

BLOOD CHEMISTRY



BASICS

OVERVIEW

- Blood chemistry analysis can be used in the evaluation of several body systems
- Chemistry profiles may be somewhat amenable to tailoring to encompass variables of interest for the particular species being assessed (*See Table 1*)
- Chemistry profiles may be utilized in selected cases to improve accuracy of diagnosis or prognosis and monitoring of treatment response, ultimately helping clients to make a more informed decision
- These profiles are ancillary tests that should be performed based on historical and physical examination findings, and should never preclude a complete clinical examination
- Use of profiles allows interpretation of each analyte in the context of other analytes
- Grouping results helps identify disease processes affecting certain body systems

Investigation of herd health problems

- Blood chemistry profiles can also be used to evaluate the nutritional and metabolic status of groups of ruminants
- It is recommended to segregate the herd into groups of similar age and physiologic status that have been managed similarly in regard to feed, water, and mineral intake
- At a minimum, samples from 8-12 animals should be collected within each group
- Clinically diseased animals should be excluded because their results may reflect an individual animal problem rather than a herd health problem

Reference intervals (RIs)

- RIs typically represent the central 95% of values of 60-120 healthy reference animals
- Conversely, 5% of healthy animals are expected to have a result outside of the RI for any single test, and therefore a single result outside of the RI should not be overinterpreted
- Repeat testing is recommended when a test result does not fit the clinical context
- Use of the term “normal range” is discouraged as a test result can be within the RI and yet may not be appropriate for the patient’s condition, and therefore a ‘normal value’ might still indicate a disease process
- Biochemical analytes vary naturally over time, both as a result of disease processes and biological variation including age, gender, diet, breed, pregnancy, lactation, exercise, and drug administration
- Use of RIs partitioned based on biological characteristics may minimize inter-individual variation (age, breed, pregnancy status...)

Preanalytical and analytical variation

- Preanalytical variation is associated with patient preparation and handling, time of collection, and sample collection, storage, and handling
- Analytical variation is associated with accuracy and precision of the biochemistry analyzer
- Assessment of the analytical performance of in-clinic analyzers is recommended following instrument purchase and should be repeated annually at a minimum

- Standardization and control of preanalytical and analytical conditions may minimize intra- and inter-individual variation
- Participation in an external quality assurance program where possible is recommended to help ensure accuracy of results

Sample collection and handling

- Blood collected in a tube containing lithium heparin to generate plasma for rapid analysis, or no anticoagulant to generate serum (after clotting) is required for blood chemistry profiles
- Blood collected in a tube containing sodium heparin, EDTA, oxalate, or citrate is not suitable as these anticoagulants may affect several analytes including sodium and calcium concentrations.
- Lithium heparin tubes should be filled to completion to ensure the proper blood-to-anticoagulant ratio and gently inverted several times immediately after filling
- Excess lithium heparin may result in false hypocalcemia and hyperchloremia
- Blood collected in a tube containing no anticoagulant should be allowed to clot at room temperature 30 minutes, centrifuged at moderate speed (450 g) at least 15 minutes, and serum separated from cells within 60 minutes after collection
- Blood collected in a lithium heparin tube should be centrifuged at moderate speed (450 g) at least 15 minutes and plasma separated from cells within 30 minutes after collection
- Delayed harvesting of serum or plasma samples may result in hemolysis and false hypoglycemia, hyperkalemia, and hyperphosphatemia
- Serum or plasma samples can be stored at refrigerator temperature (4°C) for 24-36 hours
- Serum or plasma samples should be frozen at -20°C if delayed analysis is anticipated

Interferences

- Marked lipemia (index > 100) may result in false hyponatremia or hypochloremia when measured by indirect potentiometry
- Marked hemolysis (index > 300) may result in false increase in AST, LDH, or CK activities and potassium or phosphorus concentrations
- Marked icterus (index > 40) may result in false decrease in GGT activity and total protein or creatinine concentrations
- Hemolysis can be avoided using atraumatic venipuncture, careful sample handling, and rapid separation of serum or plasma from cells

COMPONENTS OF CHEMISTRY PROFILES

Renal Variables

- Urea and creatinine (Crt) are commonly used to evaluate renal function and ideally should always be interpreted in conjunction with the results of a urinalysis
- Urea is synthesized in the liver from nitrogen absorbed as ammonia from the rumen and nitrogen arising from the deamination of endogenous amino acids
- Therefore, high protein dietary intake or increased protein catabolism can cause increased blood urea nitrogen (BUN) concentration
- Causes of increased protein catabolism include prolonged exercise, fever, upper gastrointestinal (GI) hemorrhage, and release or administration of glucocorticoids
- Conversely, low protein dietary intake or hepatic insufficiency can cause decreased BUN concentration
- Urea is excreted by the kidneys into urine at a rate proportional to the renal tubular flow
- Therefore, a decrease in glomerular filtration rate (GFR) can cause increased BUN concentration

