

Zoetis Diagnostics

Chemistry Differential Diagnoses

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LOOK DEEPER

zoetis

Virtual Lab

Anywhere. Anytime. Any device.

The Zoetis Virtual Laboratory is the next evolution in the connected veterinary practice. With access to Responsible Trending™, Vetscan Imagyst results, and clinical consultations, the Virtual Laboratory allows for efficient medical decisions and access to specialists.

Access results on any device with ZoetisDx

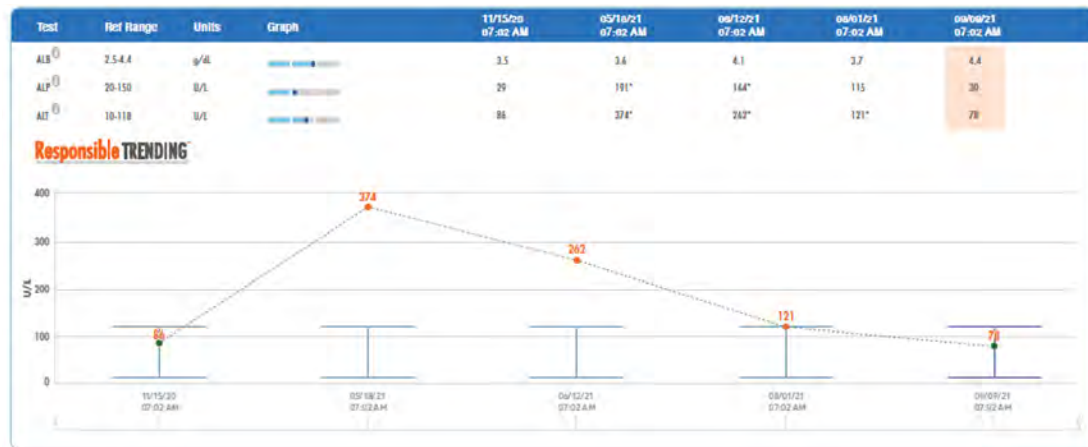
- View and share patient results
- Drive informative discussions
- Improve pet owner/veterinarian communication

Integrate results with your practice management software*

- Analyze Zoetis diagnostic information from multiple sources in a single glance
- Review easy-to-interpret graphics and Responsible Trending data
- Access patient information before appointments and surgeries

What is Responsible Trending?

Responsible Trending, available on the ZoetisDx online platform, focuses on showing test analyte results as a sequence of graphs. This visual format provides a clear story of each patient's trends in test results over time with results from different instruments and Zoetis Reference Laboratories together, but always relative to each analyte's reference interval on each instrument.



Head to ZoetisDx.com to Book a Clinical Consultation:

Request a Specialist Consult.

Choose when, where, and how:



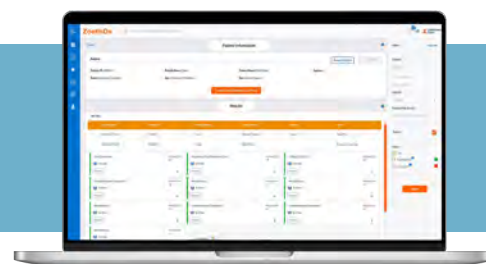
ZOOM VIDEO



ZOOM AUDIO



EMAIL



Common Examples of a Clinical Consultation:

- Internal medicine advice on managing subclinical UTIs
- Current treatment protocols for IMHA
- Oncology advice on treatment and prognosis for various neoplasias
- Dermatology advice for chronic pyoderma

*Compatible with select PIMS

For Zoetis DX application

This guide is intended to aid in interpretation of results for biochemical parameters. No differential list is meant to be exhaustive and examining only one parameter at a time could result in an erroneous diagnosis. When abnormalities are detected or suspected clinically, a Complete Blood Count (CBC), urinalysis, and additional diagnostic testing may be warranted to aid in interpretation and case management.

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Alanine Aminotransferase (ALT)

Increased

Hepatocellular Injury

Degenerative

- **Anoxia due to anemia/shock/passive congestion^{1,2}**

Anomalous

- Portosystemic shunt (generally mild increase)¹

Inflammatory

- **Infectious: leptospirosis, histoplasmosis, FIP, bacterial cholangiohepatitis^{1,2}, canine adenovirus, leishmania, toxoplasma, neospora, hepatozoon, dirofilariosis**
- **Non-infectious: chronic hepatitis, cholangitis, cirrhosis**

Inherited

- Copper storage disease
- Lysosomal storage diseases¹

Toxic (Not an exhaustive list)

- Acetaminophen (especially cats)
- Barbiturates
- Carprofen
- Glucocorticoids (dogs only)
- Phenobarbital
- Primidone
- Trimethoprim-sulfa drug
- Xylitol

Metabolic

- **Hepatic lipidosis**
- **Diabetes mellitus**
- **Feline hyperthyroidism**
- **Hyperadrenocorticism^{1,2}**

Neoplastic

- Lymphoma
- Hepatocellular carcinoma
- Metastatic neoplasia^{1,2}

Nutritional

- Copper toxicosis
- Hemochromatosis¹

Traumatic

- Hit by car (hepatocellular or skeletal muscle damage)¹

Skeletal Muscle Injury

Inherited

- Muscular dystrophy (rare)

Miscellaneous

- Hit by car/other sources of muscle injury
- Myositis

Artifacts

- Hemolysis can cause mild increase³
- Lipemia can cause artifactual increase³

Decreased

- Not clinically significant
- Can occur with hepatic atrophy due to portosystemic shunt, chronic liver failure, or cirrhosis.

Interpret With

- Bilirubin
- Hepatic enzymes
- Creatine kinase

Bold Indicates a common cause



Albumin (ALB)

Increased

Hemoconcentration

- Fluid losses/dehydration

Decreased

Decreased Albumin Synthesis

- Inflammation⁴
- Hepatic insufficiency (chronic hepatic disease)^{4,5}
- Malabsorption and maldigestion⁴
- Cachectic/catabolic state⁴
- Hypergammaglobulinemia⁴

Increased Albumin Loss

- Blood loss (hemorrhage)^{4,5}

- Protein-losing nephropathy^{4,5}

- Glomerulonephritis
- Amyloidosis

- Protein-losing enteropathy^{4,5}

- Small intestinal mucosal disease
- Lymphangiectasia
- Intestinal blood loss

- Cutaneous losses (burns/exudative skin disease)

Sequestration⁴

- Third space losses (pleural/peritoneal effusion)

Hemodilution

- Excess administration of Intravenous fluid^{4,5}
- Edematous disorders⁴
 - Congestive heart failure
 - Cirrhosis
 - Nephrotic syndrome

Artifacts

- High fibrinogen levels in heparinized plasma samples used with a BCG method may cause false increases⁸
- Hemolysis or hemoglobinemia can cause false increases
- Marked lipemia or hypertriglyceridemia can cause false decreases
- Severe hypoalbuminemia can cause a falsely elevated albumin concentration (rare)⁹

Interpret With

- Total protein
- Globulins
- Blood urea nitrogen
- Creatinine
- Liver panel +/- bile acids
- Packed cell volume
- Urinalysis

Bold Indicates a common cause



Alkaline Phosphatase (ALP)

Increased

Most Common Causes

Physiologic

- Age (young dogs with rapid bone growth)
- Endogenous corticosteroid release¹
- Ingestion and absorption of colostrum by neonatal foals and pups may increase serum ALP activity¹

Degenerative

- Hepatocyte swelling or necrosis (leads to impaired bile flow)¹

Metabolic

- Diabetes mellitus
- Hyperadrenocorticism
- Hypothyroidism (dogs) mild
- Hyperthyroidism (cats)
- Hyperparathyroidism (primary or secondary)
- Hepatic lipidosis¹ (in the initial phase of feline hepatic lipidosis, ALP activity will be markedly increased with little to no increase in GGT activity)

Cholelithiasis

Inflammatory

- Periportal hepatitis
- Chronic hepatitis
- Cholangiohepatitis/cholangitis
- Feline infectious peritonitis
- Cirrhosis/fibrosis
- Pancreatitis (local inflammation)²

Neoplastic

- Lymphoma
- Hemangiosarcoma
- Mammary neoplasia (benign and malignant)
- Hepatocellular carcinoma
- Metastatic carcinoma¹

Induction by Drugs or Hormones

(Not an Exhaustive List)

- Barbiturates
- Estrogens (urinary incontinence medication)
- Glucocorticoids (dogs only)
- Phenobarbital
- Primidone

Cardiogenic

- Chronic passive congestion from right heart failure²

Other Causes

Physiologic

- Breed (Siberian Huskies – benign familial hyperphosphatasemia; Scottish Terriers)^{10, 11}

Biliary Tract Disease

- Bile duct neoplasia
- Cholecystitis
- Gall bladder mucocele
- Ruptured gallbladder
- Pancreatic neoplasia^{1, 2}

Inflammatory

- Copper storage disease
- Toxic hepatitis
- Aflatoxin
- Certain types of mushrooms
- Sago palm
- Drug induced¹

Induction by Drugs or Hormones

(Not an Exhaustive List)

- Anabolic steroids/androgens
- Asparaginase
- Azathioprine
- Cephalosporins
- Cyclophosphamide
- Dapsone
- Erythromycin estolate
- Griseofulvin
- 6-Mercaptopurine
- Methimazole
- Methotrexate
- Nitrofurantoin
- Phenothiazines
- Progesterone
- Testosterone
- Tetracyclines
- Thiabendazole
- Trimethoprim-sulfa
- Vitamin A

Decreased

- Not clinically significant

Artifacts

- Severe hemolysis may falsely decrease ALP²

Interpret With

- Hepatic enzymes
- Cholestatic markers

Bold Indicates a common cause



Amylase (AMY)

Increased

Pancreatic Acinar Cell Damage

- **Inflammation (AMY and LIP)^{1,2}**
- **Neoplasia (AMY and LIP)**

Decreased Renal Clearance/Renal Disorder

- **Dehydration^{1,2}**
- **Acute or chronic renal diseases (AMY and LIP)¹**
- Shock (AMY and LIP)^{1,2}
- **Urinary tract obstruction (AMY and LIP)**
- Macroamylasemia¹

Miscellaneous Causes

- Gastrointestinal obstruction (AMY and LIP)
- Dexamethasone treatment
- Pancreatic or hepatic neoplasia

Decreased

- Not clinically significant

Artifacts

- Can be artifactually decreased due to Vitamin C

Interpret With

- Pancreatitis specific markers (i.e., canine pancreas-specific lipase)
- Blood urea nitrogen
- Creatinine
- Hepatic enzymes
- Bilirubin
- Urinalysis
- Lipase

Bold Indicates a common cause



Anion Gap

Increased

Metabolic Acidosis

- **Lactic acidosis: increased lactate or D-lactate**
- **Ketoacidosis: increased ketone bodies (BHB or AcAc)**
- **Renal failure: increased PO_4 , sulfate, or citrate**
- Massive rhabdomyolysis: possibly associated with increased lactate or PO_4
- Drugs/toxins
 - Ethylene glycol
 - Methanol poisoning
 - Paraldehyde
 - Metaldehyde poisoning (snail bait)
 - Penicillin
- Hyperalbuminemia

Decreased (Minimal Clinical Significance)

Decreases in Unmeasured Anions-

- **Hypoalbuminemia**
- Acidemia

Increases in Unmeasured Cations+

- Hypercalcemia
- Hypermagnesemia

Iatrogenic

- Bicarbonate-rich fluids

Artifacts

- Increased Na^+ and K^+ , decreased Cl^- can lead to false increases
- Increased Cl^- and HCO_3^- can lead to false decreases
- Potassium bromide can lead to false increases

