Clinical Pathology in the Adult Sick Horse

The Gastrointestinal System and Liver

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KEYWORDS

- Hematology • Chemistry • Enteropathy • Hepatopathy • Hyperammonemia

KEY POINTS

- Horses with acute inflammatory intestinal conditions, for example, enteritis and colitis, often present with clinical and hematologic evidence of endotoxemia, plasma volume contraction, acid-base disturbances, and electrolyte derangements.
- Horses with chronic enteropathies frequently display evidence of malabsorption and protein loss, including weight loss despite good appetite, hypoproteinemia characterized predominantly by hypoalbuminemia, and blunted glucose-absorption curves.
- Liver disease is common in horses but liver failure is uncommon.
- Liver-specific enzymes sorbitol dehydrogenase and glutamate dehydrogenase reflect hepatocellular injury, whereas γ-glutamyltransferase indicates biliary disease. Other enzymes, such as aspartate aminotransferase, lactic dehydrogenase (hepatocellular), and alkaline phosphatase (biliary), may support the diagnosis of hepatopathy, but these enzymes are not liver-specific.
- Liver function tests include conjugated and unconjugated bilirubin, ammonia, bile acids, and coagulation tests (prothrombin/partial thromboplastin times).

INTRODUCTION

The gastrointestinal tract and liver comprise key components of the equine digestive system and together have important functions in metabolism, digestion, detoxification, and synthesis. Disorders of the gastrointestinal tract and liver are common in clinical practice, whereas failure of either organ system is less common. Hematologic and biochemical analysis can be helpful for identifying organ dysfunction, narrowing down the differential diagnostic list, and, in many cases, monitoring progress and response to treatment. This article details hematologic and biochemical tests that are important

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in the evaluation of intestinal and hepatic diseases and reviews bloodwork trends frequently observed in adult horses affected by enteropathy or hepatopathy.

ACUTE GASTROINTESTINAL DISEASE

Horses with acute inflammatory intestinal conditions, for example, proximal enteritis and colitis, often present with hematologic and biochemical findings suggestive of endotoxemia (leukopenia characterized by neutropenia), plasma volume contraction (increased hematocrit, high urine-specific gravity [USG], and prerenal azotemia), and electrolyte derangements (hyponatremia, hypochloremia, and hypomagnesemia). These derangements result from intestinal inflammation and mucosal barrier disruption, leading to fluid, electrolyte, and protein loss as well as endotoxin and bacterial translocation into the blood stream. Neutropenia reflects neutrophil margination and sequestration in the intestinal tract, with left shift and toxic changes commonly observed. Strong ion acidosis characterized by hyponatremia and hyperlactatemia also is common, although a hypoproteinemic alkalosis occasionally may occur.[1] Hemoconcentration and plasma volume contraction occurs secondarily to fluid sequestration and loss via the intestines. Lower than expected total protein (especially albumin) concentration, considering the relative erythrocytosis and estimated degree of dehydration, occurs frequently in horses with acute colitis and indicates protein loss from the diseased bowel. Hypocalcemia often is observed in horses with hypoalbuminemia and reflects the high proportion of protein-bound calcium in circulation. Ionized (unbound) calcium, which better reflects physiologic calcium homeostasis, usually is normal. Clinicopathologic derangements can vary in severity between cases, depending on the degree of intestinal damage and, in 1 study, severity of electrolyte loss, hemoconcentration, and prerenal azotemia all were predictors of survival.[2]

Measurement of L-lactate concentrations in blood and/or peritoneal fluid has become an increasingly popular diagnostic and prognostic indicator in horses presented for colic and other acute intestinal disorders. Lactate is produced by mammalian cells under anaerobic conditions during global or local tissue ischemia/hypoxia.[3] In horses presented for colic, peritoneal lactate concentrations are higher than blood lactate concentrations (sampled at the same time) in horses with surgical lesions necessitating intestinal resection and anastamosis.[4] In practice, peritoneal fluid lactate concentrations that are twice that of blood are highly suggestive a strangulating surgical lesion. This diagnostic test can be particularly helpful in identifying strangulating lesions early in the course of disease (hours), during which horses may display signs of severe abdominal pain but still have normal hematologic and biochemical profiles.