- Conversely, glucosuria or diabetes insipidus can cause increased urinary excretion of urea leading to decreased BUN concentration
- However, urea is also excreted into the rumen during times of low protein dietary intake to serve as a source of nitrogen for microbial protein synthesis
- Therefore, BUN concentration can be within the RI in some ruminants with renal disease
- As opposed to urea, Crt is a waste product of muscle metabolism almost exclusively excreted by the kidneys
- Therefore, Crt concentration is considered the test of choice for evaluating renal function and increased Crt concentration is usually caused by a decrease in GFR
- Alternatively, rhabdomyolysis can rarely cause increased Crt concentration due to release from muscle
- Rate of endogenous Crt production is proportional to muscle mass, and therefore Crt concentration is higher in males compared to females, and may be low in cachexic animals with poor muscle mass.
- Azotemia is defined as an increase in BUN and/or Crt concentrations
- **Prerenal azotemia**
 - Results from decreased renal perfusion and is usually associated with a urine specific gravity (USG) >1.025
 - Hypovolemia or circulatory shock can cause decreased renal perfusion
 - Causes of hypovolemia and circulatory shock include severe dehydration, severe blood loss, endotoxemia, sepsis, anaphylaxis, and heart failure
 - Prerenal azotemia can cause reduced renal tubular flow and increased urea reabsorption leading to marked increase in BUN concentration
- **Renal azotemia**
 - Results from any renal disease or injury that markedly decreases GFR
 - Acute renal failure may be reversible or irreversible and is usually associated with hematuria and a low USG in the face of dehydration (USG < 1.020)
 - Chronic renal failure is irreversible and usually associated with polyuria and isosthenuria caused by impaired renal concentrating ability (USG 1.008 -1.016)
 - BUN and Crt concentrations are not sensitive markers of renal function because renal azotemia develops when approximately 75% of the renal functional mass is lost, urine concentrating ability is lost prior to this time (~66% function lost)
 - Evaluation of serial BUN and Crt concentrations has been used to provide better monitoring and more accurate prognosis in patients with renal azotemia
- **Causes of acute renal failure**
 - Infections
 - Leptospirosis
 - Ischemia
 - Endotoxemia/sepsis
 - Extreme ruminal distension
 - Hypovolemia or severe dehydration
 - Severe blood loss
 - Toxicants
 - Drugs
 - Aminoglycosides (especially in neonates)
 - Ionophores (monensin or lasalocid)
 - Nonsteroidal anti-inflammatory drugs

- Oxytetracycline
 - Sulfonamides
- Metals
 - Arsenic
 - Cadmium
 - Copper
 - Lead
 - Mercury
 - Zinc
- Mycotoxins
 - Citrinin
 - Fumonisin
 - Ochratoxin
- Pigments (common)
 - Hemoglobin
 - Myoglobin
- Plants (common)
 - Cocklebur
 - Day blooming jasmine
 - Easter lily
 - Oxalate-containing plants
 - Oak leaves and acorns
 - Philodendron
 - Pigweed
 - Ponderosa pine
- **Causes of chronic renal failure**
 - Congenital defects
 - Hereditary renal oxalosis in Beefmaster cattle
 - Renal hypoplasia or aplasia
 - Chronic urethral obstruction (especially in castrated small ruminants)
 - Urolithiasis (common)
 - Inflammatory disorders
 - Amyloidosis
 - Glomerulonephritis
 - Pyelonephritis
 - Neoplasia (lymphoma, carcinoma...)
- **Post renal azotemia**
 - Urinary tract obstruction or rupture usually results in postrenal azotemia and is extremely common in ruminants, and also affects camelids.
 - Postrenal azotemia is usually caused by urolithiasis, especially in castrated small ruminants

Liver Variables

Hepatocellular leakage enzymes

- Increased aspartate aminotransferase (AST), sorbitol dehydrogenase (SDH), glutamate dehydrogenase (GLDH), and lactate dehydrogenase (LDH) activities usually result from increased release from damaged hepatocytes secondary to cell injury or death

- Magnitude of increase does not correlate with the severity of the disease because focal necrosis may result in higher increases than chronic diffuse liver disease in which hepatic mass is lost
- Hepatocellular enzyme activities are not a good measure of hepatic function
- Enzyme activities may not remain increased over time with chronic focal hepatic lesions including abscesses and neoplasms
- Hepatocellular injury is often associated with cellular swelling which may also cause intrahepatic cholestasis
- AST and LDH can be found in muscle cells and erythrocytes, and therefore muscle damage or hemolysis can cause increased AST and LDH activities
- Conversely, SDH and GLDH are specific markers of hepatocellular injury
- GLDH is more stable than SDH and is the enzyme of choice for delayed analysis
- LDH, SDH, and GLDH have a shorter half-life (few hours) than AST (few days)
- Goats and camelids have higher AST concentrations than cattle and sheep