Interpret With

- Electrolytes
- Bicarbonate
- Blood-gas values/acid-base status

Bold Indicates a common cause



Aspartate Aminotransferase (AST)

Increased

Hepatic Damage

- See hepatocyte damage conditions listed for increased alanine aminotransferase (ALT) activity^{1,2}

Muscular

- See skeletal muscle damage condition listed for increased creatine kinase (CK) activity^{1,2}

Decreased

- Not clinically significant

Artifacts

- Hemolysis will increase AST serum activity¹⁹
- Icterus may affect results
- Marked lipemia may interfere with spectrophotometric assays¹⁹
- Metronidazole may artifactually depress AST activity¹⁹

Interpret With

- Alanine aminotransferase
- Alkaline phosphatase
- Total bilirubin
- Gamma-glutamyl transferase
- Bile acids
- Creatine kinase

Bold Indicates a common cause



Base Excess

Increased

Excess of base (gain of HCO_3^- or loss of acid)

- Metabolic alkalosis
- Refer to bicarbonate (HCO_3^-) and TCO_2 for additional differentials

Decreased

Insufficient Base

- Metabolic acidosis
- Refer to bicarbonate (HCO_3^-) and TCO_2 for additional differentials

Artifacts

- Exposure to room air can cause a false increase

Interpret With

- Electrolytes
- Bicarbonate
- Anion gap
- Proteins
- Renal function values

Bold Indicates a common cause



Bicarbonate (HCO_3^-)

Increased

Metabolic Alkalosis

Loss of H^+

- **Gastric loss**
- Renal loss
 - Loop or thiazide diuretics
 - Secondary to respiratory acidosis
- **Hypokalemia**
- Sweat loss

Iatrogenic

- Administration of bicarbonate solutions, lactate, citrate, or magnesium hydroxide

Decreased

Metabolic Acidosis

Generation of H^+

- **Lactic acidosis**
- **Ketoacidosis**
- **Toxins: ethylene glycol**

Decreased renal excretion of H^+

- Renal failure
- Uroperitoneum or urinary tract obstruction

Increased HCO_3^- loss

- Alimentary losses: diarrhea, sequestration, vomiting (pancreatic secretions)

- Renal losses: proximal or distal renal tubular acidosis

Other Causes

- Hypoadosteronism

Artifacts

- Severe muscle injury can cause false elevation
- Aged samples can lead to false increases or decreases
- Over dilution of heparin and prolonged venous stasis can cause false decrease
- Lipemia, hemolysis, and icterus can cause false decrease
- Dilutional acidosis (with saline) can decrease

Interpret With

- Electrolytes
- Anion gap
- Renal values
- Blood gas/acid-base status

Bold Indicates a common cause



Bile Acids (BA)

Increased

Most Common Causes

Physiologic

- Spontaneous gallbladder contraction (without feeding)²

Decreased Functional Hepatic Mass

- Diffuse hepatocellular disease²²

Decreased Portal Blood Flow to Liver

- Congenital and acquired portosystemic shunts²²
- Hepatic microvascular dysplasia²

Hepatic Cholestasis (Obstructive)

- Cirrhosis
- Cholangitis/Cholangiohepatitis
- Periportal hepatitis

Post-Hepatic Cholestasis

- Cholangitis
- Bile duct carcinoma
- Liver fluke
- Cholelithiasis
- Cholecystitis
- Pancreatitis
- Pancreatic carcinoma²²

Other Causes

Hepatic Cholestasis (Obstructive)

- Hepatic lipidosis
- Diabetes mellitus
- Steroid hepatopathy
- Lymphoma
- Histoplasmosis
- Cytauxzoonosis
- Pyrrolizidine alkaloid toxicosis²²

Functional Cholestasis

- Sepsis-associated cholestasis²²

Decreased

- Low clinical significance

Artifacts

Decreased BA value-

- Hemolysis²³
- Heparin BA²³
- Lipid-clearing agents²³
- Incomplete gallbladder contraction after feeding may result in a lower value than expected²

Increased BA Value

- Lipemia (spectrophotometry)²³
- Treatment with ursodiol (a synthetic BA)²³

Interpret With

- Pancreatic specific markers (canine or feline pancreas-specific lipase)
- Hepatic enzymes
- Cholestatic markers
- Bilirubin
- Ammonia

Bold Indicates a common cause



Blood Urea Nitrogen (BUN)

Increased

Most Common Causes

Pre-Renal Conditions

- Hypovolemia/dehydration
- Decreased cardiac output
- Shock

Renal Conditions

- Inflammatory
 - Glomerulonephritis
 - Pyelonephritis (e.g., ascending UTI, leptospirosis)
- Toxic nephrosis
 - Hypercalcemia
 - Ethylene glycol intoxication
 - NSAID intoxication²⁴
 - Lily toxicity
 - Gentamicin

- Renal ischemia or hypoxia

- Poor renal perfusion
- Infarction²⁴

Post-Renal Conditions

- Urinary tract obstruction
 - Urolithiasis
 - Urethral plugs in cats
 - Neoplasia
 - Uroabdomen^{24, 25}
 - Prostatic disease
- Urine leakage
 - Trauma
 - Neoplasia

Increased Production

- Hemorrhage into the upper gastrointestinal system
- High protein diet

Other Causes

Renal Conditions

- Inflammatory
 - Tubular-interstitial nephritis^{24, 25}
- Amyloidosis
- Toxic nephrosis
 - Myoglobin
- Renal ischemia or hypoxia
- Congenital hypoplasia or aplasia²⁴
- Hydronephrosis
- Neoplasia (renal or metastatic)^{24, 25}

Increased Production

- Exercise

Decreased

Most Common Causes

Decreased BUN Synthesis

- Hepatocellular disease
- Portosystemic shunts (congenital or acquired)

Other Causes

Decreased BUN Synthesis

- Dietary restriction of protein
- Urea cycle enzyme deficiencies^{24, 25}

Increased Renal Excretion of Urea

- Impaired proximal tubular resorption of urea: glucosuria²⁴
- Central or nephrogenic diabetes insipidus (polyuria/polydipsia)²⁴

Artifacts

- Severe hemolysis will increase BUN concentration^{24, 26}
- Severe icterus may increase BUN concentrations²⁴
- Severe lipemia may decrease BUN concentrations
- Contamination of the sample with ammonium (NH₄)^{24, 26} (e.g., benzalkonium chloride disinfectants) can increase BUN results obtained by reflectance spectrophotometry

Interpret With

- Creatinine
- Total protein
- Albumin
- Electrolytes
- Anion gap
- Calcium
- Phosphate
- Hepatic function tests
- Hematology
- Urinalysis

Bold Indicates a common cause



Total Calcium (CA)

Increased

Most Common Causes

Physiologic

- Healthy young, fast-growing dogs (young dog < 6 months, large or giant breed)^{27, 28}

Increased PTH or PTHrp Activity

- Primary hyperparathyroidism (PTH)
 - Parathyroid neoplasia²⁷
- Hypercalcemia of Malignancy / Humoral Hypercalcemia (PTHrp)
 - Lymphoma
 - Apocrine gland adenocarcinoma^{27, 28}
 - Other carcinoma
 - Multiple myeloma

Increased Vitamin D

Activity (Hypervitaminosis D)

- Exogenous Vitamin D
 - Rodenticides containing cholecalciferol
- Endogenous Vitamin D
 - Granulomatous inflammation
 - Some fungal and parasitic infections

Decreased Urinary Excretion of Calcium

- Renal failure^{27, 28}
- Hypoadrenocorticism
- Idiopathic hypercalcemia in cats³²

Other or Unknown Mechanisms

Other Causes

Increased Vitamin D

Activity (Hypervitaminosis D)

- Exogenous Vitamin D
 - Tacalcitol or calcipocriol
 - Plants containing ergocalciferol (Vitamin D₂)
 - Excess dietary supplementation^{27, 28}

Increased Protein-Bound Calcium

- Hyperglobulinemia in multiple myeloma
- Hyperalbuminemia²⁷

Iatrogenic Disorders

- Excessive calcium supplementation (Intravenous)²⁷
- Excessive oral phosphate buffers²⁷
- Calcipotriene²⁸ (psoriasis treatment)

Decreased

Most Common Causes

Hypoalbuminemia

- Hypoproteinemia^{27, 28}

Pregnancy, Parturient, or

Lactational Hypocalcemia

- Eclampsia^{27, 28}
- Milk fever in cattle

Excess Urinary Excretion of Calcium

- Ethylene glycol toxicosis (dogs and cats)

Other or Unknown Mechanisms

- Acute pancreatitis in dogs and cats
- Urinary tract obstruction

Other Causes

Primary Hypoparathyroidism

- Naturally acquired

- Post-thyroidectomy²⁷

Hypovitaminosis D

- Chronic renal disease or failure
- Protein-losing enteropathy in dogs
- Dietary vitamin D deficiency (rare)^{27, 28}

Pregnancy, Parturient, or

Lactational Hypocalcemia

- Postpartum/periparturient hypocalcemia/puerperal tetany

Hypercalcitonism

- Thyroid C-cell neoplasia
- Iatrogenic (calcitonin therapy)²⁷

Excess Urinary Excretion of Calcium

- Intravenous HCO₃ infusions
- Furosemide treatment²⁷

Calcium Binding Anticoagulants

- EDTA, citrate, oxalate (in vivo or in vitro)²⁷

Other or Unknown Mechanisms

- Exocrine pancreatic insufficiency (dogs)^{27, 28}
- Vitamin D-receptor defect rickets²⁷
- Oxalate toxicity²⁸
- Tetracycline administration²⁷
- Calcium deposition during fracture healing
- Acute and chronic renal failure
- Phosphate enema
- Sepsis
- Acute tumor lysis syndrome
- Nutritional secondary hyperparathyroidism^{27, 28}

Artifacts

- Total Ca is falsely increased by lipemia and hemolysis³³
- Total Ca can be decreased by marked bilirubinemia³³
- Prolonged occlusion during phlebotomy may mildly increase Ca³³
- Use of an inappropriate anticoagulant (EDTA, citrate anticoagulants) may cause falsely decreased results³³

Bold Indicates a common cause



Calcium (CA), Continued

Interpret With

- Albumin
- Ionized calcium
- Phosphate
- Blood urea nitrogen
- Creatinine
- Urinalysis

Note: Frequency of hypercalcemia due to listed neoplastic processes may differ by species and/or breed.