Blood lactate concentrations alone may also be of prognostic value in horses with acute intestinal disease. In one prospective study evaluating horses presented for surgical colic, higher blood lactate levels at admission and at 24 hours and 72 hours postoperatively was associated with non-survival.[5] Markedly increased blood lactate concentrations at admission are associated with poorer outcomes in horses with large colon volvulus,[6] and horses presenting for colitis with blood lactate concentrations that remain increased in the face of fluid therapy are less likely to survive to discharge.[7,8] In the latter cases, monitoring changes in blood lactate concentration after fluid resuscitation generally is of greater prognostic value than a single measurement.

It has been suggested that hyperlactatemia in horses should be categorized by the physiologic mechanism of excessive lactate production as a means to potentially increase its utility as a diagnostic and prognostic test.[9] Type A hyperlactatemia occurs

in response to inadequate tissue perfusion and oxygenation and is observed in horses with dehydration, hypovolemia, and hypoxemia. Type B hyperlactatemia is produced by inflamed and/or ischemic tissues and is observed in horses with inflammatory or strangulating intestinal lesions. Although type A hyperlactatemia generally responds rapidly to restoration of tissue perfusion (often through volume replacement and fluid therapy), type B hyperlactatemia persists until the underlying inflammatory or ischemic condition is corrected. Many horses with inflammatory or ischemic intestinal lesions also are dehydrated and volume-contracted, and increased lactate concentrations in these patients likely represented simultaneous type A and type B hyperlactatemia. Applied clinically, these concepts support serial measurement of blood lactate as a means to identify the source of hyperlactatemia and provide useful information regarding severity and prognosis for survival. This was corroborated by a prospective observational study of horses presenting for gastrointestinal disease, in which a rapid reduction in blood lactate concentration in response to correction of dehydration and restoration of perfusion (type A) was associated with increased survival, whereas persistently increased blood lactate or lactate concentrations that increased in the face of supportive therapy (type B) were associated with more severe intestinal lesions and poorer survival outcomes.[9] This also is true for peritoneal fluid, in which lactate concentrations that remain increased in the face of medical therapy is suggestive of a strangulating or severely inflamed lesion in horses presented for colic.[10]

Lactate concentrations may be measured in blood or peritoneal fluid using either benchtop or portable handheld analyzers, although variable results may be observed with handheld analyzers.[11] The same instrument should be used when comparing blood and peritoneal fluid lactate concentrations in a single patient. Compared with horses, ponies presenting for gastrointestinal disease have higher blood lactate concentrations (median 2.8 mmol/L vs 1.6 mmol/L in 1 study).[12] This difference may be explained by carbohydrate metabolism via the Cori cycle, in which blood glucose (which also was found to be higher in the study ponies) leads to the generation of lactate.[13]

Increased liver enzyme activities occasionally are observed in horses presented for acute gastrointestinal disorders and likely reflect anatomic proximity of the 2 organ systems and direct communication via the biliary system and portal circulation. A retrospective study examining horses with colic observed that increased g-glutamyl-transferase (GGT) activity was observed in 49% of horses with right dorsal displacement but only 2% of horses with left dorsal displacement of the large colon, a finding attributed to extrahepatic biliary obstruction from bile duct compression by the displaced colon.[14] Increased liver enzyme activities (GGT, alkaline phosphatase [ALP], and aspartate aminotransferase [AST]) also have been reported in horses with proximal enteritis, which is thought to be due to hepatic injury secondary to ascending enteric bacteria from the common bile duct, absorption of endotoxin from the portal circulation, and/or hepatic hypoxia from systemic inflammation.[15]

Hyperammonemia with clinical signs of encephalopathy occasionally is observed in horses with acute gastrointestinal disease in the absence of concurrent liver disease.[16] These horses present most frequently for diarrhea, colic, and neurologic signs (dullness, blindness, aimless wandering, and obtundation). Blood ammonia concentrations can range from slightly above normal to more than 1000 μmol/L (case 1, discussed later), and higher concentrations at admission were associated with nonsurvival in 1 retrospective report.[16] Hyperammonemia of gastrointestinal origin also has been reported as a cause of neurologic signs and high fatality rates in horses infected with equine coronavirus.[17,18]

Ammonia concentrations in blood samples rapidly increase with storage after collection and, therefore, special handling is required for accurate measurement. Blood should be drawn into EDTA or heparin anticoagulant tubes and centrifuged and plasma separated from red blood cells immediately. If within 1 hour of the laboratory, plasma may be chilled on ice until analysis. If analysis is greater than 1 hour from collection or the sample must be shipped, the separated plasma should be immediately frozen and shipped overnight on ice. It is imperative that the sample remain frozen until analysis, because thawed samples quickly accumulate ammonia.[19]

