Bile Acids

Bile acids have been used to evaluate enterohepatic circulation and, therefore, functional hepatic mass, in several species including dogs, cats, cattle, sheep, goats, and horses. Primary bile acids are synthesized from cholesterol in the liver, conjugated, and excreted in bile. Some conversion of unabsorbed primary bile acids to secondary bile acids occurs by intestinal bacteria. Conjugated bile acids form micelles with fat, are resorbed in the ileum, and carried via portal circulation to the liver for hepatocyte uptake and continuation of the cycle. From 90% to 95% of bile acids are removed by the liver via the portal system with a small concentration of bile acids detectable in serum or plasma. This cycle provides a maximum concentration of bile acids in the proximal small intestine where fat digestion and absorption occurs. Increases in bile acid concentrations above reference intervals are sensitive indicators of liver disease (often due to decreased enterohepatic circulation), but do not define the specific hepatopathy. Concentrations also can be increased due to cholestasis. Bile acid concentrations may be decreased due to ileal malabsorption. In monogastric carnivores with gallbladders, such as dogs and cats, there is a postprandial increase in bile acid concentrations with a defined narrow reference interval. Therefore, pre- and post-prandial samples are used.

Bile acid concentrations have been utilized to a lesser degree in the evaluation of ruminant hepatobiliary disease due to individual variation in bile acid concentrations that broaden the reference interval. Values above the reference limit are useful for the diagnosis of hepatobiliary disease. There is a continual flow of ingesta from the abomasum into the duodenum with periodic interruptions that stimulates a similar pattern in the flow of bile acids. These interruptions resulted in variability of serum bile concentrations by 60 µmol/L between hourly samples. Generally, sampling is performed at one time point.

Because horses do not have gallbladders and the sphincter of the common bile duct is weak, continuous secretion of bile into the intestine has been documented and enterohepatic circulation occurs 38 times per day. There is no statistical difference between bile acid concentrations in ponies and horses, and no effect of feeding on serum bile acid concentrations, after a 14 hour fast. Additionally, no diurnal variation and no effect of age and gender were found for equine bile acid concentrations. Bile acid concentrations in horses did increase 2- to 3- fold over baseline values after 3 and 4 days of fasting to maximum values of 20 - 25 µmol/L. Generally, sampling is performed at one time point.

Camelids, such as the llama**,** are herbivores with a unique digestive system consisting of three compartments. The first compartment (C1), holding approximately 83% of the stomach contents, is analogous to the rumen of cattle. A muscular sphincter exists between C2 and the third compartment (C3). Additionally, the llama does not have a gallbladder. Llama bile acid concentrations are reported as 1-23 µmol/L for llamas >1 year of age and 10 - 44 µmol/L for llamas $\leq$ 1 year of age. Generally, sampling is performed at one time point.

Different methods for serum bile acids result in different reference intervals. Each laboratory reference interval should be used. In our laboratory, reference intervals are:

Dogs: 12 hour fasting 5-20 µmol/L; 2 hours post-prandial 1-30 µmol/L
Cats: 12 hour fasting 1-13 µmol/L; 2 hours post-prandial 1-25 µmol/L
Horses: 1-15 µmol/L
Cattle: <30 µmol/L

Submitted by Dr. Claire Andreasen, Director of the Clinical Pathology Laboratory