Bold Indicates a common cause



Chloride (CL)

Increased

Most Common Causes

Inadequate Water Intake

- Water deprivation

Water Loss

- Pure water loss
 - Insensible loss: panting, hyperventilation, or fever

Alimentary Loss of Bicarbonate

- Bicarbonate loss/small bowel diarrhea
- GI loss/sequestration (diarrhea)

Hyperchloremic Metabolic Acidosis

- GI loss of bicarbonate
- Renal loss of bicarbonate
 - Proximal or distal renal tubular acidosis

Other Causes

Inadequate Water Intake

- Defective thirst response (hypothalamic defect)

Water Loss

- Pure water loss
 - Diabetes insipidus
- Renal
 - Osmotic diuresis
 - Hypoadrenocorticism
- Phosphate enema³⁴

Excessive Gain of Chloride Relative to Sodium

- Salt poisoning
- Diabetes mellitus
- Fluid therapy (e.g., 0.9% sodium chloride, hypertonic saline, potassium chloride-supplemented fluids)
- Therapy with chloride salts: KCl or NH₄Cl³⁵

Decreased Renal Excretion of Na and Cl

- Hyperaldosteronism³⁴

Renal Chloride Retention

- Proximal renal tubular acidosis
- Distal renal tubular acidosis

- Hypoadrenocorticism³⁶
- Drug-induced: acetazolamide, spironolactone³⁶
- Compensatory response to chronic respiratory alkalosis
 - Hyperventilation or hypocapnia
 - Hypoxemia
 - Primary pulmonary disease
 - Pain³⁵

Bicarbonate Consumption (Titration Acidosis)

- Decreased excretion of non-carbonic acid:
 - Sulfates
 - Phosphates
- **Renal Failure**
- **Toxicity (Ethylene glycol, Salicylate, Methanol)**³⁵

Decreased

Most Common Causes

Gastrointestinal

- Loss or sequestration of chloride rich fluid
 - Vomiting/diarrhea
 - Sequestration
 - Pyloric obstruction
 - Gastric rupture
 - Gastric dilation-volvulus
 - Trichuriasis

Metabolic Acidosis

- Ketoacidosis
- Lactic acidosis
- Ingestion of foreign substances generating strong anions (ethylene glycol)

Other Causes

Renal Loss

- Hypoadrenocorticism
- Osmotic diuresis (diabetes mellitus)
- Proximal renal tubular dysfunction (prolonged diuresis)
- Hypoaldosteronism
- Hyperadrenocorticism³⁶
- Glucocorticoid administration³⁶

- Ketonuria
- Sodium-wasting nephropathies
- Compensatory response to chronic respiratory acidosis
- Furosemide therapy
- Thiazide therapy

Third Space Losses

- Pancreatitis
- Peritonitis
- Uroabdomen
- Chylothorax with repeated pleural fluid drainage³⁵
- Acute internal hemorrhage
- Acute exudation
- Cutaneous (sweating)

Edematous Disorders

- Congestive heart failure
- Hepatic disease/hepatic cirrhosis
- Nephrotic syndrome
- Advanced renal failure³⁴

Expanded Extracellular Fluid Volume (Without Edema)

- Excess sodium-poor fluid administration (parenteral)³⁴

- Fluid therapy with 5% dextrose, 0.45% saline solution, or hypotonic fluids³⁵
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- Antidiuretic drugs (e.g., heparin solutions containing chlorbutanol, vincristine, cyclophosphamide, nonsteroidal anti-inflammatory drugs)³⁵
- Myxedema coma of hypothyroidism (rare)³⁵
- Psychogenic polydipsia³⁵

Extracellular Translocation of Water

- Hyperglycemia
- Mannitol infusion (intravenously)³⁴

Intracellular Translocation of Na (Cl Follows)

- Hypokalemia (to maintain the intracellular electronegativity)
- Acute muscle injury³⁴

Extravascular Fluid Translocation of Na (Cl Follows)

- Uroperitoneum (ruptured bladder, or abdominal urethra)³⁴

Bold Indicates a common cause



Chloride (CL), Continued

Artifacts

- Lipemia causing pseudo-hypochloremia (ion-exclusion effect when using the titrimetric methods) or causing pseudo-hyperchloremia (using the colorimetric method)³⁵
- Potassium bromide therapy will falsely increase the reported chloride concentration (common and important)³⁵
- Hyperviscosity may cause problems in analyzers that dilute samples before analysis³⁵

Interpret With

- Electrolytes (Na⁺, K⁺)
- Urinalysis
- Total carbon dioxide/bicarbonate
- Anion gap
- Acid-base analysis

Bold Indicates a common cause



Cholesterol (CHOL)

Increased

Most Common Causes

Postprandial Hypercholesterolemia^{28, 37, 40}

Secondary Hypercholesterolemia

- Hypothyroidism
- Diabetes mellitus^{37, 40}
- Nephrotic syndrome or protein-losing nephropathy^{28, 37, 40}
- Cholestasis^{37, 40}
- Acute pancreatitis^{38, 40}
- Hyperadrenocorticism or excess iatrogenic glucocorticoids

Other Causes

Primary Hypercholesterolemia

- Idiopathic hyperlipoproteinemia (Miniature Schnauzers and other breeds)^{28, 37, 40}
- Hypercholesterolemia in Briards (dog)⁴⁰
- Idiopathic hyper-chylomicronemia (cat)²⁸
- Lipoprotein lipase deficiency (cat)^{28, 37, 40}
- Idiopathic hypercholesterolemia^{28, 37}

Secondary Hypercholesterolemia

- Hepatic insufficiency²⁸

- Excess negative energy balance
 - Starvation/anorexia
 - Pregnancy or lactation

Drug Induced Hypercholesterolemia

- Megestrol acetate (cat)²⁸
- Glucocorticoids²⁸

Decreased

Most Common Causes

Severe Malnutrition⁴⁰

Malabsorption/Maldigestion

- Protein-losing enteropathy²⁸
- Lymphangiectasia⁴⁰
- Exocrine pancreatic insufficiency⁴⁰

Decreased Cholesterol Production

- Portosystemic shunt
- Chronic liver disease³⁷
- Liver failure⁴⁰

Altered Metabolism

- Inflammatory cytokines³⁷

Increased Lipoprotein Uptake

- Rapidly proliferating neoplastic cells (histiocytic sarcoma, multiple myeloma)^{38, 39}

Other Causes

- Hypoadrenocorticism⁴⁰

Artifacts

- Hemolysis and hyperproteinemia artifactually increase results⁴⁰
- Bilirubin and ascorbic acid negatively interfere with enzymatic assays⁴⁰
- Postprandial cholesterol increase may be mistaken for metabolic disease⁴⁰

Interpret With

- Glucose
- Blood urea nitrogen
- Creatinine
- Hepatic enzymes
- Bilirubin
- Triglycerides
- Urinalysis

Bold Indicates a common cause



Increased

Hepatocellular injury or necrosis

Endocrine

Neoplastic disorders

Decreased

Preabsorptive defect in dogs and cats

- **EPI: pancreatic atrophy, chronic pancreatitis**
- **Intestinal bacterial overgrowth: EPI, impaired gastric acid secretion, enteric disorders**

Defective absorption of cobalamin in ileum of dogs and cats

- **Ileal disease: inflammation, resection, villous atrophy (viral atrophy, hypersensitivity, cytotoxic drugs)**
- Congenital deficiency of receptor in Giant Schnauzers and Border Collies

Severe cobalamin deficiency in cats (probable congenital malabsorption defect)

Cobalt deficiency in cattle

Artifacts

- Can be increased with oral or parenteral cobalamin supplementation

Interpret With

- Folate
- Pancreatic lipase
- TLI
- Hepatic enzymes
- Glucose

Bold Indicates a common cause



Creatine Kinase (CK)

Increased

Most Common Causes

Skeletal Muscle Damage

Degenerative

- Hypoxia caused by exertion or seizures, exertional Rhabdomyolysis, saddle thrombus^{1, 43}

Traumatic

- Intramuscular injections
- Hit by car
- Prolonged recumbency
- Seizures
- Exertion
- Post-surgical¹

Other Causes

Neoplastic

- Metastatic neoplasia with striated muscle involvement

Nutritional

- White muscle disease (vitamin E-selenium deficiency), polioencephalomalacia^{1, 43}

Inflammatory

- Myositis caused by Neospora, Toxoplasma, bacteria, or other agents¹

Toxic

- Monensin, ricin (Castor Bean), mycotoxin, gossypol, snakebite¹

Inherited

- Muscular dystrophy (Cavalier King Charles Spaniel dystrophin-deficient muscular dystrophy)
- Hyperkalemic periodic paralysis
- Malignant hyperthermia¹

Other Pathologies with Uncertain Pathogeneses

- Critically ill anorectic cat⁴⁴

Decreased

- Not clinically significant

Artifacts

- May increase the measured CK activity
 - Hemolysis^{1, 43}
 - Muscle penetration during venipuncture¹
 - Underfilling of lithium heparin tube⁴⁵

Bold Indicates a common cause



Creatinine (CRE)

Increased

Most Common Causes

Pre-Renal Conditions

- Hypovolemia/dehydration
 - Hypoadrenocorticism
 - Blood loss
- Decreased cardiac output
 - Cardiac insufficiency
 - Shock
 - Hypoadrenocorticism
- Shock
 - Hypovolemic
 - Cardiogenic
 - Anaphylactic
 - Septic
 - Neurogenic¹

Renal Conditions

- Inflammatory
 - Glomerulonephritis
 - Pyelonephritis

- Toxic nephrosis
 - Hypercalcemia
 - Ethylene glycol intoxication
 - NSAID intoxication
- Renal ischemia or hypoxia
 - Poor renal perfusion
 - Infarction

Post-Renal Conditions

- Urolithiasis
- Urethral plugs in cats
- Leakage of urine from the urinary tract within the abdominal cavity: trauma, neoplasia^{1, 25}

Physiologic Increase

- Heavily muscled dogs (Greyhounds) or other heavily muscled animals¹

Other Causes

Renal Conditions

- Inflammatory
 - Tubular-interstitial nephritis
 - Amyloidosis
- Toxic nephrosis
 - Myoglobin
 - Aminoglycosides
- Renal ischemia or hypoxia
- Congenital hypoplasia or aplasia
- Hydronephrosis
- Neoplasia (renal or metastatic)^{1, 25}

Post-Renal Conditions

- Neoplasia
- Prostatic disease

Physiologic Increase

- Post-protein meal¹

Decreased

Not a clinically significant finding

Most Common Causes

Physiologic

- Young dogs⁴⁶
- Small breed dog⁴⁷
- Decreased muscle mass^{1, 25}

Other Causes

Decreased Production

- Starvation
- Cachexia
- Hepatic insufficiency: hepatocellular disease
- Portosystemic shunts (congenital or acquired)⁴⁸

Artifacts

- Presence of acetoacetate, glucose, Vitamin C, uric acid, pyruvate, cephalosporins, and amino acids in the sample¹
- Lidocaine: increases values (dry chemistries)⁴⁹
- Nitrofurantoin: increases values (Jaffe reaction)⁴⁹
- Cefoxitin: increases values (Jaffe reaction)⁴⁹
- Dobutamine: decreases values⁴⁹
- Proline from hyperalimentation fluids increases values⁴⁹

Interpret With

- Blood urea Nitrogen
- Hepatic enzyme activity
- Creatine kinase
- Lactate dehydrogenase
- Urinalysis

Bold Indicates a common cause



DGGR Lipase

Increased

- Acute pancreatitis
- Gastrointestinal disease
- Hepatic disease
- Azotemia
- Hyperadrenocorticism

Decreased

- Not clinically significant

Artifacts

- Hemolysis can lead to false decreases
- Lipemia causes false increases
- Glucocorticoids cause false increases

Interpret With

- cPL
- Folate
- Cobalamin
- TLI

Bold Indicates a common cause



Increased

Increased production by thyroid neoplasia

- **Thyroid adenoma** (common in cats, not dogs, rare in horses)
- **Thyroid adenocarcinoma** (dogs, cats, horses)
- Multiple endocrine neoplasia (type II)

Administration of T4, TSH, or TRH

Administration of compounds containing iodide

Decreased

Most Common Causes

Decreased production of T4

- **Primary hypothyroidism**
 - **Lymphocytic thyroiditis**
 - **Idiopathic thyroid atrophy**
 - **Congenital thyroid gland dysgenesis**
 - **Destruction of thyroid tissue**
 - **Neoplasia**
 - **Surgery**
 - **Radioactive iodide**

Multifactorial or unknown mechanisms

- **Nonthyroidal disease:**
hyperadrenocorticism,
inflammatory diseases

- **Drugs: glucocorticoids, trimethoprim-sulfadiazine, trimethoprim-sulfamethoxazole, phenobarbital, phenylbutazone, clomipramine**

Other Causes

Decreased production of T4

- Secondary hypothyroidism
 - TSH deficiency caused by pituitary malformation or destruction by neoplasia, radiation, or other
- Defective thyroxine production
 - Iodine organification defect

- Congenital thyroid peroxidase deficiency in Toy Fox Terriers
- Iodine deficiency

