatic, extrahepatic), drugs (dogs [glucocorticoids]), anticonvulsants (phenobarbital, primidone), hepatocellular disease (generally slight increase)

Note: Cats with hepatic lipidosis tend to have normal to mildly elevated GGT but greatly elevated alkaline phosphatase levels.

Decreased: spurious (e.g., laboratory error, lipemic sample), hemolysis

Globulin

Normal range:
Feline: 2.3-5.3 g/dL
Canine: 1.6-3.6 g/dL
Elevated in: dehydration (albumin and total protein also elevated); infection (polyclonal gammopathy; chronic pyoderma, pyometra, chronic periodontitis, feline infectious peritonitis [FIP], bacterial endocarditis, brucellosis, feline immunodeficiency virus [FIV], feline leukemia virus [FeLV], ehrlichiosis [may cause polyclonal or monoclonal gammopathy], leishmaniasis [may cause polyclonal or monoclonal gammopathy], systemic mycoses, chronic pneumonia, bartonellosis, *Mycoplasma haemofelis* infection, Chagas disease, leishmaniasis; immune-mediated disease (polyclonal gammopathy); neoplasia (polyclonal gammopathy [necrotic or draining tumors, lymphomas, mast cell tumors]); neoplasia (monoclonal gammopathy [multiple myeloma, chronic lymphocytic leukemia, lymphoma]); cutaneous amyloidosis; “idiopathic” monoclonal gammopathy

### Glucose

**Normal range:**
- Feline: 64-170 mg/dL
- Canine: 70-138 mg/dL

Elevated (hyperglycemia) in: diabetes mellitus, stress (cats), hyperadrenocorticism, pancreatitis, drugs (glucocorticoids, progestagens, megesterol acetate, thiazide diuretics), parenteral nutrition, dextrose-containing fluids, postprandial, acromegaly (cats), diestrus (bitch), pheochromocytoma (dogs), exocrine pancreatic neoplasia, renal insufficiency, head trauma

Decreased (hypoglycemia) in: hepatic insufficiency (portal caval shunts, chronic fibrosis, cirrhosis); sepsis; prolonged sample storage; iatrogenic (insulin therapy, sulfonylurea therapy); toxicity (ethanol ingestion, ethylene glycol); β-cell tumor (insulinoma); extrapancreatic neoplasia (hepatocellular carcinoma or hepatoma, leiomyosarcoma or leiomyoma, hemangiosarcoma, carcinoma [mammary, salivary, pulmonary], leukemia, plasmacytoma, melanoma); hypoadrenocorticism; hypopituitarism; idiopathic hypoglycemia (neonatal hypoglycemia, juvenile hypoglycemia [toy breeds], hunting dog hypoglycemia); renal failure; exocrine pancreatic neoplasia; glycogen storage diseases; severe polycythemia; prolonged starvation; laboratory error

### Glucose Tolerance Test

May be used to differentiate type 1 (insulin-dependent) from type 2 (non–insulin-dependent) diabetes mellitus in cats (all dogs are considered to have type 1); results inconsistent; not usually done
Glycosylated Hemoglobin
Assays measure mean blood glucose over the life span of erythrocytes (3-4 months); in dogs, values between 4% and 6% are associated with adequate glycemic control; used less often than fructosamine.

Heartworm Antibody, Feline
Should be interpreted in conjunction with a feline heartworm antigen test
Should be interpreted in light of clinical, clinicopathologic, and radiographic signs
A negative test suggests no exposure to *Dirofilaria immitis* and helps to rule out.
A positive test supports prior exposure but does not confirm active infection.

Heartworm Antigen, Canine
A negative test implies no infection.
A positive test supports active infection.
A sample hemolysis may cause a false-positive result.
A low worm burden may cause a false-negative result.
The result may remain positive for up to 16 weeks after successful adulticide therapy.

Heartworm Antigen, Feline
Should be interpreted in conjunction with a feline heartworm antibody test
Negative test is not useful; may still be positive
Positive test is highly specific; infection is likely
Should be interpreted in light of clinical, clinicopathologic, and radiographic signs
Sample hemolysis may cause false-positive result
Low worm burden or male unisex infection will cause false-negative result

Hematocrit (Packed Cell Volume, PCV)
*Normal range:*
Feline: 29-48%
Canine: 36-60%
*Increased in:* dehydration (total protein also increased), polycythemia, splenic contracture
**Decreased in:** anemia (for more detailed list, see Erythrocyte Count); color of plasma in spun-down hematocrit tube can help determine if icterus (yellow) or intravascular hemolysis (red) is present; buffy coat: may see microfilaria if patient has heartworm disease; mast cells in systemic mastocytosis

**Hemoglobin**

Hemoglobin concentrations are usually proportional to hematocrit except in rare cases where hemoglobin synthesis defects stimulate polycythemia.