Causes of hepatocellular injury

- Congenital defects
 - Hereditary hemochromatosis in Salers cattle
- Infections
 - Bacillary hemoglobinuria
 - Black disease
 - Leptospirosis
 - Liver abscesses
 - Liver flukes
- Ischemia
 - Abomasal volvulus or right displaced abomasum
 - Congestive heart failure
 - Endotoxemia/sepsis
 - Hypovolemia or severe dehydration
 - Severe blood loss
- Metabolic
 - Hepatic lipidosis (especially in overconditioned cattle)
- Neoplasia
 - Carcinoma
 - Lymphoma
- Nutritional deficiencies
 - Cobalt (especially in sheep)
- Toxicants
 - Drugs
 - Isoniazid
 - Oxytetracycline
 - Metals
 - Arsenic
 - Copper (especially in sheep)
 - Iron
 - Minerals
 - Phosphorus
 - Mycotoxins
 - Aflatoxin
 - Ochratoxin
 - Rubratoxin

- Sporidesmin (especially in sheep)
- Plants
 - Alsike clover
 - Bermudagrass
 - Blue green algae
 - Cocklebur
 - Coffeeweed
 - Cottonseed
 - Lantana
 - Lupine
 - Ponderosa pine
 - Pyrrolizidine alkaloid-containing plants (especially in cattle)

Cholestasis

- Increased gamma-glutamyl transferase (GGT) activity usually results from increased production in hepatocytes and biliary epithelial cells secondary to cholestasis
- Alternatively, colostrum intake causes increased GGT activity in neonates because GGT is present in mammary epithelial cells and colostrum
- Bilirubin is produced in macrophages by the degradation of hemoglobin and myoglobin, then conjugated in the liver and excreted into bile
- Bile acids are synthesized in the liver from cholesterol and then excreted into bile
- Therefore, cholestasis and/or hepatic insufficiency can cause increased total bilirubin and bile acid concentrations
- Alternatively, hemolysis or internal hemorrhage can cause increased bilirubin production leading to increased bilirubin concentration
- Bilirubin concentration usually exceeds 1.5 mg/dL before icterus is clinically detected

Causes of cholestasis

- Congenital defects
 - Congenital hyperbilirubinemia in Southdown and Corriedale sheep
- Intrahepatic disorders (common)
 - Severe hepatocellular injury (infections, ischemia, neoplasia, toxicants...)
- Extrahepatic disorders
 - Abdominal fat necrosis
 - Abomasal volvulus or right displaced abomasum
 - Duodenal sigmoid flexure volvulus (especially in dairy cattle)
 - Cholangitis or cholangiohepatitis
 - Cholelithiasis
 - Gallbladder neoplasia
 - Pancreatitis

Hepatic insufficiency

- Hepatic functions include albumin synthesis, uptake and excretion of bilirubin and bile acids, uptake of ammonia and conversion to urea, gluconeogenesis, and lipoprotein synthesis to export liver triglycerides (TGs)
- Therefore, hepatic insufficiency can cause increased ammonia, bilirubin and bile acid concentrations and decreased BUN, albumin, glucose, and TG concentrations
- Bilirubin, ammonia, and bile acids are not sensitive markers of liver function because abnormalities develop when approximately 75% of the hepatic functional mass is lost
- Ammonia absorption from the rumen is proportional to the ruminal ammonia production

- Therefore, high protein or urea dietary intake can cause increased blood ammonia concentration
- Plasma is the sample of choice for blood ammonia analysis but should be chilled on ice and analyzed within 30 minutes after collection or quick-frozen and analyzed within two days

Causes of hepatic insufficiency

- Congenital or acquired portosystemic shunt
- Severe and sustained hepatocellular injury (metabolic, neoplasia, toxicants...)

Plasma proteins

- Albumin, fibrinogen, and most globulins (α and β) are synthesized in the liver while γ -globulins are synthesized by B lymphocytes and plasma cells in the lymphoid organs
- Therefore, hepatic insufficiency can result in hypoalbuminemia and hypoglobulinemia
- Severe hypoalbuminemia (< 1 g/dL) usually results in ascites and dependent edema
- Acute and chronic inflammatory disorders usually cause increased fibrinogen and globulin concentrations, respectively
- Hyperalbuminemia is not clinically significant and caused by dehydration
- Plasma total protein (TP) concentration is usually higher than serum TP concentration because serum does not contain fibrinogen
- Serum TP concentration has been used to evaluate transfer of passive immunity in dairy calves, but is not a suitable method in camelids
- Less than 10% of calves sampled between 1-5 days of age should have serum TP concentration < 5.0 - 5.2 g/dL
- Decreased TP concentration has been associated with reduced growth rate, decreased first-lactation milk production, increased mortality, and increased risk of being culled