CHRONIC GASTROINTESTINAL DISEASE

Chronic enteropathies are uncommon in horses and often present clinically as weight loss, diarrhea, and/or recurrent colic. Weight loss is a consistent presenting complaint, reported in 78% of horses in 1 retrospective study.[20] Differential diagnoses for chronic enteropathy include inflammatory bowel disease and alimentary lymphoma, both of which can affect the small intestine, large colon, or both, as well as parasitism, salmonellosis, sand enteropathy, and right dorsal colitis (RDC), which primarily affect the large colon. Although intestinal biopsies (duodenal and/or rectal) can be helpful for determining the nature and extent of intestinal involvement in some horses,[20,21] clinical signs and serum biochemistry results also can provide clues as to the nature and severity of disease. Horses with chronic colonic disease often have impaired water resorption and present with chronic diarrhea. In 1 retrospective study, the clinicopathologic abnormalities detected most frequently in horses with chronic diarrhea included neutrophilia, hypoalbuminemia, hyperglobulinemia, and increased ALP activity.[22] Clinical signs of dehydration and endotoxemia typically observed in acute colitis cases are less common, and many horses with chronic enteropathies are able to compensate for excessive fecal water loss and maintain normal or nearly normal clinicopathologic profiles.

Hypoproteinemia predominantly characterized by hypoalbuminemia is a common finding in horses affected by chronic enteropathy. The severity of hypoproteinemia and hypoalbuminemia may be of prognostic value and was found positively correlated with nonsurvival in a retrospective study examining horses with weight loss despite good appetite.[23] RDC, a complication of nonsteroidal anti-inflammatory drug (NSAID) treatment, is associated with particularly marked protein loss, often resulting in plasma protein concentrations less than 5.0 g/dL and albumin concentrations less than 1.5 g/dL. Although any NSAID is thought to be capable of causing RDC, phenylbutazone, a nonselective cyclooxygenase inhibitor, frequently is implicated. Prolonged administration of phenylbutazone, at 8.8 mg/kg, orally every 24 hours, to 12 healthy adult horses resulted in consistent hypoalbuminemia in 1 clinical trial. Neutropenia also was observed (likely due to marginalization and sequestration in inflamed sections of bowel), and 2 horses developed clinical colitis.[24] The combination of phenylbutazone and flunixin increased the risk for ulcerative damage to the intestinal tract and created severe gastric ulceration and fatal colitis in 1 prospective study.[25] Serial monitoring of albumin concentrations is advisable in horses receiving NSAID administration and a diagnosis of RDC should be strongly considered in horses that develop hypoproteinemia and hypoalbuminemia during treatment. This diagnosis is supported further by observing localized right dorsal colon wall thickening on transabdominal ultrasound (**Fig. 1**).

In addition to routine hematologic and biochemical testing, the oral glucose absorption test can support a diagnosis of chronic protein-losing enteropathy. This test is simple to perform, requires no specialized equipment, and can be performed
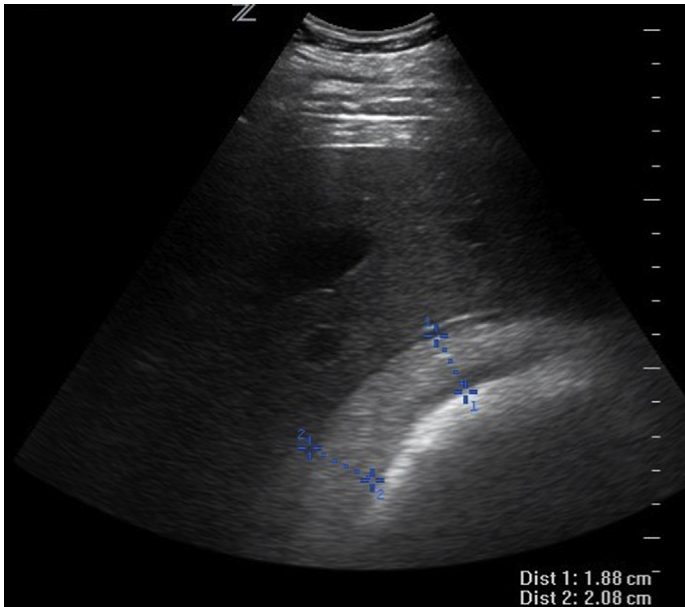
Fig. 1. Ultrasonographic image obtained from the right fourteenth intercostal space of a 3-year-old standardbred gelding with RDC secondary to chronic phenylbutazone administration. The total protein and albumin concentrations were 2.9 g/dL and 0.7 g/dL, respectively, on an initial serum biochemistry panel. The right dorsal colon wall (*blue callipers*) is markedly thickened, measuring between 1.9 cm and 2.1 cm (normal <0.4 cm). The gelding was treated successfully with colloid replacement, misoprostol, gastroprotectants, and discontinuation of the phenylbutazone.