**Hemolysis, Prevention in Laboratory Samples**

**Steps to Prevent Hemolysis:**

- Fasted patient: Lipemia increases red cell fragility.
- Minimize negative pressure (may cause vein to flutter against needle, crushing red cells).
- Reposition needle deeper, or slightly rotate to move bevel of needle away from vessel wall.
- Resist tendency to increase vacuum by using more negative force; “milk” the vein.
- Use vacuum tubes and needles instead of syringes.
- Remove needle and specimen tube stopper, and transfer sample directly into open tube.
- Aspirate small amount of air from tube to reestablish negative pressure to prevent tops from coming off in transit.

**Immunoassays**

*Assays That Detect all Immunoglobulins to a Specific Antigen in a Serum Sample*

- Complement fixation
- Hemagglutination inhibition
- Serum neutralization
- Agglutination assay
- Agar gel immunodiffusion
- Indirect fluorescent antibody

*Assays That May Be Used to Detect Specific Immunoglobulins (IgG, IgM, IgA) to Antigens in a Serum Sample*

- Enzyme-linked immunosorbent assay (ELISA)
- Western blot immunoassay

IgM usually first immunoglobulin produced; may indicate recent infection and more likely to be active infection rather than just previous exposure.
Production of immunoglobulin shifts to IgG and/or IgA in days to weeks; indicates more chronic infection and possibly exposure without active disease.

Demonstrating a rising titer with paired samples may be necessary to document active infection.

**Insulin**

*Normal range:* Feline and canine: 15-35 μIU/mL

*Elevated:* normal or elevated insulin concentration in the presence of hypoglycemia is supportive of insulinoma.

*Decreased:* decreased insulin levels are not a reliable indicator of diabetes mellitus. Patients with insulin-dependent diabetes mellitus (IDDM) should have low insulin and high glucose levels. Insulin levels in non–insulin-dependent diabetes mellitus (NIDDM) are variable.

**Iron-Binding Capacity (Total, TIBC)/Ferritin**

*Decreased TIBC and decreased ferritin:* chronic (not acute) blood loss (intestinal ulceration, hookworm anemia, bleeding from neoplasia, etc.)

*TIBC normal to increased, ferritin decreased:* iron deficiency

*TIBC normal to low, ferritin normal to high:* anemia of chronic inflammatory disease

**Joint Fluid (Arthrocentesis)**

*Gross appearance:* Evaluate for turbidity (cloudiness), viscosity (does it form a long string when allowed to drip from a needle?), and color (clear, red or hemorrhagic, yellow); yellow color (xanthochromia) may indicate previous hemorrhage, degenerative, traumatic, or inflammatory disease.

*Gross appearance, microscopic examination/cytologic evaluation:*

*Normal*

Straw-colored, clear, viscous, firm mucin clot test

1-3 mononuclear cells per high-power field (hpf)

Large and small mononuclear cells with numerous vacuoles and granules; less than 10% are neutrophils (<1 neutrophil/500 erythrocytes if blood contamination has occurred).
**Abnormal**

*Hemarthrosis*
Bloody or xanthro-chromic, turbid, reduced viscosity, normal to slightly friable mucin clot test
Hemosiderin-laden macrophage, erythrophagia, moderate neutrophils

*Chronic degenerative joint disease*
Light yellow, clear to slightly turbid, viscous, normal firm mucin clot 0-20% neutrophils, few to moderate lymphocytes and macrophages

*Immune-mediated joint disease (nonerosive)*
Yellow to blood-tinged, slight to moderate turbidity, reduced viscosity, friable mucin clot test 15-95% neutrophils, few to moderate lymphocytes, synoviocytes, macrophages

*Traumatic*
Straw-colored to blood-tinged, slight to moderate turbidity, normal to slightly turbid, normal to slightly friable mucin clot test Variable neutrophils
May see hemorrhage

*Septic*
Yellow to blood-tinged to bloody, turbid to purulent, reduced viscosity, friable mucin clot test 90-99% neutrophils
May see microorganisms within cells
Toxic changes in neutrophils

*Rheumatoid arthritis (erosive)*
Yellow to blood-tinged, turbid, reduced viscosity, friable mucin clot test 20-80% neutrophils
Systemic lupus erythematosus (SLE)–induced polyarthritis: may see LE cells

**Lipase**

*Normal range:*
Feline: 10-450 U/L
Canine: 77-695 U/L

*Elevated in:* most often seen with acute pancreatitis, pancreatic necrosis, pancreatic neoplasia, enteritis, renal disease, glucocorticoids; rarely elevated with certain neoplasms in the absence of pancreatitis.