Multifactorial or unknown mechanisms

- Diets high in energy, protein, copper, zinc, endophyte-infected fescue grass (horse)
- Food deprivation for 4 days (horses)
- Diet high *Leucaena leucocephala* (cattle)

Artifacts

- Thyroxine autoantibodies (T4AA) can interfere with some fT4 assays

Interpret With

- tT4
- TSH
- Hepatic enzymes

Bold Indicates a common cause



Fructosamine

Increased

Increased fructosamine concentration and increased glycated hemoglobin percentage or concentration

- **Diabetes mellitus/persistent hyperglycemia**
- Insulin overdose (Somogyi rebound)
- **Hypothyroidism**

Decreased

- Insulinoma
- Hyperlipidemia
- Hypoproteinemia
- **Anemia**
- **Azotemia**
- Hyperthyroidism

Artifacts

- Hemolysis will artificially increase levels (some methodologies)
- Drugs: Lexodopa and oxytetracycline increase levels

Interpret With

- Glucose
- Proteins
- CBC
- Hepatic enzymes
- Insulin levels
- Urinalysis

Bold Indicates a common cause



Gamma-Glutamyltransferase (GGT)

Increased

Biliary Tract Abnormalities (same as Alkaline Phosphatase, ALP)^{1, 2}

Hepatic Parenchyma Disease/Condition

- **Degenerative, metabolic, inflammatory, neoplastic (same as ALP)^{1, 2}**

Induction by Drugs or Hormones

- **Corticosteroids endogenous or exogenous (dog)¹**
- Phenobarbital, Phenytoin, Primidone¹

Physiologic

- Can be elevated in neonates, mainly cattle, and horses

Decreased

- Not clinically significant

Artifacts

- Hemolysis or icterus may decrease the measured GGT activity⁵⁵
- Underfilling of lithium heparin tube may increase GGT activity⁴⁵

Interpret With

- Hepatic enzymes
- Markers of cholestasis

Bold Indicates a common cause



Globulin (GLOB)

Increased

Most Common Causes

Hemoconcentration

- Dehydration^{4,5}

Iatrogenic

- Corticosteroids (dogs)

Inflammation/Infection

Infectious

- Bacterial
 - Brucellosis
 - Pyoderma (suppurative dermatopathies)
 - Bacterial endocarditis^{4,5}
 - Rickettsial
 - Ehrlichiosis⁵
- Viral
 - Feline infectious peritonitis (FIP)
 - Feline immunodeficiency virus (FIV)
 - Feline leukemia virus (FeLV)^{4,5}
- Fungal
 - Systemic fungal infections
 - Blastomycosis
 - Histoplasmosis
 - Cryptococcosis
 - Coccidioidomycosis^{4,5}

Parasitic

- Dirofilariasis
- Demodicosis
- Scabies^{4,5}

Immune-Mediated Disease

- Inflammatory (immune complex)
 - Feline cholangitis/cholangiohepatitis
 - Pyometra⁵

Neoplasia

- Multiple myeloma
- Lymphoma
- Extramedullary plasmacytoma (rare)
- Chronic lymphocytic leukemia
- Waldenström's macroglobulinemia⁵

Other Causes

Inflammation

- Acute phase response
- Nephrotic syndrome (α -globulins)⁴
- Inflammation (acute, chronic)
 - Active liver disease
 - Nephrotic syndrome (β -globulins)⁴

Immune-Mediated Disease

- Systemic lupus erythematosus (SLE)
 - Glomerulonephritis
 - Immune-mediated hemolytic anemia (IMHA), thrombocytopenia (IMT), and polyarthritis⁵
- Immune mediated hemolytic anemia (IMHA)⁵ and Immune-mediated thrombocytopenia (IMT) - not because of SLE⁵
- Pemphigus complex, bullous pemphigoid⁵
- Rheumatoid arthritis⁵
- Neoplasia^{4,5}

Infection

- Ehrlichiosis
- Leishmaniasis
- Feline infectious peritonitis (rare)
- Idiopathic
- Benign monoclonal gammopathy⁵

Miscellaneous

- Cutaneous amyloidosis⁵⁶
- Lymphocytic-plasmacytic gastroenterocolitis

Decreased

Most Common Causes

- Blood Loss (hemorrhage)⁵
- Protein Losing Enteropathy (PLE)⁵
- Markedly damaged glomeruli (protein losing nephropathy- PLN)⁵
- Skin (plasma exudation)

Other Causes

- Acquired
 - Chemotherapy, radiation therapy, or other compounds (e.g., toxins, drugs)
 - Failure of passive transfer
- Inherited
 - IgM deficiency (Dobermans)⁴
 - Primary severe combined immunodeficiency (Jack Russell Terriers, Basset Hounds,

Cardigan Welsh

Corgis, Dachshunds)^{4,56}

- IgA deficiency (Shar Peis, Beagles, Airedale Terriers, and German Shepherd Dogs)⁴
- Transient hypogammaglobulinemia (dogs)⁴
- Infectious
 - Viral: FeLV, FIV, canine parvovirus, canine distemper virus

Interpret With

- Albumin
- Packed cell volume
- Leukogram
- Renal Values
- Hepatocellular enzymes

Bold Indicates a common cause



Glucose (GLU)

Increased

Most Common Causes

Physiologic

- Post-prandial
- Excitement, fright
- Stress (endogenous corticosteroids)
- Diestrus/pregnancy^{28, 57}

Primary Pancreatic Condition

- Pancreatitis
- Pancreatic carcinoma⁵⁷

Endocrine

- Diabetes mellitus
 - Immune-mediated⁵⁷
 - Obesity
- Pancreatic insular amyloidosis (mostly cats)
- Hyperadrenocorticism (Cushing's)

Pharmacologic or Toxicological

Hyperglycemia (iatrogenic)

- Intravenous glucose administration
- Steroids (glucocorticoids)
- Ethylene glycol
- Insulin (Somogyi effect)

Other Causes

Endocrine

- Glucagonoma
- Acromegaly
- Hyperpituitarism
- Hyperthyroidism (transient, cats)
- Hypothyroidism (dogs)
- Pheochromocytoma
- Hepatocutaneous syndrome (dogs)⁵⁷

Other

- Sepsis (initial phase, transient)⁵⁷
- Anti-insulin antibodies⁵⁷
- Head trauma²⁸

Pharmacologic or Toxicological

Hyperglycemia (iatrogenic)

- Megestrol acetate
- Ketamine^{28, 57}
- Glucagon
- Thyroxine
- Alpha-2 agonists (xylazine, detomidine, medetomidine, dexmedetomidine)
- Propranolol
- Morphine
- Progestins⁵⁷

Decreased

Most Common Causes

- Pancreatic β -cell neoplasia (insulinoma)
- Hypoadrenocorticism (Addison's)
- Hepatic insufficiency/failure (acquired, congenital)
- Insulin therapy
- Xylitol toxicosis (dogs)²⁸
- Sepsis (especially with endotoxemia)

Other Causes

- Porto-systemic shunt
- Starvation, malabsorption, and severe malnutrition^{28, 57}
- Exertional hypoglycemia ("hunting dog hypoglycemia")^{28, 57}

- Growth hormone deficiency
- Hypopituitarism⁵⁷
- Glycogen storage diseases (rare) (e.g., Pompe's disease, von Gierke's disease)⁵⁷

Pharmacologic or Toxicologic Hypoglycemia

- Sulfonylurea compounds (glipizide, glyburide)
- Ethanol^{28, 57}

Uncertain Pathogeneses

- Non- β -cell neoplasms²⁸
 - Hepatocellular carcinoma
 - Hepatoma
 - Leiomyosarcoma
 - Leiomyoma
 - Hemangiosarcoma

- Pregnancy hypoglycemia
 - Bovine ketosis
 - Ovine pregnancy toxemia
- Malonic aciduria (Maltese dogs)⁵⁷
- Idiopathic hypoglycemia
 - Neonatal hypoglycemia
 - Juvenile hypoglycemia (especially toy breeds)²⁸

Artifacts

- Delayed analysis of blood sample/failure to remove serum or plasma from blood cells can cause a decrease in glucose concentration⁵⁸
- Sample bacterial contamination/bacteremia (parasitemia) can cause a decrease in glucose concentration (increased glycolysis)⁵⁹
- Extreme leukocytosis can cause a decrease in glucose concentration (increased glycolysis)^{28, 57}
- Extreme erythrocytosis can cause a decrease in glucose concentration (increased glycolysis)⁵⁷
- Bromide (KBr) interference with glucose in some of the oxidase activity used to measure glucose concentration⁵⁷

Bold Indicates a common cause



Glucose (GLU), Continued

Interpret With

- Ketones (serum, urine)
- Hepatic enzymes serum activity
- Urinalysis
- Fructosamine
- Glucose curve or continuous monitoring

Bold Indicates a common cause



Ionized Calcium

Increased

Physiologic

- Healthy young, fast-growing dogs (young dog < 6 months, large or giant breed)^{27, 28}

Primary Hyperparathyroidism (PTH)

- Parathyroid neoplasia²⁷

Hypercalcemia of Malignancy/Humoral Hypercalcemia (PTHrp)

- Lymphoma
- Apocrine gland adenocarcinoma^{27, 28}

- Other carcinoma

- Multiple myeloma

Increased Vitamin D Activity (Hypervitaminosis D)

- Exogenous Vitamin D
- Rodenticides containing cholecalciferol
- Endogenous Vitamin D
- Granulomatous inflammation
 - Some fungal and parasitic infections

Decreased Urinary Excretion of Calcium

- **Renal failure**^{27, 28}
- Hypoadrenocorticism

Other or Unknown Mechanisms

- Idiopathic hypercalcemia in cats³²

Decreased

Chronic Renal Disease in Dogs and Cats

Hypoparathyroidism (rare)

Pregnancy, Parturient, or Lactational Hypocalcemia

- Eclampsia^{27, 28}
- Milk fever in cattle

Excess Urinary Excretion of Calcium

- Ethylene glycol toxicosis (dogs and cats)

Other or Unknown Mechanisms

- **Acute pancreatitis in dogs and cats**
- Urinary tract obstruction
- Hyperthyroidism in cats

Artifacts

- Decreased pH due to physiologic causes or sample handling will falsely increase calcium
- Anticoagulants (EDTA, citrate, excess heparin) will falsely decrease calcium
- Severe lipemia may increase iCa

Interpret With

- Total calcium
- Albumin
- PTH, PTHrp
- Other minerals and electrolytes

Bold Indicates a common cause



Lactate

Increased

Insufficient Oxygen Supply (Type A)

- Relative
 - **Strenuous exercise**
 - Muscle tremors
 - Shivering
 - Seizures
 - Struggling/restraint
- Absolute
 - **Hypoperfusion/shock**
 - **Severe anemia and hypoxemia**
 - Regional ischemia
 - Carbon monoxide

Adequate Oxygen Supply (Type B)

- Disease
 - **Neoplasia: lymphoma**
 - **Diabetes mellitus**
 - **Hepatic failure**
 - Thiamine deficiency
 - Hyperthyroidism
 - Impaired gluconeogenesis
 - Alkalosis
 - **SIRS/sepsis**
 - Pheochromocytoma
 - Drugs/toxins
 - Glucocorticoids
- Xylitol
 - Glucose
 - Strychnine
 - Lactulose
 - 5-Fluorouracil
 - Epinephrine
 - Acetaminophen
 - Ethylene glycol
 - Propofol
- Congenital
 - Mitochondrial myopathy
 - PDH deficiency

Decreased

- Clinically not significant

Artifacts

- Rapid infusion of Lactated Ringers solution
- Ethylene glycol

Interpret With

- CBC
- Electrolytes
- Hepatic enzymes
- Renal enzymes
- Acid-base evaluation
- Anion Gap

Bold Indicates a common cause



Magnesium (MG)