Causes of hypoalbuminemia, hypoglobulinemia and hypoproteinemia

- Dilution of plasma proteins
 - Excessive water retention
 - Chronic hepatic insufficiency
 - Congestive heart failure
 - Overadministration of intravenous fluids
- Decreased protein synthesis
 - Chronic hepatic insufficiency
 - Severe malabsorption or maldigestion
 - Severe malnutrition or starvation
- Excessive loss of protein
 - Via GI tract
 - Abomasal ulcers
 - Intestinal lymphangiectasia
 - Johne's disease in adult cattle
 - Parasitism (especially *Haemonchus* and *Trichostrongylus* spp.)
 - Salmonellosis
 - Via high-protein effusions
 - Peritonitis
 - Pleural effusion
 - Via urinary tract
 - Bracken fern toxicosis
 - Via skin
 - Bloodsucking parasites (lice, fleas, or ticks)
 - Severe burns

Causes of selective hypoalbuminemia

- Decreased albumin synthesis
 - Chronic inflammatory disorders (pneumonia, peritonitis, liver abscesses...)
- Excessive loss of albumin
 - Via kidneys
 - Amyloidosis
 - Glomerulonephritis
 - Pyelonephritis

Causes of selective hypoglobulinemia

- Immunodeficiencies
 - Juvenile llama immunodeficiency syndrome
 - Severe combined immunodeficiency in Angus cattle
 - Selective immunoglobulin G2 deficiency in red Danish cattle
 - Thymic and lymphocytic hypoplasia in Black Pied Danish and Friesian cattle
 - Transient hypogammaglobulinemia in Simmental cattle
- Inadequate colostrum intake in neonates (common)
 - Delayed colostrum feeding (dystocia, mismothering...)
 - Inadequate volume of colostrum ingested (especially in larger calves)
 - Poor quality colostrum (especially in dairy cattle)

Causes of hyperglobulinemia, hyperfibrinogenemia and hyperproteinemia

- Concentration of plasma proteins
 - Dehydration (common)
- Increased fibrinogen and globulin synthesis
 - Chronic inflammatory disorders (pneumonia, peritonitis, liver abscesses...)
 - Neoplasia

Causes of selective hyperfibrinogenemia

- Increased fibrinogen synthesis
 - Acute inflammatory disorders (mastitis, metritis, arthritis...)

Energy and lipid metabolism

- Ingested carbohydrates are fermented to short-chain fatty acids (acetate, propionate, and butyrate) by rumen microbes, and therefore most glucose is synthesized in the liver via a metabolic pathway called gluconeogenesis
- Glucose is under tight homeostatic control to allow for functioning of the brain and other tissues, and therefore is not a sensitive marker to investigate energy metabolism disorders
- Cattle, sheep, and goats have lower blood glucose concentration (40-80 mg/dL) than non-ruminants because they utilize short-chain fatty acids as a major source of energy
- Conversely, camelids have higher glucose concentration (80-160 mg/dL)
- Neonates have higher glucose concentration than adult ruminants because they have a higher metabolic rate
- Hyperglycemia usually results from release of catecholamines and/or endogenous corticosteroids caused by excitement, pain, food competition, handling, transportation, and extreme temperatures
- Hyperglycemia can also be caused by administration of catecholamines, glucocorticoids, dextrose-containing fluids, thiazide diuretics, morphine, ketamine, or xylazine
- Hyperglycemia is common in moribund animals and ruminants with circulatory shock, severe systemic disease, or neurological disorders

- Hyperglycemia (up to 300 mg/dL) is common in adult camelids because they have lower blood insulin concentration
- Therefore, camelids are more susceptible to factors that antagonize insulin action or decrease insulin production including catecholamines and glucocorticoids
- Marked hyperglycemia accompanied by severe dehydration may lead in camelids to a hyperosmolar disorder characterized by hypernatremia and neurological signs
- Diabetes mellitus has been described in cattle and camelids and is associated with persistent hyperglycemia, glucosuria, polyuria, and polydipsia
- Hypoglycemia usually arises from a combination of increased tissue use of glucose, reduced glucose intake, inadequate gluconeogenesis and reduced storage of glycogen
- Neonates are prone to hypoglycemia because they have limited hepatic glycogen stores
- Delayed separation of serum or plasma from cells may result in false hypoglycemia
- Blood collected in a tube containing sodium fluoride is suitable for delayed analysis of glucose because sodium fluoride inhibits glycolysis