stall-side. In 2 retrospective studies, abnormal glucose absorption was demonstrated in 70% of horses with inflammatory bowel disease[20] and in 57% of horses with chronic diarrhea.[22]

To perform an oral glucose absorption test

1. Fast horse for 12 hours to 18 hours.
2. Measure blood glucose.
3. Administer glucose at 1-g/kg body weight as a 20% solution to the unsedated horse via nasogastric tube.
4. Measure blood glucose every 30 minutes for 2 hours, then every hour for 4 hours.

Accurate serial blood glucose measurements can be obtained easily stall-side using point-of-care glucometers calibrated specifically for horses.[26] In normal horses, blood glucose concentrations should rise to higher than 185% of baseline by 120 minutes post–glucose administration and should return to normal by 6 hours. Horses with malabsorptive enteropathy display a delayed rise in blood glucose and diminished peak concentrations compared with normal horses.[27]

LIVER DISEASE

Liver disease may result from toxic, infectious, hypoxic, neoplastic, vascular, or metabolic causes.[28] Liver disease is detected most commonly by measuring activity of liver-specific enzymes in serum or plasma. Increased hepatic enzyme activity often is a result of secondary liver disease from toxemia, hypoxia, and so forth, and hepatic

function remains normal in most horses with these disorders. Primary liver disease most commonly occurs from toxic, infectious, or metabolic causes and may progress to loss of function and clinical signs of hepatic failure. Liver (hepatobiliary) failure occurs when this system has lost some or all of its functionality. Failure generally occurs when greater than 70% of hepatic function is lost and this can be determined by clinical evidence (eg, jaundice, photosensitization, and central nervous system signs) of liver failure, along with abnormal liver function tests, such as bile acids, ammonia, and so forth. It is critical to remember that liver enzyme activities are not indicators of hepatic function! Interpretation of biochemical results is always best made in combination with anamnesis and a thorough clinical examination. Clinical examination, biochemical test results, ultrasonographic findings, and, if indicated, liver biopsy are best used in combination to determine the importance of the liver disease, possible causes, proper treatments, and prognosis.

LIVER ENZYME ACTIVITY IN HORSES WITH PRIMARY LIVER DISEASE

Biochemical testing is imperative when attempting to diagnose liver disease or liver failure. From a clinical perspective, biochemical results can be helpful in narrowing the differential diagnoses for liver analyte changes and, when evaluated over time, help predict prognosis. Biochemical enzyme testing, especially GGT activity, also can be used to identify subclinical hepatotoxin exposure, such as during outbreaks of pyrrolizidine alkaloid toxicity.[29] Enzyme testing can be useful in determining treatment duration, for example, serial GGT measurements to determine duration of antimicrobial treatment of bacterial cholangiohepatitis. Equine liver-specific enzymes include sorbitol dehydrogenase (SDH), glutamate dehydrogenase (GLDH), and GGT, which reflect hepatocellular injury (SDH and GLDH) and cholestasis, biliary necrosis, or hyperplasia (GGT), respectively. AST, lactic dehydrogenase (LDH), and ALP also reflect hepatocellular (AST and LDH) and biliary (ALP) disease, but these enzymes are not liver-specific[28,30,31] (**Table 1**). Increased activities of SDH, GLDH, and AST occur with even mild acute hepatocellular injury, and the magnitude of the enzyme increase may not correspond to the functional status of the liver. SDH is released from the cytosol of the hepatocyte and has a short half-life (approximately 12 hours). Thus, repeated SDH measurements can be helpful in determining resolution or progression of acute hepatocellular disease.[28] The clinical use of SDH measurements for detection of liver disease is affected by its instability in shipped or nonfrozen stored samples. Samples that are refrigerated may be relatively stable for up to 24 hours.[32] GLDH is located in the mitochondria of hepatocytes, and activities are abnormally high in many horses with acute hepatocellular disease. The calculated sensitivities of increased GLDH activity for the detection of hepatic necrosis and of hepatic lipidosis were 78% and 86%, respectively, in 1 study.[31] GLDH is more stable and has a slightly longer half-life than SDH (see **Table 1**). The improved stability of GLDH makes it a recommended test for detecting acute hepatocellular disease when sample shipping is required. Horses with severe chronic fibrosis (cirrhosis) occasionally may have SDH and GLDH activities within normal reference intervals.