Increased

Decreased urinary excretion

- **Renal failure/Insufficiency**
- **Pre-renal/Decreased GFR**
- Post-renal azotemia

Shift of fMg_2+ from ICF to ECF

- Active in vivo hemolysis

Increased [PTH]

- **Milk fever**

Increased intestinal absorption of Mg_2+ without increased PTH or PTHrp

- Antacids or cathartics in cattle
- $MgSO_4$ (horses)

Miscellaneous

- Intravenous administration of Mg^{2+}

Decreased

Hypoproteinemia

Inadequate ruminal or intestinal absorption

- **Prolonged anorexia or poor food intake**
- **Grass tetany (cattle)**
- Enteric diseases: chronic diarrhea, loss of saliva in cattle (choke, rabies), hyperaldosteronism
- Calves on whole milk diets
- Malabsorption

Excess loss

- **Osmotic diuresis**
- **Ketonuria**
- Blister beetle poisoning in horses
- Lactation
- Sweat

Artifacts

- Delayed removal of serum from blood clot leading to false increase

Interpret With

- Other minerals
- Electrolytes
- Renal enzymes

Bold Indicates a common cause



Increased

Disorders that cause increases in

- **Glucose**
- **Urea**
- **Sodium**

Administration or ingestion of

- Mannitol
- Radiographic contrast media
- Ethanol, methanol, or ethylene glycol

Decreased

Disorders that cause decreases in

- **Sodium** (see hyponatremia for more info)

Artifacts

- Radiographic contrast media

Interpret With

- Electrolytes
- Renal enzymes
- Glucose

Bold Indicates a common cause



Increased (Alkalemia)

Loss of H⁺

- **Gastric loss: vomiting or pyloric obstruction**
- **Renal Loss**
 - Loop or thiazide diuretics
 - Secondary to respiratory acidosis

- Hypokalemia
- **Respiratory alkalosis**
 - **Hypoxemia**
 - Pulmonary disease
 - Metabolic acidosis
 - **Septicemia**

- Heat stroke
- Central neurologic disease
- Pain or anxiety

Decreased (Acidemia)

Accumulation/decreased excretion of H⁺

- **Renal failure**
- Uroperitoneum
- **Ketoacidosis**
- Respiratory acidosis
 - Upper airway dysfunction
 - Inhibition or dysfunction of respiratory muscles
 - Inhibition or dysfunction of medullary respiratory center
 - Impaired gas exchange at

- pulmonary capillaries
- Restrictive disease
- Vascular disorders: right-to-left shunts
- Metabolic alkalosis

- Ethylene glycol
- Uremic acids

Increased HCO₃⁻ loss

- **GI loss**
 - Diarrhea
 - Salivary loss (ruminants)
- **Organic acidosis**
 - Lactic acidosis
 - Ketoacidosis

Artifacts

- Falsely decreased pH
 - Can occur in aged samples – increased lactate production
- Falsely increased pH
 - Can occur secondary to severe muscle injury (rare)
 - Exposure to air/air bubbles
 - Excess heparin

Interpret With

- Complete acid-base analysis
- Electrolytes

Bold Indicates a common cause



Phenobarbital (PHB)

Increased

- **High therapeutic dose**
- Severe anuric or oliguric renal failure
- Drugs: chloramphenicol, felbamate
- Low protein or fat diets

Decreased

- Malabsorption
- Increased urine flow (mannitol)
- Drugs: rifampin

Artifacts

- Serum separator tubes can produce a false decrease

Interpret With

- Liver enzymes
- CBC

Bold Indicates a common cause



Phosphorus (PHOS)

Increased

Most Common Causes

Physiologic

- Post-Prandial
- Young fast-growing dog (generally large breed dog)^{27, 28}

Renal (Decreased PHOS Excretion)

- Decreased glomerular filtration rate (GFR)
- Pre-renal azotemia
- Renal failure
- Post-renal obstruction

Other Causes

Renal (Decreased PHOS Excretion)

- Urinary bladder rupture or urine leakage into tissues
- Decreased parathyroid hormone (PTH) concentration or activity (hypoparathyroidism)

- Hyperthyroidism
- Acromegaly^{27, 28}

Intestinal (Increased PHOS Absorption)

- Increased vitamin D
 - Ingestion of cholecalciferol rodenticides and plants (e.g., Cestrum diurnum, Solanum sp.)
- Phosphate enema or ingestion of phosphate urinary acidifier
- Ischemic intestinal lesions (shift intracellular fluid to extracellular fluid)
- Granulomatous disease
 - Fungal, parasitic
- Humoral hypercalcemia of malignancy
- Diet with a low calcium/phosphorus ratio (rare)²⁷

Bone

- Osteolytic bone lesions (neoplasia)²⁸

Other or Unknown Mechanisms

- Malignant hyperthermia^{27, 28}
- Acute tumor lysis syndrome^{27, 28}
- Hyperthyroidism in cats
- Metabolic acidosis
- Hyperadrenocorticism in dogs^{27, 28}

Decreased

Most Common Causes

Intestinal (Decreased PHOS Absorption)

- Prolonged anorexia or phosphorus-deficient diet

Iatrogenic

- Treatment of diabetes ketoacidosis⁶⁵

Other Causes

Renal (Increased Renal PHOS Excretion)

- Prolonged diuresis²⁷
- Increased PTH or PTHrP activity
- Primary hyperparathyroidism (parathyroid neoplasia)^{27, 28}
- Humoral hypercalcemia of malignancy^{27, 28}
- Eclampsia
- Fanconi syndrome (dogs)²⁷

- Hyperadrenocorticism/iatrogenic steroid administration^{28, 65}

Intestinal (Decreased PHOS Absorption)

- Vomiting/diarrhea
- Phosphorus-binding agents
- Hypovitaminosis D
- Intestinal malabsorption/steatorrhea^{27, 28}

Increased Loss

- Vomiting/diarrhea
- Diabetes
- Diabetic ketoacidosis⁶⁵

Defective Mobilization of Phosphorus from Bone

- Puerperal tetany
- Eclampsia

Iatrogenic

- Glucose infusion²⁷
- Sodium bicarbonate administration
- Parenteral glucose administration
- Aggressive parenteral fluid therapy²⁸

Other Causes

- Respiratory alkalosis²⁷
- Monoclonal gammopathy⁶⁶
- Hyperinsulinism (endogenous or exogenous)
- Hepatic lipidosis (cats)
- Re-feeding syndrome⁶⁵

Bold Indicates a common cause



Phosphorus (PHOS), Continued

Artifacts

- Drugs or Substances That May Cause Increased Serum PHOS⁶⁷
 - Bilirubin (icterus)
 - Hemoglobin (hemolysis)
 - Lipemia
 - Amino salicylic acid
 - Detergents contaminating glassware
 - Fat emulsions
 - Methotrexate
 - Naproxen
 - Rifampin
- Drugs or Substances That May Cause Decreased Serum PHOS⁶⁷
 - Phenothiazine
 - Cefotaxime
 - Citrates
 - Mannitol
 - Oxalate
 - Promethazine

Interpret With

- Calcium
- Blood Urea Nitrogen
- Creatinine
- Urinalysis

Bold Indicates a common cause



Potassium (K)

Increased

Most Common Causes

Decreased Renal Excretion

- Urinary tract obstruction
- Ruptured bladder/ureter (uroabdomen)
- Renal insufficiency or failure (primarily oliguric or anuric patients)
- Hypoaldosteronism
 - Hypoadrenocorticism (pathologic)

Metabolic

- Metabolic acidosis by accumulation of inorganic acid (NH₄Cl, HCl, etc.)⁶⁸

Hypertonicity

- Diabetes mellitus

Other Causes

Decreased Renal Excretion

- Hypoaldosteronism
 - Angiotensin-converting enzyme inhibitors (iatrogenic)

- Hyporeninemic hypoaldosteronism with diabetes or renal failure (rare)³⁴

Increased Intake

- Administration of potassium-rich fluid

Drugs

- Angiotensin-converting enzyme inhibitors (e.g., enalapril)
- Potassium-sparing diuretics (e.g., spironolactone, amiloride, triamterene)
- Prostaglandin inhibitors
- Heparin
- Non-specific beta blockers (e.g., propranolol)³⁵

Hypertonicity

- Mannitol infusion
- Massive intravascular hemolysis with potassium-rich erythrocytes
- Massive tissue damage
 - Acute tumor lysis syndrome

- Reperfusion of extremities after aortic thromboembolism in cats with cardiomyopathy
- Crush injuries³⁵
- Hyperkalemic myopathy (Rhabdomyolysis or other muscle damage)³⁴

Other/Unknown Mechanism

- Repeated drainage of chylous thoracic effusions³⁵
- Peritoneal effusions in cats³⁵

Iatrogenic

- IV fluids or IV fluid line contamination with potassium supplementation
- Use of the wrong anticoagulant (K+ EDTA)

Decreased

Most Common Causes

Decreased Intake

- Anorexia

Gastrointestinal Loss

- Vomiting or sequestration of H⁺ and Cl⁻ causing metabolic alkalosis
- Diarrhea³⁴
- Excess salivation

Renal Loss

- Chronic renal failure in cats
- Post-obstructive diuresis
- Increased fluid flow in distal nephron (collecting tubule)
 - Osmotic (diabetes)
 - Sodium-losing nephropathies³⁴

Increased Renal Excretion of Anions

- Ketonuria
- Lactaturia
- Bicarbonaturia

Drugs

- Loop diuretics (e.g., furosemide)
- Glucose-containing fluids ± insulin³⁵

Other and Unknown Mechanisms

- Metabolic/respiratory alkalosis with alkalemia³⁵
- Hypokalemic renal failure in cats

Other Causes

Increased Renal Excretion of Anions

- Distal (type I) renal tubular acidosis (rare)³⁵
- Proximal (type II) renal tubular acidosis after NaHCO₃- treatment (rare)³⁵
- Hyperaldosteronism (primary)³⁴

Drugs

- Thiazide diuretics (e.g., chlorothiazide, hydrochlorothiazide)
- Amphotericin B
- Penicillin (rare)

- Albuterol overdose (rare)³⁵
- Inadequate fluid therapy
 - Inadequate potassium supplementation
 - Potassium-free fluids (e.g., 0.9% NaCl, 5% dextrose in water)³⁵

Other and Unknown Mechanisms

- Catecholamine release³⁵
- Endotoxemia³⁴
- Third space loss (body cavity effusion)³⁴
- Hypokalemic myopathy of Burmese kittens

Bold Indicates a common cause



Potassium (K), Continued

Artifacts

- Lipemia may cause a decreased measured K⁺ concentration (ionic exclusion phenomenon)⁶⁸
- Serum K⁺ is slightly higher than plasma K⁺ of healthy animals
 - Release of K⁺ from platelets during clotting³⁵
- Elevations in K⁺ levels
 - Potassium oxalate or K₂ or K₃ EDTA anticoagulants⁶⁸
 - Severe bilirubinemia: slight increase (ion-selective electrodes)³⁵
 - Marked thrombocytosis^{34, 35}
 - Marked leukocytosis (physiologic or neoplastic)⁶⁸
 - In vitro hemolysis of K-rich erythrocytes in the Akita and Shiba Inu breeds²
 - In vivo hemolysis in phosphofructokinase deficiency in predisposed canine breeds^{2, 3}
 - English Springer Spaniels, American Cocker Spaniels

Interpret With

- Electrolytes
- Blood urea nitrogen
- Creatinine
- Total carbon dioxide
- Anion gap
- Acid-base analysis
- Urinalysis

Bold Indicates a common cause



Progesterone

Increased

- **Before ovulation**
- **Mid-pregnancy**
- Ovarian tumors
- False pregnancy

Decreased

- **Before parturition**
- **Anestrus**
- **Proestrus**

Interpret With

- Vaginal cytology
- Anti-Mullerian hormone (AMH)
- Luteinizing hormone (LH)