*Note:* Not very sensitive or specific for pancreatic disease
Lymphocyte Count

**Normal range:**
Feline: 1200-8000 cells/μL  
Canine: 690-4500 cells/μL

**Elevated (lymphocytosis):** physiologic or epinephrine induced, postvaccination, leukemia (lymphocytic, lymphoblastic), chronic antigenic stimulation (e.g., chronic infection, viremia, immune-mediated, inflammatory bowel disease, cholangiohepatitis, ehrlichiosis, Chagas disease, babesiosis, leishmaniasis, hypoadrenocorticism)

**Decreased (lymphopenia):** corticosteroid or stress induced; chemotherapy; immunodeficiency (feline leukemia virus [FeLV], feline immunodeficiency virus [FIV]); loss of lymph (chylothorax, lymphangiectasia); viral disease (FeLV/FIV, feline infectious peritonitis [FIP], parvovirus, canine distemper, canine infectious hepatitis)

Magnesium (Mg)

**Normal range:**
Feline: 1.1-2.3 mEq/L  
Canine: 1.2-1.9 mEq/L

**Increased in:** renal failure or insufficiency, excessive oral intake (antacids, laxatives), excessive parenteral administration

**Decreased:** dietary, gastrointestinal (malabsorption, chronic diarrhea, pancreatitis, cholestatic liver disease), renal (glomerular disease, tubular disease, postobstructive diuresis, prolonged intravenous fluids, diuretics, digitalis administration, hypercalcemia, hypokalemia), endocrine (diabetic ketoacidosis, hyperthyroidism, primary hyperparathyroidism, primary hyperaldosteronism), multiple endocrine disorders, sepsis, blood transfusion, parenteral nutrition, hypothermia, dialysis, drugs (diuretics, amphotericin B, insulin, glucose, amino acids)

Mean Corpuscular Volume (MCV)

**Normal range:**
Feline: 37-61 fl  
Canine: 58-79 fl
Elevated (macrocytosis) in: regeneration, feline leukemia, feline immunodeficiency virus (FIV), breed-related characteristics (poodles), dyserythropoiesis (bone marrow disease), sample artifact (swelling of RBCs secondary to prolonged storage in EDTA tubes)

Decreased (microcytosis) in: iron deficiency, portosystemic shunt, polycythemia, breed-related characteristics (Akita, Shar-Pei, Shiba Inu)

Methemoglobinemia
Methemoglobin is the form of hemoglobin in which the heme iron has been oxidized from ferrous (Fe^{2+}) to ferric (Fe^{3+}) and is rendered unable to bind and transport oxygen. Methemoglobinemia is seen in oxidative damage-induced hemolytic anemias and with rare inherited erythrocyte disorders.

Methods of Sample Collection for Cytology

Fine-Needle Biopsy (Aspiration or Nonaspiration Method)
- Surface masses
- Internal masses
- Lymph nodes
- Internal organs
- Fluid collection

Impression Smear
- Exudative cutaneous lesions
- Preparation of cytology samples from biopsy specimens

Scraping
- Flat cutaneous lesions not amenable to fine-needle biopsy
- Preparation of cytologic samples from poorly exfoliative biopsy specimens

Swab
- Vaginal smears
- Fistulous tracts
- Otic swabs
- Nasal, conjunctival swabs

Monocyte Count

Normal range:
Feline: 0-600 cells/μL
Canine: 0-840 cells/μL
**Elevated (monocytosis)** in: infection (pyometra, abscess, peritonitis, pyothorax, osteomyelitis, prostatitis, *Mycoplasma haemofelis*, blastomycosis, histoplasmosis, *Cryptococcus, Coccidioides*, heartworm disease, other bacteria [e.g., nocardiosis, actinomycosis, mycobacteriosis]); stress or corticosteroid induced; immune-mediated disease (hemolytic anemia, dermatitis, polyarthritis); trauma with severe crushing injury; hemorrhage into tissues or body cavities; neoplasia (tumor necrosis, lymphoma, myelodysplastic disorders, leukemias, myelomonocytic leukemia, monocytic leukemia, myelogenous leukemia)

### Myoglobinuria
Brown to dark-red urine with an absence of red blood cells (RBCs) in urine sediment and a positive test for occult blood; seen with generalized muscle disease