GGT is an excellent screening test for hepatic disease in the horse.[33] In the authors' experience, it is rare that a horse with moderate to severe liver disease does not have increased GGT activity. Increases in GGT activity also are highly specific for liver disease because diseases in other body organs (kidney and pancreas) that contain GGT do not result in abnormal serum or plasma GGT activity. GGT activity may continue to increase for several days after an acute hepatic insult has resolved, presumably due to biliary hyperplasia.[28] Although the greatest increase in GGT activity is seen with biliary disease,

Table 1
Serum biochemical enzymes commonly used to detect equine hepatic disease[a]

| | Hepatocellular Injury | | | Biliary Injury/Cholestasis | |
	Glutamate Dehydrogenase	Sorbitol Dehydrogenase	Aspartate Aminotransferase	γ-Glutamyltransferase	Alkaline Phosphatase
~Half-life	12–24 h	<12 h	7 d	3 d	3 d
Sensitivity	+++	+++	+++	++++	++
Specificity	+++	++++	+	+++	+
Stability	++	+	++++	++++	++++

+, Lowest; ++++, highest.
  [a] These are estimated numbers based on review of available reports.[28,30,31,33,34]

small amounts of GGT can be released after hepatocellular injury.[34] If multiple horses stabled together have increased GGT activity, toxic causes should be considered.

In horses with hepatic disease, relative increases in hepatocellular versus biliary enzyme activities can be helpful when formulating a causative differential diagnostic list. For example, if GGT activity is markedly increased and SDH, GLDH, or AST activities are increased only modestly, diseases that predominantly affect the biliary system, for example, cholangiohepatitis, should be considered most likely. Conversely, if hepatocellular-derived enzyme activity is very high and GGT activity is increased only mildly, then diseases that predominantly affect hepatocytes, for example, serum hepatitis, are more likely.[28] Although somewhat dependent on the duration of disease, many causes of severe liver disease may result in a similar increase in hepatocellular and biliary enzyme activities, for example, pyrrolizidine alkaloid toxicity and hepatic lipidosis.

The magnitude of increase in hepatocellular-derived enzymes may not correspond to hepatic function, and enzyme results should be viewed as a measure of disease and not a measure of function. In addition, the magnitude of changes in hepatocellular enzymes does not determine prognosis. For example, during a 2-year farm investigation of a forage-associated hepatopathy in Europe, more than 70 weanlings, yearlings, and adults had increased GGT (up to 1000 IU/L) and GLDH (up to 1200 IU/L) activities, yet total bilirubin and bile acid concentrations remained within the reference interval in almost all of the horses and no horses demonstrated signs of hepatic failure (Divers TJ 2016, personal observation). Instead, the prognosis for horses with liver disease is best determined by function test abnormalities (discussed later), etiology, fibrosis on liver biopsy, and presence or absence of hepatic encephalopathy.[35]

LIVER ENZYME ACTIVITY IN HORSES WITH SECONDARY LIVER DISEASE

Hepatocellular enzyme activities often are increased with many systemic disorders. This likely reflects inflammatory, vascular, hypoxic, and toxic insults to the liver secondary to the primary disorder and, in these cases, diagnostic and therapeutic attention should focus on the primary disease. Bile acid concentrations, which generally are considered a liver function test, can be increased in some horses with intestinal disorders, such as colic, enteritis, and equine dysautonomia. Moderate to markedly increased bile acid concentrations in horses with colic are associated with a guarded prognosis.[36] Horses with displacement of the left colon to the right occasionally have increases in GGT activity along with increased concentrations of direct (conjugated) bilirubin and bile acids, resulting from obstruction of bile flow.[14] These horses have an excellent prognosis after correction of the displacement.

A small number of racehorses may have moderate increases in GGT (50–140 IU/L) activity with either no or only mild increases in other liver-derived enzyme activity, including ALP. The serum/plasma GGT activity generally remains in the 50-IU/L to 140-IU/L range for weeks in these horses if kept in work. Studies have demonstrated that GGT activity is correlated to cumulative training load and racing frequency and considered a maladaptation to training.[37–40] Oxidative stress has been hypothesized as a cause.[28] The incidence of this increased GGT activity in racehorses in 1 study was 18%,[41] but in some stables it may be higher. This abnormality has not been proved to affect performance, although many trainers believe there is a correlation between the high GGT syndrome and reduced performance.