Bold Indicates a common cause



Sodium (NA)

Increased

Most Common Causes

Inadequate Water Intake

- Water deprivation (inadequate access to water)

Excess Pure Water Loss

- Panting
- Fever
- Hyperventilation³⁴

Renal Water Loss

- Diabetes mellitus
- Chronic renal failure

Extra-Renal Water Loss

- Vomiting
- Osmotic diarrhea
- Osmotic sequestration (small intestinal obstruction)
- Peritonitis, pancreatitis, cavity effusions³⁵

Other Causes

Inadequate Water Intake

- Primary adipsia/hypodipsia (defective thirst response secondary to hypothalamic disease or lesion)³⁴

Excess Pure Water Loss

- Diabetes insipidus
- Central
- Nephrogenic

Renal Water Loss

- Osmotic
- Mannitol infusion
- Chemical diuresis (pharmacologic)
- Post-obstructive diuresis
- Non-oliguric renal failure³⁵

Extra-Renal Water Loss

- Third space water losses
- Cutaneous water losses
- Burn lesions

Excess Intake of Sodium

- Salt poisoning (with concurrent water deprivation)
- Administration of hypertonic fluid
 - Hypertonic saline
 - Sodium bicarbonate
 - Parenteral nutrition
 - Sodium phosphate enema

Increased Renal Sodium Retention

- Hyperaldosteronism³⁵

Other/Unknown Mechanism

- Hyperadrenocorticism³⁵

Therapeutics

- Administration of hypertonic saline or sodium bicarbonate

Decreased

Most Common Causes

Gastrointestinal Sodium Loss

- Vomiting/diarrhea
- Sequestration
- Canine whipworm infection
- Excess salivation
- Bovine hemorrhagic bowel syndrome

Renal Sodium Loss

- Hypoadrenocorticism
- Osmotic diuresis (diabetes mellitus)
- Hypoaldosteronism
- Ketonuria
- Sodium-wasting nephropathies³⁴

Third Space Sodium Loss

- Pancreatitis
- Peritonitis
- Uroabdomen

Edematous Disorders

- Congestive heart failure causing ascites

Extracellular Translocation of Water

- Hyperglycemia

Extravascular Fluid Translocation of Sodium

- Uroperitoneum (ruptured bladder or abdominal urethra)³⁴

Other Causes

Renal Sodium Loss

- Proximal renal tubule dysfunction (prolonged diuresis)

Third Space Sodium Loss

- Chylothorax with repeated pleural fluid drainage³⁵
- Acute internal hemorrhage or acute exudation^{34, 35}

Cutaneous Loss

- Sweating
- Exudative skin lesions

Edematous Disorders

- Hepatic disease/hepatic cirrhosis causing ascites
- Nephrotic syndrome causing effusion
- Advanced renal failure (primarily oliguric or anuric)³⁵

Expanded Extracellular Fluid Volume (Without Edema)

- Excess sodium-poor fluid administration (parenteral)
- Inappropriate fluid therapy with 5% dextrose, 0.45% saline solution, or hypotonic fluids³⁵

- Syndrome of inappropriate antidiuretic hormone secretion (SIADH)^{34, 35}
- Antidiuretic drugs (e.g., heparin solutions containing chlorbutanol, vincristine, cyclophosphamide, nonsteroidal anti-inflammatory drugs)³⁵
- Myxedema coma of hypothyroidism (rare)³⁵
- Psychogenic polydipsia³⁵

Extracellular Translocation of Water

- Mannitol infusion (intravenously)³⁴

Intracellular Translocation of Sodium

- Hypokalemia
- Acute muscle injury³⁴

Bold Indicates a common cause



Sodium (NA), Continued

Artifacts

- Lipemia may cause pseudo-hyponatremia (ion-exclusion effect)³⁵
- Marked hyperproteinemia may cause a false decrease in measured sodium³⁵
- Hemolysis may cause a decreased sodium concentration
- Sample dehydration may cause artefactually increased sodium³⁴
- Anticoagulant: Na2EDTA will increase the Na plasma concentration
 - Use of Na-Heparin will not cause clinically relevant changes in heparinized plasma Na³⁴

Interpret With

- Electrolytes (K⁺, Cl⁻)
- Total protein
- Blood urea nitrogen
- Creatinine
- Osmolality
- Urinalysis
- Hematocrit

Bold Indicates a common cause



Symmetric Dimethylarginine (SDMA)

Increased

Physiologic

- Neonatal foals⁷¹
- Greyhounds/sighthounds⁷²
- Birman cats⁷²
- A small percentage of puppies and kittens may have values slightly above the adult reference interval

Non-azotemic

- **Lymphoma**⁷³
- Pancreatitis⁷⁴
- Dermatopathies⁷⁵
- Psychogenic polydipsia⁷⁵

Pre-renal

- **Dehydration**

Renal disease

- **Acute kidney injury**
- **Chronic kidney disease**

Decreased

- Not clinically significant

Artifacts

- No known artifacts/interferents

Interpret With

- Urinalysis including urine specific gravity
- Renal values (BUN and creatinine)
- Electrolytes
- CBC

Bold Indicates a common cause



Thyroxine (Total T4)

Increased

Most Common Causes

Hyperthyroidism

- **Thyroid adenoma/adenomatous hyperplasia (common in cats, rare in dogs)**^{28, 76, 77}

Other Causes

Hyperthyroidism

- Thyroid carcinoma/adenocarcinoma (cats, rare in dogs)^{28, 76, 77}
- Hyperplasia⁷⁶
- Multiple endocrine neoplasia (Type II)⁷⁶

Drugs (Dogs)²⁸

- Amiodarone
- Iodate
- Overdose of levothyroxine supplementation⁷⁶

Decreased

Most Common Causes

Primary Hypothyroidism (Dogs)

- Lymphocytic thyroiditis
- Idiopathic thyroid atrophy
- Congenital thyroid gland dysgenesis
- Destruction of thyroid gland (neoplasia, surgery, radioactive iodide treatments, etc.)^{28, 76, 77}

Non-Thyroidal Illnesses: "Euthyroid Sick Syndrome"⁷²⁸

- Acute diseases
 - Bacterial bronchopneumonia
 - Sepsis
 - Distemper
 - Autoimmune hemolytic anemia
 - Systemic lupus erythematosus
 - Intervertebral disk disease
 - Polyradiculoneuritis
 - Acute renal failure
 - Acute hepatitis
 - Acute pancreatitis
- Chronic diseases
 - Generalized demodicosis
 - Generalized bacterial furunculosis

- Systemic mycoses
- Lymphoma
- Chronic renal failure
- Diabetes mellitus
- Congestive heart failure
- Cardiomyopathy
- Chronic hepatitis, cirrhosis
- Gastrointestinal disturbances
- Megaesophagus

Other Causes

Secondary Hypothyroidism

- Hyperadrenocorticism⁷⁶
- Pituitary failure
- May be normal for some breeds

Defective Thyroxine Production

- Iodine organification defect⁷⁶
- Congenital thyroid peroxidase deficiency in Toy Fox Terriers⁷⁶
- Iodine deficiency⁷⁶

Drugs

- Dogs²⁸
 - Aspirin
 - Carprofen

- Glucocorticoids
- Clomipramine
- Furosemide
- Methimazole
- Phenobarbital
- Phenylbutazone
- Progestagens
- Propylthiouracil
- Sulfonamides
- Cats
 - Following radioactive iodine or methimazole therapy for hyperthyroidism⁷⁶

Bold Indicates a common cause



Thyroxine (Total T4), Continued

Variables That May Affect Baseline T4 in Dogs

Age Inversely proportional effect²⁸

- Neonate (< 3 mo) Increased T4
- Aged (> 6 yr) Decreased T4

Body size Inversely proportional effect²⁸

- Small (< 10 kg) Increased T4
- Large (> 30 kg) Decreased T4

Breed

- Sight Hounds (e.g., Greyhound) T4 may be lower than normal range established for dogs²⁸
- Nordic breeds (e.g., Huskies)

Strenuous exercise²⁸ Increased T4

Pregnancy (progesterone)²⁸ Increased T4

Surgery/anesthesia²⁸ Decreased T4

Concurrent illness

(Euthyroid Syndrome)²⁸ Decreased T4

Artifacts

- Presence of anti-T4 autoantibodies can cause an artefactual increase in T4 (radioimmunoassay) (dogs)²⁸
- Administration of compound containing iodine

Interpret With

- Cholesterol
- Free T4
- Thyroid Stimulating Hormone (canine)
- Alanine Aminotransferase (feline)
- Kidney values (feline)

Bold Indicates a common cause



Trypsin-Like Immunoreactivity (TLI)

Increased

Increased release from acinar cells

- **Pancreatitis**
- Gastrointestinal obstruction
- Endotoxic shock

Decreased renal clearance

- **Pre-renal, renal, or post-renal disorders**

Decreased

Decreased cellular release

- **Chronic pancreatitis**
- **Pancreatic acinar atrophy/exocrine pancreatic insufficiency (EPI)**

Artifacts

- No known interferences
- Recommended patient fasted for testing

Interpret With

- PLI
- Cobalamin
- Folate
- DGGR lipase

Bold Indicates a common cause



Total Bilirubin (TBIL)

Increased

Most Common Causes

Fasting/Anorexia (Especially Horses)

Hemolysis

Immunological Alterations

- Immune Mediated Hemolytic Anemia (IMHA)^{79, 80}
- Blood transfusion reaction

Infectious

- Mycoplasma haemofelis
- Mycoplasma haemocanis
- Babesia canis
- Cytauxzoon felis
- Anaplasma spp.
- Feline leukemia virus (FeLV)
- Bacteremia⁷⁹

Oxidative Damage

- Heinz body anemia

Erythrocyte Fragmentation in Blood

- Disseminated intravascular coagulation
- Hemangiosarcoma

Hepatobiliary Disease

Cirrhosis

- Chronic active hepatitis

Metabolic or Endocrine

- Hepatic lipidosis
- Diabetes mellitus
- Hyperadrenocorticism
- Hyperthyroidism

Immunological

- Chronic active hepatitis
- Feline lymphocytic or suppurative cholangiohepatitis
- Cirrhosis

Neoplasia

- Lymphoma
- Hepatocellular carcinoma
- Hepatoma

Biliary Disorders

- Cholangitis (bile sludge)
- Gall bladder stones
- Pancreatic disease (extrahepatic biliary obstruction)
- Neoplasia (gallbladder, bile duct adenocarcinoma)
- Biliary mucocele

Other Causes

Hemolysis

Immunological Alterations

- Drug induced hemolytic anemia
- Vaccine associated^{79, 80}

Toxins

- Lead poisoning
- Zinc/copper toxicity^{79, 80}

Oxidative Damage

- Methemoglobinemia
- Eccentric hemolysis (acquired or inherited)⁷⁹

Defect in Adenosine Triphosphate (ATP) Generation

- Pyruvate kinase (PK) deficiency^{79, 80}
- Phosphofructokinase deficiency^{79, 80}
- Hypophosphatemic hemolysis⁸⁰

Erythrocyte Fragmentation in Blood

- Vasculitis
- Microangiopathic disease

- Rheological processes
 - Caval syndrome of dirofilariasis
 - Cardiac valvular disease⁷⁹

Other Unknown Pathogenesis

- Envenomation⁷⁹
- Hemophagocytic histiocytic sarcoma⁷⁹
- Increased osmotic fragility⁷⁹
- Hereditary non-spherocytic hemolytic anemia of Beagles⁷⁹
- Idiopathic hemolytic anemia of Abyssinian and Somali cats⁷⁹