### Neutrophil Count

**Normal range:**
- Feline: 2500-8500 cells/μL
- Canine: 2060-10600 cells/μL

**Elevated (neutrophilia):** increased production (infection [bacterial, systemic mycoses, protozoal], inflammation [immune-mediated disease, neoplasia, tissue trauma, tissue necrosis]); demargination (stress, hyperadrenocorticism, glucocorticoids); metabolic (uremia, diabetic ketoacidosis); associated with regenerative anemia (hemolytic anemia, hemorrhagic anemia); chronic granulocytic leukemia

**Decreased (neutropenia):** decreased production (myelophtisis [myeloproliferative disease, lymphoproliferative disease, metastatic neoplasia], myelofibrosis, drug induced [chemotherapeutics, griseofulvin, chloramphenicol, trimethoprim-sulfa, azathioprine, estrogen, phenylbutazone, phenobarbital], infectious [parvovirus, ehrlichiosis, FIV, FeLV {aplastic anemia, myelodysplasia, panleukopenia-like syndrome}], hypersplenism, idiopathic hypoplasia/aplasia [cyclic neutropenia, immune mediated]); increased consumption (bacteremia/septicemia, severe systemic infection, endotoxemia); hypoadrenocorticism; margination

### Osmolality
Plasma osmolality is expected to be decreased in primary polydipsia (psychogenic polydipsia); diabetic ketoacidosis; azotemia; hypernatremia; hyperglycemia; and intoxication with ethylene glycol, ethanol, or methanol.
Plasma osmolality is expected to be increased in primary polyuria (diabetes insipidus, DI). There may be considerable overlap in values of primary polyuria and polydipsia. However, osmolality of less than 280 mOsm/kg suggests psychogenic polydipsia, whereas osmolality of greater than 280 mOsm/kg suggests central DI, nephrogenic DI, or psychogenic polydipsia.

**Packed Cell Volume**

*See Hematocrit.*

**Parathyroid Hormone (PTH)/Ionized Calcium**

*Normal range:*

**PTH:**
- Feline: 0.0-40.0 pg/mL
- Canine: 20.0-130.0 pg/mL

**Ionized Calcium:**
- Feline: 1.16-1.34 mmol/L
- Canine: 1.24-1.43 mmol/L

*Elevated in:* primary hyperparathyroidism (elevated ionized calcium and mid- to high-elevated PTH), renal or nutritional secondary hyperparathyroidism (normal or decreased ionized calcium and elevated PTH), hypercalcemia of malignancy, vitamin D toxicity, granulomatous inflammatory disease

*Decreased in:* primary hypoparathyroidism (decreased ionized calcium and low or low-normal PTH)

**Phosphorus (P)**

*Normal range:*
- Feline: 2.4-8.2 mg/dL
- Canine: 2.5-6.0 mg/dL

*Elevated in:* young, growing animal (also see elevated alkaline phosphatase); reduced glomerular filtration rate (GFR, acute renal failure, chronic renal failure); postrenal obstruction, primary hypoparathyroidism, nutritional secondary hyperparathyroidism, hyperthyroidism, acromegaly, hemolysis, intoxication (hypervitaminosis D, jasmine ingestion); hypoparathyroidism; dietary excess; metabolic acidosis; iatrogenic (phosphate enemas,
parenteral administration); osteolysis; osteolytic neoplasia; rhabdomyolysis; tumor cell lysis syndrome; sample hemolysis/delayed serum separation

**Decreased in:** primary hyperparathyroidism (also see increased calcium); nutritional secondary hyperparathyroidism; renal tubular acidosis; vomiting/diarrhea; neoplasia (PTH-like hormone, C-cell thyroid tumors); insulin therapy; diabetic ketoacidosis; Fanconi syndrome; dietary deficiency; decrease intestinal absorption; eclampsia; hyperadrenocorticism; vitamin D deficiency; hyperaldosteronism; aggressive fluid therapy; bicarbonate administration; respiratory or metabolic acidosis

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**Platelet Count**

**Normal range:**
Feline: 200-500 \(10^3/\mu \text{L}\)
Canine: 170-400 \(10^3/\mu \text{L}\)

**Elevated in:** essential thrombocytosis, rebound thrombocytosis, polycythemia vera

**Decreased (see p. 160):** decreased production (infectious retroviruses: feline immunodeficiency virus, feline leukemia virus; *Ehrlichia*); increased destruction (immune-mediated thrombocytopenia); sequestration (hypersplenism); increased consumption (hemorrhage, disseminated intravascular coagulation); breed idiosyncrasy (King Charles Spaniels [macrothrombocytes], Greyhounds)

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**Polymerase Chain Reaction**

