Interpretation of the bovine CBC and chemistry

Meredyth Jones, DVM, MS, DACVIM
Oklahoma State University, Stillwater, OK 74075
Large Animal Consulting & Education, Perkins, OK 74059

Abstract
The complete blood count (CBC) and serum chemistry can be an important extension of the physical examination and may be used to suggest certain disease processes when exam findings are vague and can be useful for establishing a prognosis in many cases. The CBC is of greatest value in ruminants for characterizing anemia and in cases where inflammatory processes are suspected. The serum chemistry may be used to provide a direct diagnosis of organ dysfunction, but is also useful in helping to determine supportive care, prognosis and progression of a case over time.

Key words: CBC, chemistry, bloodwork

Complete blood count (CBC)
Whole blood in EDTA is the preferred sample for CBC, with the vacuum volume of the tube fully replaced by the sample. An unstained, air-dried blood film should be made within 15 minutes of collection and submitted with the remaining sample in the tube for laboratory analysis if the time to analysis is greater than 2 hours. An accurate CBC can be achieved in properly stored samples in tubes up to 24 hours. If samples are to be shipped to an outside laboratory, they should be wrapped in packing material to protect from breakage and shipped on ice. Automated analyzers must be properly calibrated for the species of interest and stained smears should undergo manual examination. Samples for serum chemistry may be obtained from red top tubes with the serum removed or from green top (heparin) tubes for more rapid analysis.

Anemia and inflammatory leukograms are among the most common abnormalities present on the CBC in ruminants.

Anemia
Anemia results from the loss of red blood cells by hemorrhage, hemolysis, chronic illness or nutritional deficiencies which result in decreased red cell production or lifespan. Reduced numbers of functional erythrocytes result in diminished oxygen delivery to the tissues.

A CBC or packed cell volume (PCV) with total plasma protein determination (TPP) should be performed on animals where anemia is suspected to differentiate between hemorrhagic and hemolytic causes of anemia.

If a decreased PCV is accompanied by a normal or increased TPP, hemolysis is more likely, as RBCs are being lost without loss of plasma proteins. If the TPP is decreased proportionate to the decrease in the PCV, hemorrhage is more likely, because RBCs and plasma proteins are lost in whole blood. In cases of acute hemorrhage, the PCV remains normal initially because red blood cells and plasma have been lost together and fluid shifts to restore blood volume may have not yet occurred.

Red blood cell parameters provided by the CBC can classify anemia into regenerative and non-regenerative. Evidence of regeneration in ruminants includes polychromasia, reticulocytes, basophilic stippling, Howell-Jolly bodies, nucleated red blood cells, increased mean corpuscular volume and decreased mean corpuscular hemoglobin concentration. Manual review of blood slides can be valuable to detect blood-borne parasites, such as *Anaplasma* spp. and *Mycoplasma* spp.

Inflammatory leukogram
The inflammatory leukogram is a phenomenon noted on the CBC in cases where there is a significant inflammatory process which overwhels the small marginalized pool of mature neutrophils, resulting in neutropenia and/or increased numbers of immature neutrophils.

When evaluating the complete blood count of ruminants, the neutrophil to lymphocyte ratio (N:L) is important to consider, in addition to the absolute number of cells. In adult cattle, the normal N:L ratio is 1:2, while in younger calves, neutrophils predominate.

The characteristics of an inflammatory leukogram include an initial neutropenia for the first 24-48 hours of severe inflammation, decreasing the N:L ratio. Generally, within the first 24 hours of acute inflammation, immature neutrophils (bands or earlier forms) will appear in the circulation, termed a left shift. A degenerative left shift refers to values in which immature forms outnumber segmented (mature) neutrophils or a left shift is present with concurrent neutropenia. A regenerative left shift indicates bone marrow response to inflammation where mature neutrophils outnumber immature cells. The bone marrow is generally able to replenish the bone marrow pool in 4-5 days, resulting in normal counts when inflammation is resolved.

The presence of hyperfibrinogenemia would further support a diagnosis of an acute inflammatory process. As inflammation progresses from days to weeks, the N:L will increase, often eventually returning to normal, even in the presence of ongoing inflammation. Additionally, there may be slight increases in lymphocyte and monocytes. The inflammatory leukogram should be differentiated from a stress leukogram, where there is a mildly increased N:L (usually 2-3:1) ratio with no left shift, accompanied by lymphopenia and eosinopenia.