Hepatobiliary Disease

Infectious

- Viral
- Bacterial
- Systemic fungal infection

Toxins

- Mushrooms
- Chemicals – insecticides, carbon tetrachloride
- Numerous pharmaceuticals
- Plants – aflatoxins, pyrrolizidine alkaloids, glycosides (sago palm)

Sepsis Associated Cholestasis

- Escherichia coli, Staphylococcus intermedius infection
 - Pneumonia
 - Peritonitis
 - Endocarditis
 - Urinary tract infection

Decreased

- Not clinically significant

Artifacts

- Hemolysis or lipemia may artifactually increase values⁸¹
- Exposure to ultraviolet light (including sunlight) will decrease bilirubin levels⁸¹

Bold Indicates a common cause



Total Bilirubin (TBIL), Continued

Interpret With

- Hepatic enzyme activity
- Creatine kinase
- Lactate dehydrogenase, if available
- Complete blood count
- Hematocrit

Bold Indicates a common cause



Total Carbon Dioxide (TCO₂)

Increased

Most Common Causes

Metabolic Alkalosis

- Gastrointestinal loss/sequestration H⁺ and Cl⁻
- Vomiting, gastric atony/torsion/pyloric obstruction (functional or mechanical)

Renal Loss of H⁺

- Hypokalemia³⁴

Iatrogenic

- Administration of bicarbonate containing solutions

Other Causes

Metabolic Alkalosis

- Contraction alkalosis secondary to vomiting³⁴

Renal Loss of H⁺

- Loop or thiazide diuretics (e.g., furosemide)³⁴
- Renal compensation for respiratory acidosis (chronic)³⁴

Decreased

Most Common Causes

Bicarbonate Consumption (Titration Acidosis)

- Lactic acidosis
- Ketoacidosis (diabetes mellitus)
- Decreased excretion of non-carbonic acid
 - Sulfates
 - Phosphates
 - Renal failure
- Toxicity (ethylene glycol, paraldehyde, salicylate, methanol)³⁴

Decreased Renal Excretion of H⁺

- Hypoadrenocorticism³⁴

Bicarbonate Loss (Hyperchloremic Metabolic Acidosis)

- Vomiting (biliary and/or pancreatic fluids)
- Diarrhea
- Sequestration or GI fluids³⁴

Other Causes

Decreased Renal Excretion of H⁺

- Proximal renal tubular acidosis

- Distal renal tubular acidosis (Type I)³⁴
- Uroperitoneum and/or urinary tract obstruction³⁴

Compensation for Primary Respiratory Alkalosis

- Hyperventilation – hypoxemia
- Primary pulmonary disease
- Pain

Dilutional Acidosis

- Rapid infusion of saline

Iatrogenic

- Ammonium chloride administration

Artifacts

- Increased contact with room air may decrease tCO₂⁸²
 - Underfilling the sample tube (heparin or plain tube)
 - Failure to properly cap the sample or repeatedly opening the tube
- Prolonged venous stasis will decrease tCO₂⁸²
- Use of EDTA, oxalate, or fluoride anticoagulants will decrease tCO₂⁸²
- Prolonged contact with the clot can cause decrease in tCO₂⁸²

Interpret With

- Acid-Base analysis
- Anion gap
- Electrolytes
- Glucose
- Blood Urea Nitrogen
- Creatinine
- Urinalysis

Bold Indicates a common cause



Total Protein (TP)

Increased

Most Common Causes

Decreased Blood Volume

- Hemoconcentration – dehydration (most common cause)^{4, 5}

Increased Protein Production

- Inflammatory Disease
 - Infectious
 - Bacterial

- Viral
- Fungal
- Protozoal⁴
- Noninfectious
 - Necrosis
 - Neoplasia
 - Immune-mediated disease⁴

Other Causes

B-Lymphocyte Neoplasia

- Plasma cell (monoclonal gammopathy): multiple myeloma, plasmacytoma⁴
- Lymphocyte: lymphoma, lymphocytic leukemia⁴

Decreased

Most Common Causes

Protein Loss

- Blood loss
- Protein-losing nephropathy
 - Glomerulonephritis
 - Amyloidosis
- Protein-losing enteropathy
 - Small intestinal mucosal disease
 - Lymphangiectasia
 - Intestinal blood loss
- Plasma loss (sequestration/third space losses)
 - Peritonitis/pleuritis

Decreased Protein Synthesis/Increased Protein Catabolism

- Hepatic insufficiency
- Malabsorption or maldigestion
 - Intestinal mucosal disease

- Exocrine pancreatic insufficiency (EPI)^{4, 5}
- Cachectic state
 - Chronic disease
 - Neoplasia
 - Malnutrition
 - Starvation

Hemodilution

- Edematous disorders
 - Congestive heart failure

Other Causes

Protein Loss

- Plasma loss (sequestration/third space losses)
 - Vasculitis
 - Exudative dermatopathies^{4, 5}

Decreased Protein Synthesis/Increased Protein Catabolism

- Cachectic state
 - Lymphoid hypoplasia^{4, 5}

Hemodilution

- Excess administration of intravenous fluid
- Edematous disorders
 - Cirrhosis
 - Nephrotic syndrome
 - Excess ADH secretion (SIADH)^{4, 5}

Artifacts

- Hemolysis or gross lipemia may cause an increase in measured TP^{4, 85}
- Icterus may falsely decrease the measured total protein value^{4, 5, 83, 84, 85}
- Plasma > serum (very slight difference)
 - Fibrinogen may slightly increase the plasma TP concentration⁸⁵

Bold Indicates a common cause



Total Protein (TP), Continued

Interpret With

- Albumin
- Globulin
- Blood urea nitrogen
- Liver enzymes
- Creatinine
- Hematology
- Urinalysis
- Urine protein:creatinine ratio

Bold Indicates a common cause



Triglycerides (TGA)

Increased

Increased triglyceride production

- **By enterocytes:** Postprandial hyperlipemia/hyperlipidemia
- **By hepatocytes:** Equine hyperlipemia/hyperlipidemia

Decreased lipolysis or intravascular processing of lipoproteins

- Hypothyroidism
- Nephrotic syndrome

Other, unknown, or multiple mechanisms

- **Acute pancreatitis**
- **Diabetes mellitus**
- High lipid diet
- Endogenous or exogenous glucocorticoids
- Idiopathic hyperlipidemia of Miniature Schnauzers

Increased lipolysis

- **Metabolic syndrome (obesity + insulin resistance)**

- Pregnancy
- Stress
- Lactation in horses
- Pregnancy toxemia
- Ketosis in camelids

Decreased

May not be clinically significant

- **Exocrine pancreatic insufficiency**
- **Protein-losing enteropathy**

- Portosystemic shunt
- Inflammatory bowel disease
- Hepatic insufficiency

- Hypoadrenocorticism
- Hematopoietic neoplasia
- Hyperthyroidism

Interpret With

- Glucose
- ALT
- ALP
- GGT
- Total bilirubin
- Cholesterol

Bold Indicates a common cause



Uric Acid (UA)

Increased

Increased production

- **Post-prandial in carnivorous species**
- **Gout**
- Starvation
- Tissue necrosis

Decreased excretion

- **Renal disease**
- **Severe dehydration**

Decreased

- Not clinically significant

Artifacts

- Can be artifactually increased in samples from toenail clippings due to fecal urate contamination

Interpret With

- Calcium
- Phosphorus
- BUN
- +/- Creatinine
- Electrolytes

Bold Indicates a common cause



References

1. Stockham SL, Scott MA. Enzymes. In: *Fundamentals of Veterinary Clinical Pathology*. 2nd Edition. Wiley-Blackwell; 2008:639-674.
2. Willard MD, Tvedten H. Gastrointestinal, Pancreatic, and Hepatic Disorders. In: *Small Animal Clinical Diagnosis by Laboratory Methods*. 5th Edition. Saunders Elsevier; 2012:191-225.
3. Vaden SL, Knoll JS, Smith FWK, and Tilley, LP. Alanine Aminotransferase. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:32-33.
4. Stockham SL, Scott MA. Proteins. In: *Fundamentals of Veterinary Clinical Pathology*. 2nd Edition. Wiley-Blackwell; 2008: 369-413.
5. Willard MD, Tvedten H. Immunologic and Plasma Protein Disorders. In: *Small Animal Clinical Diagnosis by Laboratory Methods*. 5th Edition. Saunders Elsevier; 2012:278-293.
6. Cooper ES, Wellman ML, Carsillo ME. Hyperalbuminemia Associated With Hepatocellular Carcinoma in a Dog. *Vet Clin Pathol*. 2009;38(4):516-520.
7. Torrente C, Manzanilla EG, Bosch L, Fresno L, Rivera Del Alamo M, Andaluz A, Saco Y, Ruiz de Gopegui R. Plasma Iron, C-Reactive Protein, Albumin, and Plasma Fibrinogen Concentrations in Dogs With Systemic Inflammatory Response Syndrome. *J Vet Emerg Crit Care* (San Antonio). 2015; 25(5):611-619.
8. Stokol T, Tarrant JM, Scarlett JM. Overestimation of Canine Albumin Concentration With the Bromocresol Green Method in Heparinized Plasma Samples *Vet Clin Pathol*. 2001; 30(4):170-176.
9. Vaden SL, Knoll JS, Smith FWK, Tilley, LP. Albumin. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:34-35.
10. Lawler DF, Keltner DG, Hoffman WE, Nachreiner RF, Hegstad RL, Herndon PA, Fischer BJ. Benign Familial Hyperphosphatasemia in Siberian Huskies. *Am J Vet Res*. 1996;57(5):612-617.
11. Gallagher AE, Panciera DL, Panciera RJ. Hyperphosphatasemia in Scottish Terriers: 7 Cases. *J Vet Intern Med*. 2006;20(2):418-421.
12. Karayannopoulou M, Polizopoulou ZS, Koutinas AF, Fytianou A, Roubies N, Kaldrymidou E, Tsioli V, Patsikas MN, Constantinidis TC, Koutinas CK. Serum Alkaline Phosphatase Isoenzyme Activities in Canine Malignant Mammary Neoplasms With and Without Osseous Transformation. *Vet Clin Pathol*. 2006;35(3):287-290.
13. Thomas JS. Introduction to Serum Chemistries: Artifacts in Biochemical Determinations. *Small Animal Clinical Diagnosis by Laboratory Methods*. 4th Edition. 2004:113-116.
14. Vaden SL, Knoll JS, Smith FWK, Tilley, LP. Lipase. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:399-400.
15. Stockham SL, Scott MA. Monovalent Electrolytes and Osmolality. In: *Fundamentals of Veterinary Clinical Pathology*. 2nd Edition. Wiley-Blackwell; 2008:534-538.
16. DiBartola, Stephen P. Introduction to Acid-Base Disorders. In: *Fluid, Electrolyte, and Acid-Base Disorders*. 4th Edition. Elsevier-Saunders; 2012:243-244, 255-269, 307.
17. Funes, S, et. al. A Quick Reference on High Anion Gap Metabolic Acidosis. *Vet Clin Smal Anim*. 2017;47:205-207.
18. Hopper, Kate. Small Animal Critical Care. In: *Traditional Acid-Base Analysis*, 2nd Edition. Elsevier-Saunders; 2015:289-291.
19. Vaden SL, Knoll JS, Smith FWK, Tilley, LP. Aspartate Aminotransferase. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:72-73.
20. Stockham SL, Scott MA. Monovalent Electrolytes and Osmolality. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:525-534.
21. DiBartola, Stephen P. Introduction to Acid-Base Disorders and Metabolic Acid-Base Disorders. In: *Fluid, Electrolyte, and Acid-Base Disorders*, 4th Edition. Elsevier-Saunders; 2012:234-243, 253-280.
22. Stockham SL, Scott MA. Liver Function. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008: 675-706.