- PCR amplifies small quantities of DNA to detectable levels.
- Can also be used to detect RNA with a reverse transcriptase step (RT-PCR)
- In general PCR is more sensitive than cytologic, serologic, or histopathologic techniques and is comparable to culture.
- PCR is of great benefit for demonstration of infectious agents, especially if the organism is difficult to culture or cannot be cultured.
- Specificity can be quite high depending on the primers used in the reaction. For example, primers can be designed to detect one bacterial genus but not others. Primers can also be designed to identify one species (e.g., all *Ehrlichia* spp. or only *E. canis*).
- False-positive if sample is contaminated during collection or in laboratory.
- False-negative if sample is handled inappropriately.
Potassium (K)

**Normal range:**
Feline: 3.4-5.6 g/dL  
Canine: 3.6-5.5 g/dL

**Elevated in:** renal failure (distal renal tubular acidosis, oliguric/anuric); postrenal (obstruction, ruptured bladder); hypoadrenocorticism; acidosis (diabetic ketoacidosis); gastrointestinal (trichuriasis, salmonellosis, perforated duodenal ulcer); chylothorax with repeated pleural fluid drainage; massive muscle trauma; postischemic reperfusion; dehydration; hypoadrenocorticism; drugs (potassium-sparing diuretics, ACE inhibitors, propranolol); thrombocytosis; severe leukocytosis (>100,000/μl, hemolysis in breed with high RBC potassium concentration (Akita, English Springer Spaniel, neonates, individuals); hyperkalemic periodic paralysis

**Decreased in:** alkalosis; dietary deficiency (feline); potassium-free fluids; bicarbonate administration; drugs (penicillins, amphotericin B, loop diuretics, thiazide diuretics); gastrointestinal fluid loss (vomiting and diarrhea, potassium rich); hyperadrenocorticism; hyperaldosteronism; insulin therapy; diuresis caused by diabetic ketoacidosis; renal (postobstructive diuresis, renal tubular acidosis, dialysis); hypokalemic periodic paralysis (Burmese cat, Pit Bull Terrier); renal failure (chronic polyuria); total parenteral nutrition; hypokalemic periodic paralysis (Burmese cats)

Protein, Total (TP)

**Normal range:**
Feline: 5.2-8.8 g/dL  
Canine: 5.0-7.4 g/dL

**Elevated in:** dehydration (albumin and globulin increased); hyperglobulinemia (chronic inflammation, infection, neoplasia [e.g., multiple myeloma]); spurious (hemolysis, lipemia)

**Decreased in:** hemorrhage, hypoalbuminemia, liver failure, external plasma loss, gastrointestinal fluid loss, malassimilation, starvation, overhydration, glomerular loss, tumor cachexia

Prothrombin Time (PT)

**Normal range:**
Feline: 6-11 seconds  
Canine: 6-12 seconds

Determines abnormalities in the extrinsic coagulation pathway
Prolonged with deficiencies of factors II, VII, and X
Becomes prolonged before any changes seen in activated coagulation time (ACT) or activated partial thromboplastin time (APTT)
Prolonged with DIC, acquired vitamin K deficiency (rodenticide poisoning), bile insufficiency, and liver failure

Red Blood Cell (RBC) Count

See Erythrocyte Count.

Reticulocyte Count

Elevated reticulocyte count is the best indicator of effective erythropoiesis.

Step 1: Multiply percent reticulocytes by red cell count to determine absolute quantity.

Step 2: Correct for reduced red cell mass; multiply absolute reticulocytes by patient’s hematocrit divided by mean species hematocrit to obtain the number of reticulocytes per milliliter.

Step 3: Correct for the effect of erythropoietin on the bone marrow reticulocyte release; divide the number of reticulocytes per milliliter by average number of days that a reticulocyte circulates in peripheral blood at that patient’s hematocrit to obtain a corrected absolute reticulocyte count.

A corrected absolute reticulocyte count of less than 105,000/mL is indicative of a nonregenerative anemia, whereas strongly regenerative anemias will have a reticulocyte count of greater than 150,000/mL.

