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Jaundice, icterus, hyperbilirubinemia

Jaundice

Affected Animals:

Any dog can develop jaundice. It is very unusual, however, to see jaundice in young puppies.

Overview:

Dogs with jaundice have a yellow discoloration of body tissues such as the eyes, gums, and skin. The condition results from increased levels of bilirubin in the body, which is one of the by-products of heme, a red blood cell protein. Jaundice generally is not a disease; rather it is a symptom of a number of canine illnesses.

The causes of jaundice are classified as pre-hepatic, hepatic, or post-hepatic in origin. Pre-hepatic jaundice occurs when red blood cell breakdown, or hemolysis, produces bilirubin faster than the liver can metabolize it. Hepatic jaundice results from primary and secondary diseases within the liver that interfere with the liver cells' ability to metabolize bilirubin or excrete it normally into the biliary tract. Post-hepatic jaundice can result from obstruction to the flow of bilirubin-containing bile within the bile duct or from injury that causes leakage from the gallbladder or bile duct.

Once identified on physical examination, jaundice needs to be assessed further to determine the type and cause. Bloodwork is useful for measuring the bilirubin level and identifying concurrent abnormalities. It will also help determine if anemia is a factor in the affected dog's jaundice. If a pet is not anemic, then the jaundice is likely to be due to liver disease or to post-hepatic biliary abnormalities. Some patients may have jaundice that has multiple causes.

The outlook for a jaundiced dog depends on the cause of the jaundice. In general, jaundice is a significant and serious sign, and the prognosis for most disorders causing it is guarded, or uncertain. However, many diseases associated with jaundice can be managed successfully with specific, supportive therapy based on timely and accurate diagnostic test results.

Clinical Signs:

Jaundice is a clinical sign associated with many diseases. Light-colored tissues will present the characteristic yellowish discoloration of jaundice. It is usually first recognized in the mucous membranes in the mouth and in the eyes or skin. Additional signs depend on the underlying cause of the jaundice in the affected dog. In general, non-specific signs such as lethargy, weakness, and reduced appetite will occur in many dogs, although some jaundiced dogs are otherwise asymptomatic. Many owners report the presence of

dark or discolored urine due to the presence of bilirubin in the urine. Bilirubinuria may appear before the body tissues are discolored.

Symptoms:

See Clinical Signs.

Description:

Jaundice is a yellowish discoloration of the skin, sclera -- the whites of the eyes -- and mucous membranes of the mouth. It occurs when the amount of bilirubin produced in the body exceeds the liver's -- and to a lesser extent, the kidneys' -- ability to excrete it. An elevated serum bilirubin level will also result in bilirubin deposition in many other tissues of the body. However, jaundice is not apparent in darker tissues and internal organs. Jaundice becomes noticeable when serum bilirubin reaches 2 mg/dl.

Bilirubin is an end product of heme metabolism. Heme is the iron-containing component of hemoglobin, which is the molecule in red blood cells responsible for carrying oxygen to the body's tissues. Heme is also a component of myoglobin, which resembles hemoglobin, and is present in muscle protein for oxygen transport. When red blood cells break down, or hemolyze, heme is separated from the other part of the hemoglobin molecule and is metabolized to bilirubin. A small amount of bilirubin in the blood is a normal consequence of the destruction of old red blood cells. The normal wear and tear of muscle protein also contributes to this normal level of serum bilirubin, although not as much as red blood cell hemolysis produces.

Any disease process that produces excess bilirubin or interferes with its metabolism and excretion from the body produces the characteristic signs of jaundice. In dogs, there are three basic classes of disease processes that cause jaundice: pre-hepatic, hepatic, and post-hepatic. Pre-hepatic jaundice is due to excessive red blood cell breakdown, or hemolysis, which results in anemia and an abnormal increase in serum bilirubin. Pre-hepatic jaundice may also occur when significant muscle damage occurs. When muscles are significantly injured, heme is released from myoglobin and is metabolized to bilirubin.

Hepatic jaundice is due to a disease or disorder located within the liver. Such intra-hepatic disease may be primary or secondary. Primary liver diseases originate in the liver; secondary ones develop elsewhere in the body and then spread to the liver or by other means cause disease within it. If a jaundiced dog is not anemic and if there is no evidence of bile duct obstruction or gallbladder disease on x-ray and ultrasound studies, then intra- hepatic disease is likely.