References

23. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Bile Acids. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009: 91-93.
24. Stockham SL, Scott MA. Urinary System. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:415-494.
25. Willard MD, Tvedten H. Urinary Disorders. In: *Small Animal Clinical Diagnosis by Laboratory Methods*, 5th Edition. Saunders Elsevier; 2012:126-155.
26. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Urea Nitrogen. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:660-661.
27. Stockham SL, Scott MA. Calcium, Phosphorous, Magnesium and Their Regulatory Hormones. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:593-638.
28. Willard MD, Tvedten H. Endocrine, Metabolic, and Lipid Disorders. In: *Small Animal Clinical Diagnosis by Laboratory Methods*, 5th Edition. Saunders Elsevier; 2012:156-190.
29. Bergman PJ. Paraneoplastic Hypercalcemia. *Topics Companion Anim Med*. 2012;27(4):156-158.
30. Robat CS, Cesario L, Gaeta R, Miller M, Schrempp D, Chun R. Clinical Features, Treatment Options, and Outcome in Dogs With Thymoma: 116 Cases (1999-2010). *J Am Vet Med Assoc*. 2013;243(10):1448-1454.
31. Hirt RA, Kneissl S, Teinfalt M. Severe Hypercalcemia in a Dog With a Retained Fetus and Endometritis. *J Am Vet Med Assoc*. 2000;216(9):1423-1425.
32. Midkiff AM, Chew DJ, Randolph JF, Center SA, DiBartola SP. Idiopathic Hypercalcemia in Cats. *J Vet Intern Med*. 2000;14(6):619-626.
33. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Calcium. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:148-150.
34. Stockham SL, Scott MA. Monovalent Electrolytes and Osmolality. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:495-558.
35. Willard MD, Tvedten H. Electrolyte and Acid-Base Disorders. In: *Small Animal Clinical Diagnosis by Laboratory Methods*, 5th Edition. Saunders Elsevier; 2012:112-125.
36. DiBartola SP, Willard MD. Disorders of Chloride: Hypochloremia and Hyperchloremia. In: *Fluid, Electrolyte, and Acid-Base Disorders in Small Animal Practice*. Ed. S DiBartola, Saunders Elsevier; 2006:82-91.
37. Stockham SL, Scott MA. Lipids. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:763-782.
38. Moore PF, Affolter VK, Vernau W. Canine Hemophagocytic Histiocytic Sarcoma: A Proliferative Disorder of CD11d+ Macrophages. *Vet Pathol*. 2006;43(5):632-645.
39. Patel RT, Caceres A, French AF, McManus PM. Multiple Myeloma in 16 Cats: A Retrospective Study. *Vet Clin Pathol*. 2005;34(4):341-352.
40. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Cholesterol. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:174-175.
41. Kather, Stafanie et. Al. Review of Cobalamin and Disorders of Cobalamin Metabolism in Dogs. *J Vet Intern Med*. 2020;34:13-28.
42. Stockham SL, Scott MA. Exocrine Pancreas and Intestine. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:747-750.
43. Willard MD, Tvedten H. Neurologic Disorder. In: *Small Animal Clinical Diagnosis by Laboratory Methods*, 5th Edition. Saunders Elsevier; 2012:304-314.
44. Fascetti AJ, Mauldin GE, Mauldin GN. Correlation Between Serum Creatine Kinase Activities and Anorexia in Cats. *J Vet Intern Med*. 1997;11(1):9-13.
45. Lippi G, Avanzini P, Cosmai M, Aloe R, Ernst D. Incomplete Filling of Lithium Heparin Tubes Affects the Activity of Creatine Kinase and Gammaglutamyl Transferase. *Br J Biomed Sci*. 2012;69(2):67-70.
46. Rørtveit R, Saevik BK, Eggertsdóttir AV, Skancke E, Lingaas F, Thoresen SI, Jansen JH. Age-Related Changes in Hematologic and Serum Biochemical Variables in Dogs Aged 16–60 Days. *Vet Clin Pathol*. 2015;44(1):47-57.



References

47. Misbach C, Chetboul V, Concordet D, Médaille C, Gruet P, Speranza C, Hoffmann AC, Rocha A, Balouka D, Petit AM, Trehieu-Sechi E, Pouchelon JL, Lefebvre HP. Basal Plasma Concentrations of Routine Variables and Packed Cell Volume in Clinically Healthy Adult Small-Sized Dogs: Effect of Breed, Body Weight, Age, and Gender, and Establishment of Reference Intervals. *Vet Clin Pathol*. 2014;43(3):371-380.
48. Deppe TA, Center SA, Simpson KW, Erb HN, Randolph JF, Dykes NL, Yeager AE, Reynolds AJ. Glomerular Filtration Rate and Renal Volume in Dogs With Congenital Portosystemic Vascular Anomalies Before and After Surgical Ligation. *J Vet Intern Med*. 1999;13(5):465-471.
49. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Creatinine. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:198-199.
50. Hope, A. et. Al. Retrospective Study Evaluation of DGGR Lipase for Diagnosis, Agreement With Pancreatic Lipase and Prognosis in Dogs With Suspected Acute Pancreatitis. *Journal of Small Animal Practice*. 2021;62:1092-1100.
51. Lim, Sue Yee, et. al. TThe 1,2-O-Dilauryl-Rac-Glycero-3-Glutaric Acid-(6'-Methylresorufin) Ester (DGGR) Lipase Assay in Cats and Dogs Is Not Specific for Pancreatic Lipase. *Veterinary Clinical Pathology*. 2020;49:607-613.
52. Stockham SL, Scott MA. Thyroid Function. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:786-788, 793.
53. Reusch CE and Haberer B. Evaluation of Fructosamine in Dogs and Cats With Hypo- or Hyperproteinaemia, Azotaemia, Hyperlipidaemia, and Hyperbilirubinaemia. *Vet Record*. 2001;148(12):365-383.
54. Gal A, Trusiano B, et al. Serum Fructosamine Concentration in Uncontrolled Hyperthyroid Diabetic Cats Is Within the Population Reference Interval. *Vet Sci*. 2017;41(1):17.
55. Ji, J. Z., & Meng, Q. H. Evaluation of the Interference of Hemoglobin, Bilirubin, and Lipids on Roche Cobas 6000 Assays. *Clinica Chimica Acta*. 2011;412(17-18), 1550-1553.
56. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Globulins. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:341-343.
57. Stockham SL, Scott MA. Glucose, Ketoamines, and Related Regulatory Hormones. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:707-737.
58. Collicutt NB, Garner B, Berghaus RD, Camus MS, Hart K. Effect of Delayed Serum Separation and Storage Temperature on Serum Glucose Concentration in Horse, Dog, Alpaca, and Sturgeon. *Vet Clin Pathol*. 2015;44(1):120-127.
59. Burkhard MJ, Garry F. Artifactual Hypoglycemia Associated With Hemotrophic Mycoplasma Infection in a Lamb. *Vet Clin Pathol*. 2004;33(4):244-248.
60. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Glucose. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:347-349.
61. Rosenstein PG, Tennent-Brown BS, et al. Clinical Use of Plasma Lactate Concentration. Part 1: Physiology, Pathophysiology, and Measurement. *Journal of Vet Emergency and Critical Care*. 2018;28(2):85-105.
62. Stockham SL, Scott MA. Blood Gases, Blood pH, and Strong Ion Difference. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:559-592.
63. DiBartola, Stephen P. Introduction to Acid-Base Disorders and Respiratory Acid-Base Disorders. In: *Fluid, Electrolyte, and Acid-Base Disorders*, 4th Edition. Elsevier-Saunders; 2012:287-299.
64. Boothe DM. *Small Animal Clinical Pharmacology and Therapeutics*, 2nd ed. WB Saunders; 2001.
65. DiBartola SP, Willard MD. Disorders of Phosphorus: Hypophosphataemia and Hyperphosphataemia. In: *Fluid, Electrolyte, and Acid-Base Disorders in Small Animal Practice*. Ed. S DiBartola, Saunders Elsevier; 2006:195-209.
66. Kristensen AT, Klausner JS, Weiss DJ, Schultz RD, Bell FW. Spurious Hyperphosphatemia in a Dog With Chronic Lymphocytic Leukemia and an IgM Monoclonal Gammopathy. *Vet Clin Pathol*. 1991;20(2):45-48.
67. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Phosphorous. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:479-481.



References

68. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Potassium. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:492-494.
69. Hinderer J, Ludeke J, et al. Progesterone Concentrations During Canine Pregnancy. *Animals*. 2021;11:3369.
70. Hokamp JA and Nabity MB. Renal Biomarkers in Domestic Species. *Vet Clin Pathol*. 2016;45(1):28-56.
71. Siwinska N et al. Serum Symmetric Dimethylarginine Concentration in Healthy Horses and Horses With Acute Kidney Injury. *BMC Vet Res*. 2020;16(1):396.
72. International Renal Interest Society: IRIS Staging of CKD (modified 2023). Accessed November 13, 2023. http://www.iris-kidney.com/pdf/2_IRIS_Staging_of_CKD_2023.pdf
73. Coyne MJ et al. The Association Between Symmetric Dimethylarginine Concentrations and Various Neoplasms in Dogs and Cats. *Vet Comp Oncol*. 2022;20:846-853.
74. Gori E et al. Evaluation of Symmetric Dimethylarginine (SDMA) in Dogs With Acute Pancreatitis. *Vet Sci*. 2020;7(2):72.
75. McKenna M et al. Relationship Between Serum Iohexol Clearance, Serum SDMA Concentration, and Serum Creatinine Concentration in Non-azotemic Dogs. *J Vet Intern Med*. 2020;34:186-194.
76. Stockham SL, Scott MA. Thyroid Function. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:783-803.
77. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Thyroxine Total. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:624-626.
78. Stockham SL, Scott MA. Exocrine Pancreas and Intestine. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:739-762.
79. Stockham SL, Scott MA. Erythrocytes. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:110-221.
80. Willard MD, Tvedten H. Erythrocyte Disorders. In: *Small Animal Clinical Diagnosis by Laboratory Methods*, 5th Edition. Saunders Elsevier; 2012:38-62.
81. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Bilirubin. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:94-95.
82. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Bicarbonate. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:88-90.
83. Garner BC, Priest H, Smith J. Pseudo-Hypoproteinemia in a Hyperbilirubinemic Dog With Immune-Mediated Hemolytic Anemia. *Vet Clin Pathol*. 2014;43(2):266-269.
84. Gupta A, Stockham SL. (2014). Negative Interference of Icteric Serum on a Bichromatic Biuret Total Protein Assay. *Vet Clin Pathol*. 2014;43(3):422-7.
85. Vaden SL, Knoll JS, Smith FWK, Tilley LP. Total Protein. In: *Blackwell's Five-Minute Veterinary Consult: Laboratory Tests and Diagnostic Procedures, Canine & Feline*. Wiley-Blackwell; 2009:634-635.
86. Stockham SL, Scott MA. Lipids. In: *Fundamentals of Veterinary Clinical Pathology*, 2nd Edition. Wiley-Blackwell; 2008:771-782.
87. Radin MJ. Laboratory Evaluation of Lipids. In: *Veterinary Hematology and Clinical Chemistry*, 2nd edition. Wiley-Blackwell; 2012:480-496.
88. Harr KE. Clinical Chemistry of Companion Avian Species: A Review. *Vet Clin Pathol*. 2002;31(3):140-151.
89. Scope A, Schwendenwein I. Laboratory Evaluation of Renal Function in Birds. *Vet Clin Exot Anim*. 2020;23(1):47-58.
90. Campbell TW. Clinical Chemistry of Reptiles. In: *Veterinary Hematology and Clinical Chemistry*, 2nd Edition. Wiley-Blackwell; 2012:599-605.