Sodium (Na)

Normal range:
Feline: 145-158 mEq/L
Canine: 139-154 mEq/L

Elevated in: dehydration; renal failure; gastrointestinal (GI) fluid loss (Na⁺ poor) (vomiting, diarrhea); insensible fluid loss (panting, high ambient temperature, fever); third space loss (i.e., pancreatitis, peritonitis); cutaneous loss (e.g., burns); decreased water intake (limited access to water, primary adipsia); hyperaldosteronemia; increased salt intake (oral, intravenous); spurious (evaporation of serum sample)

Decreased in: hypoadrenocorticism; GI fluid loss (Na⁺ rich) (vomiting, diarrhea); severe liver disease; hookworms; renal failure (polyuric); nephrotic syndrome causing effusion; chronic
effusions; diuretics; hypotonic fluids; diabetes mellitus; man- 
nitol infusion; burns; excess antidiuretic hormone (ADH); diet 
(severe sodium restriction); antidiuretic drugs (e.g., vincristine, 
cyclophosphamide, NSAIDs); myxedema coma of hypothyroid-
ism; psychogenic polydipsia; spurious (hyperlipidemia, marked 
hyperproteinemia)

**Thoracocentesis Fluid**

*Pyothorax (septic)*
Extremely high nucleated cell counts (>50,000/μl), protein 
> 3.0 g/dL
Primarily degenerate neutrophils and macrophages
Bacteria seen in white blood cells (WBCs)
Penetrating wounds, foreign body (grass awns), extension of 
bacterial pneumonia or discospondylitis, postoperative 
infection

*Nonseptic*
Moderate nucleated cell counts (>5000/μl)
Neutrophils, macrophages, eosinophils, lymphocytes
Feline infectious peritonitis (FIP), neoplasia, diaphragmatic 
hernia, lung lobe torsion

*Chylous Effusion*
Low to moderate nucleated cell counts (400-10,000/μl)
Predominant cell type is small lymphocyte; also neutrophils 
and macrophages
Triglyceride concentration of pleural fluid is greater than that 
of serum.
Idiopathic
Congenital
Secondary to neoplasia, trauma, cardiac disease, fungal 
granuloma, pericardial disease, dirofilariasis, lung lobe 
torsion, diaphragmatic hernia, pericardial diaphragmatic 
hernia, vena caval thrombosis

*Hemorrhagic Effusion*
Trauma
Coagulopathy
Neoplasia
Lung lobe torsion
Rupture of vessels associated with parasitic infection (Spirocerca 
lupi, Dirofilaria immitis)

*Transudates and Modified Transudates*
Protein concentrations less than 2.5-3.0 g/dL
Low nucleated cell count (<500-1000/μL)
Macrophages, lymphocytes, mesothelial cells
Right-sided heart failure, pericardial disease, hypoalbuminemia, neoplasia, diaphragmatic hernia

*Note: Neoplastic cells may or may not be present in effusions caused by neoplastic processes.*

**Eosinophilic Effusion**

>10% of leukocytes are eosinophils.
Reported in dogs in association with heartworm disease, systemic mastocytosis, interstitial pneumonia, and disseminated eosinophilic granulomatosis

**Thrombocyte Count**

See Platelet Count.

**Thyroid Function Tests**

*Total T₄ (thyroxine, tetraiodothyronine):*
Measures free T4 and protein-bound T4.
Below-normal values suggest hypothyroidism (dogs).
Above-normal values in cats are likely caused by hyperthyroidism.
Below-normal values are also seen with underlying illness (sick, euthyroid).

*Free T₄ (FT₄):*
Below-normal values suggest hypothyroidism (dogs).
Above-normal values in cats are likely caused by hyperthyroidism.
Not as affected by the suppressive effects of concurrent illness as total T4.
Modified equilibrium dialysis assay is not affected by circulating antithyroid hormone antibodies and therefore is the preferred assay for fT4.

*Thyroid-stimulating hormone (TSH) concentration:* Must be interpreted in conjunction with serum T4 and fT4.
Low value for serum T4 and fT4 with a high TSH supports diagnosis of hypothyroidism.
Normal T4 and fT4 and normal TSH rule out hypothyroidism.

*TSH and thyroid-releasing hormone (TRH) stimulation tests:* Used to differentiate hypothyroidism from euthyroid sick syndrome.
These tests are not typically done because of availability and expense of reagents.

$T_{3}$ (3,5,3′-triiodothyronine) concentration:
Poor indicator of thyroid function in dogs and cats; not recommended.

Tests for lymphocytic thyroiditis:
Autoantibodies to circulating thyroid hormone (T4 and T3) and thyroglobulin (Tg) correlate with lymphocytic thyroiditis. Tg autoantibodies may be present when T4 and T3 are not; therefore testing for Tg autoantibodies is considered the better screening test. Provides no information about the severity of disease or the extent of thyroid gland involvement Hypothyroid dogs may be negative, and euthyroid dogs may have Tg autoantibodies. May be used as a prebreeding screening test in breeding dogs

$T_{3}$ suppression test:
Administration of T3 to normal cats should suppress pituitary TSH secretion, decreasing the serum T4 concentration. Administration of T3 to hyperthyroid cats should have no suppressive effect. Confirms hyperthyroidism in cats with occult disease

Toxoplasmosis Antibody Titer
Positive titer indicates exposure but not necessarily active infection. Positive IgM titer greater than 1:256 is consistent with active infection, especially with typical clinical signs. Fourfold rise in IgG titer of paired samples 2 to 3 weeks apart also supports active infection.