Causes of hypoglycemia

- Excessive use of glucose
 - Extreme leukocytosis
 - Endotoxemia/sepsis (especially in neonates)
 - Insulin overdose
 - Lactation (especially in dairy cattle)
 - Neoplasia
 - Pregnancy toxemia (especially in beef cattle and small ruminants)
- Decreased gluconeogenesis
 - Hepatic insufficiency
 - Inadequate colostrum intake or fasting in neonates
 - Severe malabsorption or maldigestion
 - Severe malnutrition or starvation
- Reduced hepatic storage of glycogen
 - Hepatic insufficiency
- Decreased glucose availability induces fat mobilization by activation of hormone-sensitive lipases in adipose tissue leading to release of non-esterified fatty acids (NEFAs) in the blood
- NEFAs can be used directly as a source of energy by muscle, mammary gland, and liver
- NEFAs can also be partially oxidized to produce ketone bodies (acetone, acetoacetic acid, and beta-hydroxybutyric acid [BHBA]) or stored as TGs in the liver
- Excessive and sustained release of NEFAs usually causes fat accumulation in the liver and low TG concentration because ruminants have limited ability to export liver TGs
- Overconditioned animals are prone to develop hepatic lipidosis and excessive fat deposits at parturition are associated with higher postpartum NEFA concentration
- Increased BHBA, NEFA, and TG concentrations have been described in camelids with severe systemic disease secondary to decreased insulin production, increased insulin resistance, and/or azotemia
- Small ruminants and camelids have lower BHBA concentration than cattle, and therefore concentrations greater than 0.5-0.8 mmol/L should be considered clinically relevant
- Plasma is the sample of choice for NEFA but should be kept refrigerated or frozen until analysis because some TGs may otherwise degrade to NEFAs after collection
- Blood BHBA and NEFA concentrations have been used to evaluate dietary energy intake and transition period management in dairy cattle

- High prepartum and postpartum BHBA and NEFA concentrations have been associated with a greater risk of displaced abomasum, clinical ketosis, retained placenta, and metritis
- Less than 15% of cows sampled between 5-50 days after calving should have BHBA and NEFA concentrations greater than 1.2-1.4 mmol/L and 0.7 mEq/L, respectively
- Less than 15% of cows sampled between 2-14 days before calving should have BHBA and NEFA concentrations greater than 0.6 mmol/L and 0.3-0.5 mEq/L, respectively

Causes of increased BHBA, NEFA, and TG concentrations

- Decreased energy dietary intake
 - Ingestion of straw or poor-quality forages
 - Prolonged anorexia
 - Starvation
- High-energy demand
 - Lactation (especially in dairy cattle)
 - Late gestation (especially in beef cattle and small ruminants)
- Decreased insulin production and/or sensitivity
 - Diabetes mellitus
 - Excessive release of catecholamines or corticosteroids (especially in camelids)
 - Circulatory shock
 - Extreme temperatures
 - Food competition
 - Pain
 - Parturition
 - Severe systemic disease
 - Transportation
 - Overuse of catecholamines or corticosteroids

Muscle Variables

- Increased AST, creatine kinase (CK), and LDH activities usually result from increased release from damaged muscle cells secondary to cell injury or death
- As opposed to AST and LDH, CK is a specific marker of skeletal muscle injury
- CK is a very sensitive marker and therefore only increases of CK activity greater than 5,000 IU/L are considered clinically relevant
- CK and LDH have a shorter half-life (few hours) than AST (few days)

Causes of muscle injury or dysfunction

- Congenital defects
 - Chloride-channel myotonia in goats
 - Lysosomal α -1,4-glucosidase deficiency in Shorthorn and Brahman cattle
 - Myophosphorylase deficiency in sheep and Charolais cattle
- Infections
 - Clostridial myositis
 - Sarcocystosis
- Nutritional deficiencies
 - Selenium/vitamin E
 - Severe hypokalemia
- Toxicants
 - Coffeeweed
 - Cottonseed
 - Envenomation

- Ionophores (monensin or lasalocid)
 - White snakeroot
- Trauma (common)
 - Capture myopathy
 - Intramuscular injection
 - Prolonged recumbency
 - Strenuous exercise
 - Transportation

Acid-base status

- Bicarbonate (HCO_3^-) is the major extracellular buffer that helps maintain blood pH
- Acid-base disorders associated with a change in the HCO_3^- concentration are called “metabolic” disorders
- Total carbon dioxide (TCO_2) is the total extractable carbon dioxide from blood by addition of an acid and equals 95% of blood HCO_3^- concentration. It serves as a useful measure of blood bicarbonate status in chemistry profiles.