LIVER FUNCTION TESTS

Liver function tests become abnormal only after 70% or more of hepatic function is lost.[42] Liver function test include increased direct (conjugated) and indirect

(unconjugated) bilirubin concentrations, ammonia and bile acid concentrations, and coagulation tests, such as the prothrombin and activated partial thromboplastin times.[28,42,43] In the authors' experience, an increase in conjugated bilirubin above the normal upper limit of the reference interval is a common finding in horses with liver failure. When the abnormally high conjugated bilirubin concentration comprises 25% or more of the total bilirubin concentration, this is suggestive of a predominant biliary and obstructive disease.[44] Increases in conjugated bilirubin (which is water-soluble) result in bilirubinuria, which may be detected by urine test strips or observing green-colored bubbles after shaking the urine. Rarely, a horse without liver disease has a positive bilirubin reading on the urine test strip. Increased unconjugated bilirubin concentration is a moderately sensitive test for liver failure but lacks specificity because increases also may occur with anorexia and hemolysis or, on rare occasions, may be seen in a healthy horse.[31] The latter condition may be caused by a congenital deficiency in glucuronyl transferase, and affected horses can maintain total bilirubin concentrations of 9 mg/dL or greater.[45]

Bile acid concentrations above 20 μmol/L are a good predictor of liver failure.[33,35] Milder increases (up to 20 μmol/L) may occur in a few horses without hepatic disease that are anorexic for 2 or more days.[46] Horses with chronic liver disease and persistently increased bile acid concentrations greater than 20 μmol/L have a guarded to poor prognosis.[35,47] Bile acid concentrations should not be used as a predictor of prognosis in horses with acute liver disease.

In states of negative energy balance, triglyceride concentrations frequently are increased in horses but hepatic lipidosis resulting in liver failure rarely occurs unless visible lipemia is noted.[48] Therefore, high triglyceride concentrations alone should not be used to diagnose hepatic lipidosis and liver failure.

Albumin concentrations rarely are low in horses with acute (6%) or chronic (18%) liver failure, and hypoalbuminemia is neither a sensitive nor specific test for liver failure in the horse.[49] Conversely, globulins are increased in 48% of horses with liver failure.[49] The albumin-to-globulin ratio is more likely to be low in horses with chronic versus acute liver disease and failure.[49] Although an inconsistent finding, urea nitrogen concentrations may be low with liver failure, presumably due to decreased synthesis in the urea cycle.[50]

Clotting times often are increased in horses with liver failure due to insufficient hepatic synthesis of clotting factors II, V, VII, IX, X, XI, and XII.[51] Coagulation abnormalities may not be detected in some horses with liver failure, even in those with obstructive biliary disease and failure.[44] This is somewhat surprising considering the importance of bile acids in the absorption of vitamin K and the importance of vitamin K in synthesis of activated coagulation factors II, VII, IX, and X, along with the inhibitors proteins C and S.[44] Regardless, clinical bleeding is uncommon and liver biopsies can be performed safely in most cases.[51] One explanation for the safety of liver biopsy in horses with fulminant hepatic disease could be that platelet counts often remain within reference intervals in most horses with liver failure. Fibrinogen, an acute-phase protein made in the liver, usually is normal or mildly decreased in horses with acute or chronic liver failure, except in horses with cholangiohepatitis, where it may be high secondary to inflammation.[44]

OTHER CLINICOPATHOLOGIC ABNORMALITIES IN LIVER DISEASE

Lactate concentrations frequently are high and bicarbonate concentrations are usually low in horses with fulminant hepatic failure.[28] The high lactate concentration likely is due to a combination of decreased hepatic clearance and increased production

from hemodynamic alterations found with hepatic failure and likely responsible for the low bicarbonate concentration. Glucose concentrations often are surprisingly normal in most adult horses with hepatic failure but, in some cases, glucose may be very low.[52,53] Hematocrit, iron concentrations, and percentage iron saturation occasionally are high in horses with severe liver disease, in particular those with acute necrosis. The erythrocytosis can persist despite adequate rehydration. These clinicopathologic findings should not be interpreted as iron toxicity because that diagnosis can be confirmed only by histologic evidence of hemochromatosis.