Triglycerides

Normal range:
Feline: 25-160 mg/dL
Canine: 29-291 mg/dL

Elevated in: postprandial, familial triglyceridemia (Miniature Schnauzer, other breeds); hyperchylomicronemia of cats (also observed in dogs); lipoprotein lipase deficiency (cat); endocrine disorders (hypothyroidism, hyperadrenocorticism, diabetes mellitus); nephrotic syndrome; pancreatitis; cholestasis; drugs (glucocorticoids, megestrol acetate)
**Decreased in:** not clearly associated with any disease; severe malabsorptive protein-losing enteropathy, hyperthyroidism

### Trypsinogen-Like Immunoreactivity (TLI)/Pancreatic Lipase Immunoreactivity (PLI)

**Normal range:**
- **TLI:**
  - Feline: 12.0-82.0 μg/L
  - Canine: 5.7-45.2.0 μg/L
- **PLI:**
  - Feline: 0.1-3.5 μg/L
  - Canine: 0-200 μg/L

Low TLI values (<2.5 μg/L for dogs and <8.0 μg/L for cats) are diagnostic for exocrine pancreatic insufficiency; values between 2.5 and 5.0 μg/L for dogs and 8.0 and 12.0 μg/L for cats are considered equivocal, and the assay should be repeated in 1 month.

High values for TLI are supportive of a diagnosis of acute or chronic pancreatitis.

Elevated values for PLI (>12 μg/L for cats and > 400 μg/L for dogs) are consistent with a diagnosis of pancreatitis.

Patients must be fasted at least 12 hours.

**Note:** These tests are species specific, and samples must be labeled “dog” or “cat” so that the test can be performed correctly.

### Urinalysis

**Appearance**

**Color**
- **Yellow (normal):** may be dark amber when concentrated and pale to colorless when diluted. However, color does not always correlate with concentration.
- **Red or reddish-brown:** hematuria, hemoglobinuria, myoglobinuria
- **Dark brown or black:** methemoglobinuria
- **Yellow-brown to yellow-green:** concentrated sample, bilirubinuria, Pseudomonas infection
- **Orange:** bilirubinuria

**Turbidity**
- Normally clear; cloudy urine may contain cellular material, crystals, lipid, and mucus.
Odor
Excess ammonia odor may be detectable in urine infected with urease-producing bacteria.

Specific Gravity

**Normal**
Feline: 1.025-1.060  
Canine: 1.020-1.050

**Isosthenuria (1.008-1.012)**
Renal failure  
Rare cases of polydipsia

**Hyposthenuria (<1.008)**
Polydipsia/polyuria (e.g., hyperthyroidism, hypercalcemia, hypokalemia, hepatic failure, psychogenic)  
Diabetes insipidus

Chemical Properties

**pH**

**Normal:** 5.5-7.5 (feline and canine)

*Causes of acidic urine:* meat-based diet; administration of acidifying agents (e.g., D,L-methionine, NH₄Cl); metabolic acidosis; respiratory acidosis; protein catabolic states; severe vomiting with chloride depletion

*Causes of alkaline urine:* vegetable-based diet; administration of alkalinizing agents (e.g., NaHCO₃, citrate); urinary tract infection by urease-producing bacteria; postprandial alkaline tide; metabolic alkalosis; respiratory alkalosis; renal tubular acidosis (distal tubule)

**Protein**

**Normal:** 0-30 mg/dL

Must be interpreted in light of urine specific gravity  
Commonly used dipsticks are more sensitive to albumin than globulin.

Increased with glomerular or inflammatory disease

**Glucose**

Appears in urine if the renal threshold is exceeded  
Diabetes mellitus, stress (especially in cats, infusion of dextrose-containing fluids, pheochromocytoma, proximal renal tubular diseases (aminoglycoside toxicity, acute renal failure, Fanconi syndrome, primary renal glucosuria)
Ketones
Test pad measures acetoacetate and acetone but not beta-hydroxybutyrate, which is responsible for acidosis

*Elevated in:* diabetes ketoacidosis, starvation, prolonged fasting, glycogen storage disease, low-carbohydrate diet, persistent fever, persistent hypoglycemia

Occult Blood
Does not differentiate among erythrocytes (RBCs), hemoglobin, and myoglobin
Always interpreted in light of urine sediment (evaluation for RBCs)
Erythrocytes—hematuria
Hemoglobin—hemolysis
Myoglobin—rhabdomyolysis

Bilirubin
Detectable in urine before it is elevated in serum
May be found in trace amounts in concentrated samples, especially in intact males
Bilirubinuria seen in hemolysis, liver disease, extrahepatic obstruction, fever, starvation

Urobilinogen
Presence indicates normal enterohepatic bilirubin circulation.