A number of mechanisms underlie the development of hyperbilirubinemia associated with liver disease, both primary and secondary. Necrosis, or death, of liver cells will impair the liver's functional capacity to store and metabolize bilirubin. The formation of scar tissue in the liver in response to injurious agents can cause obstruction of bile flow within the liver, thus preventing its excretion. Compression of the intrahepatic duct system by tumors can block the flow of bilirubin-containing bile flow also. Inflammatory conditions of the liver can cause intrahepatic congestion that can block the flow of bile through the liver as well.

Post-hepatic jaundice occurs with bile duct obstruction or biliary tract leakage. Normally bile is eliminated in the gastrointestinal tract. When this normal elimination of bilirubin is impaired, serum concentrations of bilirubin will rise. Obstruction to bile flow outside the liver will cause secondary bile flow obstruction in the liver. When post-hepatic bile flow is obstructed, leakage of bile from the obstructed biliary tract into the abdominal cavity can

readily occur. The bile, including bilirubin, will be absorbed through the abdominal cavity wall and enter the blood stream.

A persistently high level of serum bilirubin, as evidenced by jaundice, can have secondary toxic effects on various tissues, including the kidney and liver. A pre-hepatic or post-hepatic disease process associated with hyperbilirubinemia could result in secondary hepatic toxicosis that could further impair the affected dog's ability to process bilirubin.

Diagnosis:

The diagnosis of jaundice usually is based on the yellow discoloration of the skin or mucous membranes noted by the veterinarian upon physical examination. Bloodwork will document elevation of the serum bilirubin concentration, which in dogs is normally less than 1.0 mg/dl. Urinalysis will demonstrate an abnormal amount of bilirubin in the urine as well. Although elevated levels of bilirubin may be present in the blood and urine, jaundice may not become clinically evident until the serum bilirubin level reaches 2.0 mg/dl.

When jaundice is noted, additional tests will be needed to determine its cause. A complete blood count, or, at the very least, measurement of the packed cell volume, is typically done to rule out anemia. If anemia is present, then the jaundice may be due to red blood cell breakdown, a condition known as hemolysis, and additional tests will be needed to look for the cause of the anemia.

Jaundiced dogs that are not anemic most likely have liver or post-hepatic biliary tract disorders. A blood chemistry profile provides confirmation of elevated total serum bilirubin concentrations, and documentation of liver enzyme, serum electrolyte, and glucose levels and kidney function values. Urinalysis is important to confirm the presence of bilirubin in the urine. Small amounts of bilirubin can be found in the urine of many normal dogs, but large amounts are abnormal. Minor serum bilirubin elevations unaccompanied by jaundice or the presence of bilirubin in the urine may be incidental findings related to blood sample collection technique or recent ingestion of food, and therefore may not be significant.

Imaging studies provide important information in the diagnosis of hepatic and post-hepatic causes of jaundice. Abdominal radiographs, or x-rays, are routinely performed to assess liver size and to look for evidence of stones in the biliary tract. Abdominal ultrasound is the most readily available non-invasive diagnostic tool used to detect bile duct obstruction or primary gallbladder abnormalities not otherwise revealed by conventional radiographs. Ultrasound can also be used to guide needle biopsy of the liver. A liver biopsy provides tissue for microscopic detection of liver tissue abnormalities. This is typically done if anemia is not present and there is no evidence on ultrasound examination of bile duct obstruction or gallbladder disease. When the ultrasound study reveals obstruction, exploratory surgery is often necessary to identify and correct the obstruction's cause. Such surgery is also performed when a cause for the jaundice remains unclear after other diagnostic tests and procedures have been performed.

Prognosis:

As with all disease signs, the outcome in a jaundiced dog depends primarily on the underlying cause of the jaundice and on the animal's response to treatment. Dogs with pre-hepatic jaundice due to hemolysis may recover completely if their respective diseases are identified and treated successfully. However, the mortality rate for patients with pre-hepatic jaundice can also be quite high, as many dogs succumb to their underlying diseases.

Patients with jaundice due to primary liver disease may recover completely, especially if the problem was drug or toxin related. Prognosis in these cases is good if further exposure to the drug or toxin is avoided and supportive care is provided as necessary. Some types of liver disease, particularly chronic hepatitis and cirrhosis, follow a chronic course, characterized by relatively quiescent periods interspersed with periods of more active disease. Jaundice may come and go in these patients. Many veterinarians used to think that the presence of jaundice in a dog invariably signaled a fatal illness. Today, however, the outcome may be more favorable for many affected dogs when treatment is given based on the results of accurate and appropriate diagnostic tests.