CASE 1

A 19-year-old Appaloosa gelding was examined because of an acute onset of diarrhea and fever. Heart rate was 56 beats per minute, mucous membranes were abnormally red, and capillary refill time was 5 seconds. Blood samples were submitted for hemogram, biochemical profile, lactate concentration, and blood polymerase chain reaction (PCR) testing for *Neorickettsia risticii,* along with fecal testing for other common enteric infectious agents. Initial treatment included intravenously administered crystalloids and oxytetracycline. Supportive treatment with misoprostol and di-tri-octahedral smectite (Bio-Sponge Platinum Performance, Buellton Calif. USA) administered orally and flunixin meglumine administered intravenously, and distal limb cryotherapy occurred within 1 hour of hospital admission. The horse had a good clinical response to treatment over the first 18 hours but on day 2 developed acute neurologic signs, which included circling, head pressing, and ataxia. The ammonia concentration was markedly increased (**Table 2**) and treatment with orally administered lactulose and intravenously administered mannitol was initiated. Commercial equine plasma and a synthetic colloid also were administered intravenously on days 3 and 4, respectively. The blood PCR for *N risticii* was positive. The horse made a full recovery and was discharged from the hospital after 5 days.

Case Discussion

Hyperammonemia may develop in a small number of horses with acute gastrointestinal disease. The magnitude of the hyperammonemia is somewhat unique to the horse and may be related to microbiome changes in the gut (increased amounts of ammonia-producing bacteria) and/or increased intestinal permeability. In these cases, neurologic signs develop quickly and may lead to death in less than 24 hours, although some horses may have a rapid (<48 hours) decrease in ammonia concentrations and complete recovery if the primary intestinal disease resolves. The authors are not aware of a horse with ammonia concentrations this high that survived.

Interpretation of clinical pathologic data

- HCT of 66%, due to hypovolemia from gastrointestinal fluid losses (dehydration)
- Inflammatory leukogram: the most common leukogram findings in acute severe colitis is leukopenia, due to a neutropenia with a left shift and concurrent toxic change in neutrophils. Not all horses have neutropenia, as observed in this case. A mild monocytosis is a commonly observed feature of *N risticii* infection in horses.
- Lower than expected total protein (especially albumin) concentration considering the relative erythrocytosis and estimated degree of dehydration. This combination occurs frequently in horses with acute colitis and indicates protein loss from the diseased bowel. The marked decrease in total protein and albumin concentrations between days 1 and 3 also is common in horses with colitis due to

Table 2
Pertinent clinical pathologic findings for case 1

	Day 1	Day 3	Reference Interval
HCT	66	41	34%–46%
White blood cell count	12.2	6.3	5.2–10.1 thou/μL
Neutrophils	4.4	3.3	2.7–6.6 thou/μL
Band neutrophils	3.2	0	0.0–0.1 thou/μL
Monocytes	1.8	0.8	0.0–0.6 thou/μL
Platelets	Adequate[a]	Adequate[a]	94–232 thou/μL
Sodium	115	132	134–142 mEq/L
Potassium	3.2	3.2	2.4–4.8 mEq/L
Chloride	69	106	95–104 mEq/L
Bicarbonate	9	19	24–31 mEq/L
UN	84	24	10–22 mg/dL
Creatinine	5.5	1.4	0.8–1.5 mg/dL
Total protein	6.3	3.0	5.4–7.0 g/dL
Albumin	2.3	1.5	2.9–3.6 g/dL
L-Lactate	9.16	1.6	<1.5 mmol/L
Ammonia	1495 (day 2)	695 23 (day 4)	<150 μg/dL

[a] Platelet clumping noted on smear precluded quantification.

ongoing protein-losing enteropathy. The resultant decrease in colloid osmotic pressure can make crystalloid therapy less effective in maintaining intravascular volume because the administered crystalloid fluids tend to shift more rapidly out of the intravascular space.

- Severe prerenal azotemia, which largely resolved with appropriate fluid therapy.
- Hyponatremia and hypochloremia are both common findings with acute colitis in horses. In this horse, the measured decrease in the negatively charged ions, chloride (change of −31 mEq/L) and albumin (−0.6 g/dL or −2.0 mEq/L)[a], were greater than the decrease in the positively charged sodium (change of −23 mEq/L)[a], indicating that other negatively charged ions are likely increased. In this horse, the bicarbonate concentration was also very low (change of −18 mEq/L)[a] and L-lactate concentration was very high, indicating a metabolic acidosis due to L-lactate. Other unmeasured anions, such as D-lactate or acids accumulating from the severe prerenal azotemia, also may have been present to help explain both the strong ion difference and the metabolic acidosis.
- Hyperlactemia often is present in horses with acute severe colitis as a result of hypovolemia and endotoxin/cytokine effects on global tissue perfusion (type A) with additional lactate production from the local damage to the bowel wall (type B). This horse had an excellent initial response to treatment and lactate concentrations decreased quickly following fluid therapy. Horses that do not have substantial decreases in lactate concentrations after fluid resuscitation have a more guarded prognosis.[8,9]

[a] Changes in ions calculated by subtracting patient value from mid normal range value.

