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Understanding the physiological derangements that occur in horses with liver disease or liver failure requires knowledge of basic hepatic anatomy and metabolic, secretory, excretory and storage functions. The equine liver has 4 lobes: right, left, quadrate and caudate. It lies predominantly to the right of midline, behind the diaphragm, primarily within the rib cage. It does not normally contact the ventral abdominal floor. The hepatic artery carries oxygenated blood from the heart to support hepatic metabolic activities. The portal vein enters the liver carrying nutrients absorbed from the gastrointestinal tract destined for metabolism, storage and/or transformation. Blood from the liver drains into central veins and hence into the hepatic vein and caudal vena cava.

The liver synthesises many proteins including coagulation and fibrinolytic factors, albumin, transport proteins (haptoglobin, transferrin etc.) and acute phase proteins. It deaminates amino acids for use as energy substrates or precursors of gluconeogenesis. The major toxic by-product of amino acid catabolism, ammonia, is eliminated by formation of new amino acids or conversion to urea which is excreted in urine. The liver plays an important role in regulation of the synthesis, storage, and release of glucose, fatty acids and triglycerides.

Bile, produced by hepatocytes, is excreted into bile canaliculi and exits through bile ducts that converge to form the hepatic duct, which drains into the proximal duodenum. Because there is no gallbladder or sphincter to regulate flow as the bile enters the duodenum, bile flow in the horse is continuous. Bile is an isotonic fluid composed of bile acids, conjugated bilirubin, cholesterol, lecithin, electrolytes and water. Bile acids facilitate excretion of phospholipid and absorption of lipids and lipid-soluble molecules including vitamins A, D, E and K. Bile acids are reabsorbed in the ileum and returned to the liver through the portal vein in a process of enterohepatic circulation.

Bilirubin is a breakdown product of haemoglobin, myoglobin and some nonhaem pigments. Haemoglobin is removed from the blood by mononuclear phagocytes and converted to bilirubin. This unconjugated bilirubin is released into the blood and binds albumin for transport to the liver. Unconjugated bilirubin is removed from the blood by hepatocytes and conjugated to glucuronide. Conjugated bilirubin is excreted via bile into the intestinal tract where it is reduced by microflora to urobilinogen and stercobilin. Urobilinogen undergoes enterohepatic circulation; a small amount is excreted in the ileum and returned to the liver through the portal vein in a process of enterohepatic circulation.

Kupffer cells are the fixed tissue macrophages of the liver. They are important for phagocytosis of soluble and particulate matter in the portal blood and for presentation of antigens to lymphocytes. They synthesise and release a wide variety of inflammatory mediators including prostaglandins, interleukins and cytokines.

Hepatic insufficiency or failure occurs when there is a loss of at least 60–80% of hepatic mass and the liver can no longer perform its normal functions. Therefore, horses with mild to moderate hepatic disease may not show recognisable clinical signs until disease is well advanced. The prognosis for horses with liver failure is usually poor, unless the disease process is acute and regeneration is occurring. A wide variety of clinical signs may occur with hepatic disease, insufficiency, or failure. Unfortunately, most of those signs are nonspecific and highly variable depending on the extent and duration of disease.

A variety of serum enzyme activities are used to assess hepatocyte or biliary epithelial damage. Sorbitol dehydrogenase (SDH) is the most sensitive and specific enzymatic indicator of hepatocellular damage. It is a leakage enzyme that is highly labile necessitating rapid processing of blood samples for accurate results. Its short half-life in vivo makes it an excellent enzyme for monitoring acute ongoing liver disease. Aspartate aminotransferase (AST, SGOT) is a leakage enzyme that increases with hepatocyte or muscle damage. Total lactate dehydrogenase (LDH) is a leakage enzyme that may be elevated with a wide variety of systemic disease process and is not a useful or specific indicator of liver damage. LDH-5 is the isoenzyme of LDH that is most specific for hepatocyte leakage. Biliary cell damage is assessed by measurement of gamma glutamyl transferase (GGT) and alkaline phosphatase (AP). GGT is a specific indicator of biliary tract damage and cholestasis. This enzyme takes a long time to return to normal serum concentrations after cholestatic disease. AP may be elevated in horses with biliary tract, gastrointestinal, bone, or placental pathology.

Assessment of hepatic function is more difficult than assessment of cell damage. Hypoglycaemia may indicate failure of gluconeogenesis but is uncommon in adult horses with liver failure. Hypoalbuminaemia and hypofibrinogenaemia may reflect decreased hepatic protein production but are not sensitive or specific for liver disease. Hyperglobulinaemia is common in horses with liver failure and when present, is a negative prognostic indicator. A decreased blood urea nitrogen (BUN)
indicates an inability of the liver to process ammonia but may also occur with inappetance or overhydration. When present due to liver failure, it occurs concomitantly with increased ammonia and is considered a poor prognostic indicator. Hyperbilirubinaemia may occur as a result of haemolysis, hepatocellular disease, or cholestatic disease. The most common cause is inappetance or anorexia. Increases in unconjugated (indirect) bilirubin occur with anorexia, haemolysis, or hepatic disease. Increases in conjugated (direct) bilirubin indicate cholestatic disease. Increases in bile acids are a sensitive indicator of hepatocellular and/or biliary disease or portosystemic shunts. Because the horse does not have a gallbladder, there is no post prandial increase in circulating bile acid concentrations; therefore, recent feeding does not impact evaluation of bile acids in horses. Coagulation times may be prolonged in horses with liver failure due to decreased production of soluble coagulation factors.

Of the widely available diagnostic tests, serum bile acids concentration is the most sensitive for detection of abnormal hepatic function. Histological assessment of hepatic biopsy samples, however, is an extremely valuable method to assess hepatic function and prognosis. Severe fibrosis, megalocytosis, necrosis, leucocyte infiltration and biliary hyperplasia are negative prognostic indicators.

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