Patients with post-hepatic jaundice often have resolution of the jaundice after the obstruction is relieved or once the leaking part of the biliary tract is repaired or removed. Nevertheless, the long-term outlook depends more on the cause of the obstruction or bile duct injury. Patients with traumatic injury to the gallbladder or bile duct, or obstruction due to stones, may do well indefinitely once the problem is addressed, but dogs with bile duct or gallbladder cancer usually do not survive for long periods of time. In dogs with bile duct obstruction secondary to pancreatitis, the prognosis is best if the obstruction resolves without surgical intervention. Some dogs that require surgical intervention and re-routing procedures to establish normal bile flow also do quite well, but others experience chronic problems with infection, inflammation, or progressive liver disease once surgery is completed.

Transmission or Cause:

There are many different diseases that can cause jaundice in dogs. These are pathophysiologically classified as pre-hepatic, hepatic, and post-hepatic, depending on the anatomic/functional location of the underlying disease process.

There are many pre-hepatic causes of jaundice, most of which are associated with hemolysis of red blood cells and the anemia that results. These include toxins and certain drugs, severe heartworm disease, red blood cell parasites and other infectious diseases such as ehrlichiosis and leptospirosis. Immune-mediated red blood cell-destructive diseases, such as autoimmune hemolytic anemia and systemic lupus erythematosus, inherited red blood cell enzyme abnormalities and cancer also may produce profound jaundice. Non-hemolytic disorders of muscle, including trauma and certain muscle degenerative diseases can also cause pre-hepatic jaundice.

Various liver diseases that interfere with the liver's role in controlling bilirubin levels can cause hepatic jaundice. Exposure to certain toxins and drugs can cause liver cell necrosis and hepatic dysfunction. Anti-seizure drugs, such as phenobarbital and phenytoin, acetaminophen, sulfa-type antibiotics, and mebendazole, an anti-parasitic medication, are some of the drugs commonly prescribed for dogs that can cause hepatic jaundice.

Various liver cancers -- both arising in the liver as well as metastasizing, or spreading, to it -- may cause intra-hepatic obstruction to bilirubin excretion and jaundice. Inflammatory disorders such as chronic active hepatitis and cholangitis, and infectious liver diseases of bacterial, viral or fungal origin often produce jaundice in the early stages of the disease process. Cirrhosis, where the functional tissue of the liver becomes scarred due to a number of disorders, produces hepatic jaundice in severe cases. Congenital or breed-related genetic liver diseases in Bedlington terriers, Doberman pinschers and some other breeds may also be associated with hepatic jaundice.

Post-hepatic jaundice occurs when the common hepatic duct or the bile duct becomes

obstructed or when bile leaks from any point along the biliary tract, including the gallbladder. Possible causes of duct obstruction include pancreatitis, gallstones, and cancer. Traumatic injury to the gallbladder or bile duct can lead to obstructing blood clots or structural damage. Spontaneous rupture of the bile duct or gallbladder can result in leakage of bile into the abdomen. Such ruptures often occur as a result of a long-standing obstruction.

Treatment:

There is no specific treatment for jaundice. The main goal is to identify the cause of the jaundice and to treat it as specifically as possible. If the jaundice is due to excessive hemolysis, the cause of the hemolysis dictates its treatment. Any potential toxins that can cause hemolysis should be identified and removed, and further exposure should be prevented. Antibiotics or anti-parasitic agents may be needed for infectious or parasitic causes of hemolysis. Immune system-suppressing drugs such as corticosteroids are used to treat immune-mediated hemolysis. Blood transfusions may be needed to treat anemia symptomatically until its cause is identified, or to allow time for other medical treatments to work.

When jaundice is caused by a primary or secondary liver disease, treatment is directed at the underlying disorder. Some liver diseases respond to specific treatments, while the majority can only be managed symptomatically and supportively. Treatment of liver disease in dogs may include fluid administration, antibiotics, antacids, anti-inflammatory drugs, vitamin K, drugs to suppress scar tissue formation or to influence bile flow, and vitamin E and fatty acid supplements. Some liver diseases resolve with time, but many, such as chronic hepatitis and cirrhosis, do not resolve and may progress with time. Nevertheless, treatment is frequently helpful in managing patients during the active stages of the disease and in improving the quality of life between episodes.

Bile duct obstruction or leakage, or primary gallbladder diseases identified on ultrasound usually require surgery. One exception is bile duct obstruction secondary to pancreatitis, which may resolve with time and without surgical intervention.

Prevention:

There are no specific means of prevention for most disorders that cause jaundice in dogs. Routine vaccinations protect against infectious hepatitis caused by adenovirus and *Leptospira* species of bacteria.