**Urinary Sediment Examination**

Red Blood Cells (RBCs)
Normally, zero to occasional RBCs; excessive RBCs termed *hematuria* (see p. 34)

White Blood Cells (WBCs)
Normally, zero to occasional WBCs
Excessive WBCs termed *pyuria*; indicates urinary tract infection but does not localize the site of infection

Epithelial Cells
Squamous and transitional cells, little diagnostic significance
Increased transitional cells may be seen with infection, neoplasia, and irritation of the urinary tract.

Casts
Cylindrical molds of renal tubules composed of aggregated proteins or cells that localize disease to the kidney
Occasional hyaline or granular cast may be normal; cellular casts are always abnormal.
Hyaline casts: protein precipitates (Tamm-Horsfall mucoprotein and albumin); seen with proteinuric renal disease (glomerulonephritis, amyloidosis), small numbers with fever and exercise

Granular casts: degeneration of cells in casts or precipitation of filtered plasma proteins; suggest ischemic or nephrotoxic renal tubular injury

Cellular casts: WBC casts (pyelonephritis), RBC casts (fragile, rare in dogs and cats), renal epithelial cell casts (acute tubular necrosis or pyelonephritis)

Fatty casts: lipid granules (nephrotic syndrome or diabetes mellitus)

Waxy casts: final stage of degeneration of granular casts (suggest intrarenal stasis)

Organisms: Small numbers of bacteria may contaminate voided or catheterized samples but usually not enough to be seen in urine sediment unless sample is allowed to incubate. Presence of large numbers of bacteria in sediment suggests urinary tract infection. Yeast and fungal hyphae usually are contaminants.

Crystals
Usually of little diagnostic value; typically found in normal urine
Acidic urine may contain urate, calcium oxalate, and cystine crystals.
Alkaline urine may contain struvite, calcium phosphate, calcium carbonate, amorphous phosphate, and ammonium biurate crystals.
Bilirubin crystals may be seen with concentrated samples or with bilirubinuria.
Urate crystals may be seen in Dalmatians and with liver disease or portosystemic shunts.
Struvite crystals are seen in cats with idiopathic lower urinary tract disease, dogs, and cats with struvite urolithiasis.
Calcium oxalate in oliguric acute renal failure (ARF) suggests ethylene glycol intoxication.
Cystine crystals, when abnormal, suggest cystinuria.

Other Findings in Sediment
Sperm in intact male dogs
Parasite ova; Dioctophyma renale, Capillaria plica
Microfilariae
Lipid droplets (diabetes mellitus, nephrotic syndrome, in cats with degeneration of lipid-laden tubular cells)
Common Bacteria Seen in Urinary Tract Infections
Escherichia coli
Proteus spp.
Staphylococcus spp.
Pasteurella multocida
Enterobacter spp.
Klebsiella spp.
Pseudomonas aeruginosa

Urine Cortisol/Creatinine Ratio
Very sensitive, but not very specific test for hyperadrenocorticism
Good test to rule out hyperadrenocorticism but not to diagnose

Urine Protein/Creatinine Ratio
More accurate than dipstick protein estimation
Normal values: dogs less than 0.3, cats less than 0.6

von Willebrand Factor
Variable degrees of expression of factor for von Willebrand disease (vWD), a common, inherited hemostatic disorder (rare in cats)
Dogs with levels less than 30% are prone to spontaneous bleeding (e.g., epistaxis).
Classification of vWD in dogs:
Type I: low concentration of normal von Willebrand factor
Type II: low-normal concentration of abnormal von Willebrand factor
Type III: absence of von Willebrand factor
Hemostatic screening tests usually are normal in dogs with vWD. Buccal mucosal bleeding time is the exception—best screening test.

White Blood Cell (WBC) Count
Normal range:
Feline: 3.5-16.0 10^3/μL
Canine: 4.0-15.5 10^3/μL
Elevated in: infection (bacterial, systemic mycoses); physiologic leucocytosis; metabolic (stress, glucocorticoids); inflammation (immune-mediated disease, neoplasia, tissue trauma, tissue necrosis); leukemia, associated with responsive anemia (hemorrhagic anemia, hemolytic anemia)
Decreased in: decreased production, increased consumption, neutropenia secondary to phenobarbital administration
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