Causes of decreased HCO_3^- concentration (metabolic acidosis)

- Excessive generation of H^+ (common)
 - Ketosis
 - Lactic acidosis
- Decreased urinary excretion of H^+
 - Renal failure
 - Urinary tract obstruction or rupture
 - Distal renal tubular acidosis
- Excessive loss of HCO_3^-
 - Via GI tract
 - Diarrhea (especially in young ruminants)
 - Via kidneys
 - Proximal renal tubular acidosis

Causes of increased HCO_3^- concentration (metabolic alkalosis)

- Excessive loss or sequestration of H^+
 - Via GI tract (common)
 - Upper GI obstruction or stasis
 - Via kidneys
 - Respiratory acidosis
 - Hypokalemia
 - Overuse of diuretics (especially furosemide)
- Excess bicarbonate intake or production
 - Overuse of NaHCO_3 , lactate, citrate or $\text{Mg}(\text{OH})_2$
- Anion gap (AG) is defined as the difference between unmeasured anions and cations, and can be calculated as follows: $\text{AG} = ([\text{Na}^+] + [\text{K}^+]) - ([\text{Cl}^-] + [\text{HCO}_3^-])$
- Increased AG is usually caused by an increase in unmeasured anions including lactate, ketone bodies, and uremic acids
- Samples should be processed quickly to prevent a false increase in lactate concentration
- Only L-lactate concentration is measured by most biochemistry analyzers

Causes of increased AG

- Increased production of D-lactate caused by alterations in GI microbial flora
 - Diarrhea (especially in young ruminants)
 - Grain overload
 - Ruminal drinking syndrome in calves
 - Urea toxicosis
- Increased production of L-lactate caused by tissue hypoxia
 - Endotoxemia/sepsis
 - Hypovolemia or severe dehydration
 - Methemoglobinemia
 - Respiratory disorders
 - Severe anemia
 - Strangulating lesions of the GI tract
 - Strenuous exercise
- Increased production of ketone bodies
 - Decreased energy dietary intake
 - High-energy demand
 - Decreased insulin production and/or sensitivity (especially in camelids)
- Accumulation of uremic acids
 - Renal failure

Electrolytes

- Electrolyte concentrations are the net result of intake, excretion, and shifts between intracellular and extracellular fluids
- Sodium (Na^+) and chloride (Cl^-) concentrations are dependent on regulation of blood volume and plasma osmolality, and therefore should be interpreted with consideration of patient's hydration and volume status
- Camelids have higher Na^+ and Cl^- concentrations than other ruminants and appropriate reference intervals should be applied
- Shifting of potassium (K^+) into and out of cells and urinary excretion of Cl^- vary in response to changes in hydrogen ion (H^+) concentration, and therefore K^+ and Cl^- concentrations should be interpreted with consideration of patient's acid-base status
- Hemolysis and marked leukocytosis or thrombocytosis may result in false hyperkalemia

Causes of hyponatremia, hypochloremia, and hypokalemia

- Excessive loss or sequestration of Na^+ , Cl^- , and K^+
 - Via GI tract (common)
 - Blood loss
 - Diarrhea
 - Excess salivation
 - Upper GI obstruction or stasis (displaced abomasum, indigestion...)
 - Via kidneys
 - Ketonuria
 - Overuse of diuretics (especially furosemide and acetate isoflupredone)
 - Overuse of hypotonic fluids (dextrose 5%)
 - Renal failure (especially pyelonephritis)
 - Via third-space
 - Ascites
 - Peritonitis
 - Pleural effusion

- Uroperitoneum

Causes of selective hyponatremia and hypochloremia

- Increased shifting of water out of cells
 - Extreme hyperproteinemia
 - Overuse of osmotic diuretics (mannitol or glucose)
 - Persistent hyperglycemia
- Excessive water retention
 - Congestive heart failure
 - Chronic hepatic insufficiency
- Electrical neutrality must be maintained at all times in the blood and Na^+ and Cl^- are the major cation and anion, respectively
- Therefore, hypochloremia in the absence of hyponatremia suggests an increased concentration of an anion other than Cl^- including HCO_3^- , ketone bodies, and lactate

Causes of selective hypochloremia

- Metabolic alkalosis (increased HCO_3^- concentration)
- Metabolic acidosis with high AG (common)
 - Increased production of D-lactate
 - Increased production of L-lactate
 - Increased production of ketone bodies

Causes of selective hypokalemia

- Decreased dietary intake of K^+
 - Prolonged anorexia (common)
- Increased uptake of K^+ into cells
 - Excessive administration or release of catecholamines
 - Excessive administration or release of insulin
 - Metabolic alkalosis

Causes of hypernatremia and hyperchloremia

- Inadequate water intake +/- excessive salt intake
 - Administration of improperly mixed milk replacer or oral electrolytes
 - Lack of access to palatable water
 - Overuse of hypertonic saline
- Excessive loss of water
 - Via respiratory tract or skin
 - Fever
 - Heat stress
 - Prolonged tachypnea
 - Via GI tract
 - Grain overload
 - Via kidneys
 - Diabetes insipidus
 - Hyperosmolar syndrome in camelids
 - Overuse of osmotic diuretics (mannitol or glucose)
- Abomasal secretion of HCl is dependent on the generation of HCO_3^- , and therefore excessive loss of HCO_3^- can cause impaired secretion of HCl and accumulation of H^+ and Cl^- in the blood