The presence of a degenerative left shift is considered a poor prognostic sign if persistent, but it is not unusual in ruminants because of their initial neutropenic response to severe inflammation. An increasing number of septic sites is associated with commensurate decreases in prognosis, particularly in cases where polyarthritis or meningitis are present. Potential sequelae to sepsis should be anticipated including abscessation, adhesions and bacterial seeding of growth plates.

Plasma proteins
Plasma of cattle should appear grossly clear and colorless, but may have a yellow cast if animals are fed green feeds. Pathologic yellow plasma can occur with icterus, suggesting hemolysis (intravascular or extravascular) or liver disease. A red discoloration indicates hemolysis, either in vitro or in vivo (intravascular), which must be differentiated. This may be done by repeat sampling with strict attention to sample handling.
A TPP level can be achieved in house by use of a handheld refractometer. In order to interpret alterations in the TPP, one should consider the differential values of albumin and globulins. This will require additional testing than what is typically included on a CBC. If TPP is elevated, it must be determined if albumin or globulins are elevated, or both (panhyperproteinemia). Conversely, decreases in TPP may be due to low albumin, low globulins or both (panhypoproteinemia). The normal albumin:globulin (A:G) ratio is 0.84-0.94 in cattle.

### Panhyperproteinemia
- Dehydration
- Panhypoproteinemia
  - Nematode parasitism, Johne's disease, salmonellosis
  - Hemorrhage
- Hyperalbuminemia
  - Dehydration
  - Hypoalbuminemia
    - Inadequate production: Severe, chronic liver disease, poor intake
    - Loss: Renal, GI disease, hemorrhage, exudation
- Hyperglobulinemia
  - Chronic inflammatory disease: traumatic reticuloperitonitis, liver abscess, chronic pneumonia
- Hypoglobulinemia
  - Not common alone in mature ruminants
  - Neonates with failure of passive transfer

**Fibrinogen** is an acute phase protein, readily analyzed by most laboratories. Fibrinogen increases over a period of 2 days after initiation of inflammation of bacterial, viral or chemical origin or trauma. Dehydration may cause a relative hyperfibrinogenemia in addition to a relative hyperproteinemia. To correct an increased fibrinogen for hydration status, a TPP:fibrinogen ratio should be considered. If the ratio is <10:1, there is an absolute increase in fibrinogen, indicating inflammation. A potential problem with this analysis is that inflammation may also increase globulins, causing an absolute increase in the TPP, so clinical hydration status should always be considered when interpreting plasma proteins. A decreased fibrinogen is unusual, but may be caused by liver disease and disseminated intravascular coagulation.

### Serum chemistry
A routine serum chemistry includes values of electrolytes, macrominerals and organ-associated enzymes. The serum chemistry is of most value in cases of primary metabolic disease, monitoring systemic fluid and acid-base response to various disease processes, and detecting liver or kidney disease.

#### Chloride
Chloride generally moves in proportion to sodium. Hypochloremia with proportional decrease in sodium can be seen with diarrhea, blood loss, ascites, ruptured bladder or renal disease. In ruminants, a large amount of chloride is sequestered in the abomasum in the form of HCl. Hypochloremia without proportional decrease in chloride is seen in cases of gastrointestinal stasis and metabolic acidosis. Syndromes resulting in lack of adequate abomasal outflow, such as abomasal volvulus, displacement, lymphosarcoma near the pylorus and proximal intestinal obstruction can profoundly reduce chloride in the peripheral blood. Hyperchloremia is uncommon in ruminants but may be seen in cases of water deprivation and salt toxicity.

### Potassium
The primary location of potassium in the body is within the cell, resulting in relatively low levels in the circulating blood. Hypokalemia may be seen in cases of anorexia as forage is the primary source of potassium for ruminants, alkalosis, insulin or dextrose administration, mineralocorticoid administration, diuretic use, diarrhea and renal disease. Recumbency may be seen when blood levels fall below 2.5 mg/dL. Hyperkalemia is less common than hypokalemia in ruminants but may occur in cases of acidosis, urinary obstruction or may be an artifact of blood handling resulting in cell rupture.

