

Bilirubin

Interpretive Summary

Description: Bilirubin is an indicator of liver disease, gall bladder disease or hemolysis.

Decreased Bilirubin

Common Causes

- Not clinically significant

Increased Bilirubin

Common Causes

- Prehepatic
 - RBC destruction (hemolysis)
 - Immune-mediated hemolytic anemia
 - Zinc or onion toxicity
 - RBC parasites
- Diffuse hepatocellular disease
 - Infectious
 - Bacterial cholangiohepatitis
 - Leptospirosis
 - Feline infectious peritonitis (FIP)
 - Histoplasmosis
 - Toxoplasmosis
 - Inflammatory (noninfectious)
 - Immune mediated chronic hepatitis
 - Toxic
 - NSAIDS
 - Copper or iron accumulation in liver
 - Ragwort
 - Hepatic Lipidosis
 - Neoplasia
 - Cirrhosis/fibrosis
 - Copper storage diseases (breed predispositions)
 - Hypoxia from anemia or congestion
 - Trauma
- Cholestatic disorders
 - Intrahepatic cholestasis
 - Lipidosis
 - Severe structural disease
 - Neoplasia
 - Posthepatic obstruction
 - Cholangitis/cholangiohepatitis
 - Gall bladder mucocoele
 - Pancreatitis
 - Bile duct neoplasia
 - Bile duct or gall bladder rupture
- Fasting or anorexia (horses)
- Artifact due to hemolysis, lipemia (varies by methodology)

Uncommon Causes

- Prehepatic: hemolytic anemia
 - Pyruvate kinase deficiency
 - Phosphofructokinase deficiency
 - Decreased phosphorus
- Diffuse hepatocellular disease
 - Toxic
 - Sago palm toxicity
 - Mushroom toxicity
 - Blue-green algae toxicity
 - Lysosomal storage disease
- Cholestatic disorders
 - Intrahepatic cholestasis
 - Cytotoxicosis (S. Eastern United States)
 - Mycotoxin
 - Alsike clover intoxications (horses)
 - Posthepatic obstruction
 - Gall stones
 - Pancreatic neoplasia
 - Liver flukes
- Functional cholestasis associated with sepsis
- Portosystemic shunt (end stage)

Related Findings

- Hemolytic anemia
 - Decreased hematocrit, RBC, hemoglobin
 - Increased reticulocytes, increased MCV and decreased MCHC, polychromasia
 - Increased WBC count
 - Spherocytosis (in dogs), autoagglutination
 - Inclusions may be seen with infectious causes of hemolysis
 - Positive serology or PCR testing for infectious causes
 - Bilirubinuria and hemoglobinuria
 - Increased serum zinc concentrations or evidence of zinc foreign body on radiographs
 - Positive Coombs or saline agglutination test may or may not be present with IMHA
- Hepatocellular liver disease
 - Increased ALT, AST
 - Decreased BUN, albumin, cholesterol, glucose in end-stage cirrhosis/fibrosis
 - Positive serology/PCR testing for infectious causes
 - Consistent liver biopsy or cytology results
 - Increased liver copper concentration
- Cholestatic liver disease
 - Increased ALP, GGT
 - Consistent liver biopsy or cytology results
- Pancreatitis
 - Increased amylase and lipase
 - Increased Spec cPL® or Spec fPL®

Additional Information

Physiology

- Bilirubin is a waste product resulting from the breakdown of heme in a variety of proteins, mainly the red blood cell protein hemoglobin.

- Hemoglobin is broken down to heme, iron, and globin in the liver, spleen, and bone marrow. Following several additional steps, the heme molecule is further degraded to bilirubin (unconjugated) before release back into the circulation.
- Unconjugated bilirubin binds to albumin, is transported to the liver, and bound by receptors within the membrane of the liver cell. Bilirubin is released from albumin, and is taken into the cell by transport molecules. Bilirubin is then joined with glucuronic acid (conjugated), which allows bilirubin to become water-soluble.
- Conjugated bilirubin is released into the biliary system to be excreted into the intestinal tract via the bile duct. Intestinal bacteria convert conjugated bilirubin to the final products that are excreted in the feces.
- Serum concentrations of bilirubin are proportional to the rate of hemoglobin breakdown, subsequent removal from the serum by the liver, and excretion into the intestinal tract.
- Horses have higher total bilirubin than other domestic animals; most is unconjugated.

Diagnostic Methodology

- Most methods of bilirubin measurement are based on the diazo reaction. With the addition of a reagent, color develops rapidly (direct reaction). After the addition of alcohol, further color development occurs (indirect reaction).
- The direct reacting component is equal to conjugated bilirubin and the indirect reaction gives a measurement of the total serum bilirubin. The difference between these two results, gives a calculated value of unconjugated bilirubin.
- The proportions of conjugated and unconjugated bilirubin have been investigated in order to differentiate between red blood cell destruction and liver disease. However, the proportions vary greatly and are of limited clinical use.

References

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