CASE 2

A 5-year-old previously healthy miniature horse mare presented with acute depression, icterus, anorexia, and inability to open the jaw. The mare was diagnosed with selenium-deficient masseter myopathy with secondary negative energy balance and hepatic lipidosis. Blood analysis included hemogram, biochemical profile, and lactate concentrations (Table 3). A free-catch urine sample was dark brown, with a USG of 1.025, and a urine dipstick test revealed bilirubinuria and positive heme (blood) reaction. The mare was treated with intramuscular and oral selenium and vitamin E and supported with partial parenteral nutrition and made a full recovery. The prognosis for hepatic lipidosis can be excellent regardless of the triglyceride concentration if the triggering disease is resolved promptly and proper nutritional support is provided.

Interpretation of Laboratory Findings

- Liver disease and failure: this mare has evidence of liver disease (increased hepatocellular and biliary enzyme activities) in addition to muscle disease (increased creatine kinase [CK] activity). The increase in total and direct bilirubin concentration along with the clinical signs and other biochemical findings support a diagnosis of liver dysfunction (failure). The increased AST activity was a result of both muscle and liver disease.
  - The marked increase in SDH (>30 times the upper reference limit) and milder increase in GGT (slightly >3 times the upper reference limit) with 11% of the total bilirubin being direct bilirubin suggest that hepatocellular injury is more severe than cholestasis.
  - The normal SDH activity on day 5 reflects both the rapid improvement in the disease and the short half-life of SDH. GGT activity is still increased on day 5 due to the longer half-life of GGT and likely from some continued biliary proliferation.
- Rhabdomyolysis: increased muscle enzyme activities (CK and AST) and positive heme reaction on urine dipstick due to myoglobin, all of which improved during hospitalization. The greater decrease in CK activity during 5 days of hospitalization is due to the shorter half-life (hours) compared with AST (days).

Table 3
Pertinent clinical pathologic findings for case 2

	Day 1	Day 3	Day 5	Reference Interval
Packed cell volume	43	42	42	34%–46%
Total solids (by refractometer)	7.2	6.9	6.8	5.2–7.8 g/dL
pH (venous)	7.29	7.35	—	7.32–7.43
Bicarbonate	20	26	26	25–32 mEq/L
L-Lactate	3.5	1.8	—	0.8–1.8 mmol/L
Creatinine	2.2	1.6	1.5	0.8–2.0 mg/dL
CK	57,040	21,984	1142	142–548 U/L
AST	13,030	10,780	4474	199–374 U/L
SDH	362	118	5	0–11 U/L
GGT	77	146	103	8–29 U/L
Total bilirubin	6.2	2.6	1.9	0.5–2.1 mg/dL
Direct bilirubin	0.7	0.3	0.2	0.1–0.3 mg/dL
Triglycerides	1929	75	27	14–65 mg/dL

- Negative energy balance with hypertriglyceridemia: miniature horses are at increased risk for developing hypertriglyceridemia, hyperlipemia, and hepatic lipidosis in response to anorexia. The increase in circulating lipids reflects increased mobilization of fat stores as well as decreased clearance/metabolism of lipids by the liver. Treatment with intravenous dextrose, parenteral nutrition, and/or enteral nutrition often results in rapid reduction in triglyceride concentrations and resolution of hepatic lipidosis.
- The acidemia with a metabolic acidosis (low venous pH and low bicarbonate), mildly increased creatinine concentration (likely prerenal azotemia), and abnormally high L-lactate concentration are likely a result of dehydration and diminished tissue perfusion, although some of the increase in L-lactate may have occurred because of decreased hepatic dysfunction/metabolism. Dehydration is further supported by the USG of 1.025. Venous pH and creatinine and lactate concentrations all normalized rapidly in response to intravenous crystalloid fluid therapy.

DISCLOSURE

The authors have nothing to disclose.

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