### Calcium
Albumin and acid-base balance can alter calcium levels and the available calcium to participate in muscular function. The most accurate picture of calcium status is best obtained by measuring ionized calcium, which is available in some stall side analyzers, but it typically not included in a standard serum chemistry offered by reference laboratories. Hypocalcemia may be seen with onset of lactation, endotoxemia, oxalate-containing plant ingestion, chronic renal failure and ethylene glycol ingestion. Further, accidental analysis of EDTA-anticoagulated blood, which chelates calcium, can create an artificial low calcium on a blood report. Recumbency in cattle may occur in animals with a total calcium of < 5 mg/dL. Hypercalcemia in cattle is rare but may be seen with the ingestion of Vitamin D-containing plants.

### Phosphorus
Phosphorus is hormonally controlled similarly to calcium, with active movement in and out of the storage pool in bone. Hypophosphatemia may be seen in cases of milk fever with hypocalcemia (and is a common cause of poor response to calcium therapy alone), dextrose boluses, dietary deficiency/anorexia and ingestion of Brassica spp. While hypokalemia is a common early indicator of anorexia, hypophosphatemia generally quickly follows and is a good indicator of prolonged anorexia in ruminants. Recumbency due to hypophosphatemia occurs at levels < 1.0 mg/dL. Hyperphosphatemia is rare in ruminants.

### Magnesium
Magnesium has no specific hormonal control within the body; it is a simple in-and-out control with little storage. For this reason, daily and consistent intake of magnesium is critical to maintain physiologic levels. Hypomagnesemia may occur during lactation in adult cows eating high moisture, high potassium forages, cattle consuming poor quality hay in winter, calves on wheat pasture, and in transported animals on marginal diets. Recumbency occurs when blood levels fall below 1.1 mg/dL. Hypomagnesemia is rarely seen in cattle, but may be seen with renal disease and is associated with a poor prognosis.

### Blood urea nitrogen (BUN) and creatinine
Blood urea nitrogen and creatinine represent the waste products of protein and intestinal microflora metabolism (BUN) and muscle metabolism (creatinine). These waste products are excreted via the kidneys and, as such, these are generally considered indicators of renal disease. In ruminants, diet and the ability to recycle urea in the gastrointestinal tract limit the
sensitivity of BUN elevations in diagnosing inadequate excretion of the toxin. Creatinine is considered the more reliable indicator as it is generally elevated in disease prior to elevations in BUN. Azotemia may be pre-renal, renal, or post-renal. Pre-renal indicating poor renal perfusion or reduced glomerular filtration rate, renal indicating true renal insufficiency or post-renal, indicating urinary outflow obstruction. Mild elevations in creatinine may be observed in very heavily muscled bulls.

**Alkaline phosphatase (ALP)**
Alkaline phosphatase is associated with both the biliary tract and osteoblasts of bone. Outside of elevations in growing young animals due to osteoclastic activity, elevated ALP is an indicator of biliary obstruction. Elevations may be seen with pyrrolizidine alkaloid toxicity, hepatic lipidosis and liver fluke infestation.

**Gamma-glutamyltransferase (GGT)**
Although GGT may be found in a variety of organs, including the mammary gland, pancreas, gastrointestinal tract and urinary and reproductive tracts, serum levels are not impacted by alterations in these organs. Rather, its association with the biliary tract impacts serum levels and elevations in GGT reliably indicate liver disease and biliary obstruction. Common causes of GGT elevations in ruminants include pyrrolizidine alkaloid toxicity and liver fluke infestation. Because GGT is found in the mammary gland, serum GGT is elevated in nursing neonates.

**Aspartate aminotransferase (AST)**
AST is both a muscle and liver enzyme, but clinical elevations are most often seen with muscle injury or crush, as in recumbent cattle. AST is less sensitive and specific than CK, but has a longer half-life of 20 hours to 10 days. For this reason, it is not very useful for monitoring of recovery at regular intervals post-injury. It has been shown to have faculty in predicting non-recovery in dairy cattle. Cattle with an AST of > 171 IU/L had an 80% greater chance of non-recovery than those with levels < 171 IU/L.³

**Creatine kinase (CK)**
Creatine kinase is sensitive and specific for cardiac and skeletal muscle. It has a very short half-life in cattle (4 hours) and therefore is useful to monitoring an animal’s recovery over time. After injury to muscle, CK levels will begin to use significantly at 12 hours, peaking usually at 48 hours and will gradually go down, sometimes if the animal remains recumbent. A persistent rise in CK over time indicates ongoing injury to the muscle, as is often seen in very heavy animals that are recumbent.

**References**