Causes of selective hyperchloremia

- Inadequate water intake +/- excessive Cl^- intake
 - Overuse of KCl or NH_4Cl
- Excessive loss of HCO_3^-
 - Via GI tract
 - Diarrhea
 - Excess salivation
 - Via kidneys
 - Renal tubular acidosis

Causes of selective hyperkalemia

- Decreased urinary excretion of K^+
 - Oliguric or anuric renal failure
 - Urinary tract obstruction or rupture
- Increased shifting of K^+ out of cells
 - Metabolic acidosis
 - Severe intravascular hemolysis
 - Severe muscle injury

Minerals

- Phosphorus exists as either organic or inorganic phosphates (PO_4) in the blood
- However, only inorganic phosphate (Pi) concentration is measured and therefore is often referred to as the phosphorus concentration
- Calcium (Ca^{2+}) and magnesium (Mg^{2+}) are either free or bound to anionic molecules (albumin, globulins, citrate, and phosphate) in the blood
- Therefore, hypoalbuminemia can cause decreased total Ca^{2+} and Mg^{2+} concentrations
- Ca^{2+} and Pi concentrations are dependent on dietary absorption, urinary excretion, and osteoclastic bone resorption of Ca^{2+} and PO_4
- Intestinal absorption, urinary excretion, and bone resorption are modulated by parathyroid hormone (PTH) and vitamin D blood levels
- Pi concentration usually correlates well with short-term dietary PO_4 intake but is a very insensitive marker of chronic PO_4 deficiency
- Pi concentration is usually higher in growing animals because they have an enhanced dietary absorption of PO_4
- Mg^{2+} concentration is nearly totally dependent on dietary Mg^{2+} absorption
- Hypomagnesemia is a major risk factor for hypocalcemia because it reduces tissue sensitivity to PTH and PTH secretion in response to hypocalcemia
- Collecting blood in tubes containing Ca^{2+} -chelating anticoagulants (EDTA, oxalate, or citrate) may result in false hypocalcemia
- Blood Ca^{2+} and Mg^{2+} concentrations have been used to evaluate transition period management in dairy cattle
- Low postpartum serum Ca^{2+} concentration has been associated with higher postpartum NEFA concentration and greater risk of metritis
- Less than 15% of cows sampled within 12-24 hours after calving should have serum total Ca^{2+} concentration less than 8 mg/dL (2 mmol/L)
- Less than 15% of cows sampled between 5-50 days after calving should have serum total Mg^{2+} concentration less than 1.8 mg/dL (0.8 mmol/L)

Causes of hypocalcemia and hypophosphatemia

- Decreased intestinal absorption of Ca^{2+} and PO_4
 - Prolonged anorexia (common)
- Decreased vitamin D synthesis
 - Chronic renal disease
- Excessive loss of Ca^{2+} and PO_4
 - Via fetus
 - Late gestation (especially in beef cattle)
 - Multiple fetuses (especially in small ruminants)
 - Via kidneys
 - Polyuric renal failure
 - Overuse of furosemide
 - Via mammary gland
 - Milk or colostrum (especially in dairy cattle)
- Reduced tissue response to PTH
 - High dietary cation-anion difference (metabolic alkalosis)
 - Hypomagnesemia

Causes of selective hypocalcemia

- Hypoalbuminemia (common)
- Decreased intestinal absorption of Ca^{2+}
 - Dietary Ca^{2+} deficiency
 - Excess dietary PO_4 intake (low $\text{Ca}^{2+}:\text{PO}_4$ ratio)
 - Ingestion of oxalate-containing plants

Causes of selective hypophosphatemia

- Decreased intestinal absorption of PO_4
 - Dietary PO_4 deficiency
- Excessive loss of PO_4
 - Via kidneys
 - Prolonged diuresis
- Increased shifting of PO_4 into cells
 - Excessive administration or release of insulin

Causes of hypomagnesemia

- Hypoalbuminemia (common)
- Decreased ruminal or intestinal absorption of Mg^{2+}
 - Prolonged anorexia
 - Dietary Mg deficiency in milk-fed animals
 - Dietary nonprotein nitrogen excess (heavily fertilized, lush pastures)
- Increased urinary excretion of Mg^{2+}
 - Ketonuria
 - Overuse of osmotic diuretics (mannitol or glucose)

Causes of hypercalcemia and hyperphosphatemia

- Increased vitamin D activity
 - Excess dietary vitamin D intake
 - Ingestion of vitamin D-containing rodenticides
 - Ingestion of ergocalciferol-containing plants

Causes of selective hyperphosphatemia

- Decreased urinary excretion of PO_4
 - Renal failure
 - Urinary obstruction or rupture
- Excess P intake
 - Excess dietary PO_4 intake (low $\text{Ca}^{2+}:\text{PO}_4$ ratio)
 - Overuse of monosodium PO_4
 - Overuse of PO_4 enemas
- Increased shifting of PO_4 out of cells
 - Hemolysis

Causes of hypermagnesemia

- Decreased urinary excretion of Mg^{2+} (common)
 - Renal failure
- Excess Mg intake
 - Overuse of MgSO_4
- Increased intestinal absorption of Mg^{2+}
 - Overuse of MgO or $\text{Mg}(\text{OH})_2$
- Increased urinary resorption of Mg^{2+}
 - Increased PTH activity secondary to hypocalcemia

COMMON BLOOD BIOCHEMICAL FINDINGS IN ADULTS

- Upper GI obstruction or stasis is often associated with hypokalemia, hyponatremia, hypocalcemia, and metabolic alkalosis
- Oliguric or anuric renal failure and uroperitoneum are often associated with azotemia, hyponatremia, hypochloremia, hyperphosphatemia, and metabolic acidosis
- Hepatic lipidosis is often associated with hepatocellular injury, cholestasis, hypoglycemia, increased BHBA and NEFA concentrations, and metabolic acidosis
- Grain overload is often associated with azotemia, hyperphosphatemia, hypocalcemia, and metabolic acidosis
- Pregnancy toxemia is often associated with hypoglycemia and increased BHBA and NEFA concentrations

COMMON BLOOD BIOCHEMICAL FINDINGS IN NEONATES

- Failure of passive transfer is often associated with hypoglycemia and hypoglobulinemia
- Neonatal diarrhea is often associated with hypoglycemia, hyponatremia, hypochloremia, hyperkalemia, and metabolic acidosis
- Hyperosmolar syndrome in crias is often associated with hypernatremia, hyperkalemia, hyperchloremia, hyperglycemia, hypertriglyceridemia, azotemia, and metabolic acidosis

Table 1: components of commonly available blood biochemistry panels

General panel	Liver panel	Renal panel	GI panel	Muscle panel	Metabolic panel
Total protein	Total protein	Albumin	Total protein	AST	Total protein
Albumin	Albumin	BUN	BUN	CK	Albumin
Globulin	Globulin	Creatinine	Creatinine	Creatinine	Globulin
SDH or GLDH	SDH or GLDH	Calcium	Calcium	Calcium	AST
AST	AST	Phosphorus	Phosphorus	Magnesium	GGT

GGT	GGT	Bicarbonate	Glucose	Potassium	Total bilirubin
Total bilirubin	Total bilirubin	Sodium	Bicarbonate		BUN
CK	BUN	Potassium	Sodium	Optional	Creatinine
BUN	Glucose	Chloride	Potassium	Blood gases	Glucose
Creatinine	Triglycerides	Anion gap	Chloride		Calcium
Calcium			Anion gap		Phosphorus
Phosphorus	Optional	Optional	Optional		Magnesium
Magnesium	Ammonia	Lactate	BHBA		BHBA
Glucose	Bile acids		Blood gases		NEFA
Bicarbonate			Lactate		
Sodium					
Potassium					
Chloride					
Anion gap					

ABBREVIATIONS

- AG = anion gap
- AST = aspartate aminotransferase
- BHBA = beta-hydroxybutyric acid
- BUN = blood urea nitrogen
- Ca^{2+} = calcium
- CK = creatine kinase
- Crt = creatinine
- Cl^- = chloride
- EDTA = ethylenediaminetetraacetic acid
- GFR = glomerular filtration rate
- GGT = gamma-glutamyl transferase
- GI = gastrointestinal
- GLDH = glutamate dehydrogenase
- H^+ = hydrogen ion
- HCl = hydrogen chloride
- HCO_3^- = bicarbonate
- K^+ = potassium
- KCl = potassium chloride
- LDH = lactate dehydrogenase
- Na^+ = sodium
- Mg^{2+} = magnesium
- MgO = magnesium oxide
- $\text{Mg}(\text{OH})_2$ = magnesium hydroxide
- MgSO_4 = magnesium sulfate
- Na^+ = sodium
- NaHCO_3 = sodium bicarbonate
- NEFA = non-esterified fatty acid
- NH_4Cl = ammonium chloride
- Pi = inorganic phosphate
- PO_4 = phosphate
- PTH = parathyroid hormone
- RI = reference interval

- SDH = sorbitol dehydrogenase
- T_{CO_2} = total carbon dioxide
- TG = triglyceride
- TP = total protein
- USG = urine specific gravity

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Consulting Editor Erica C. McKenzie