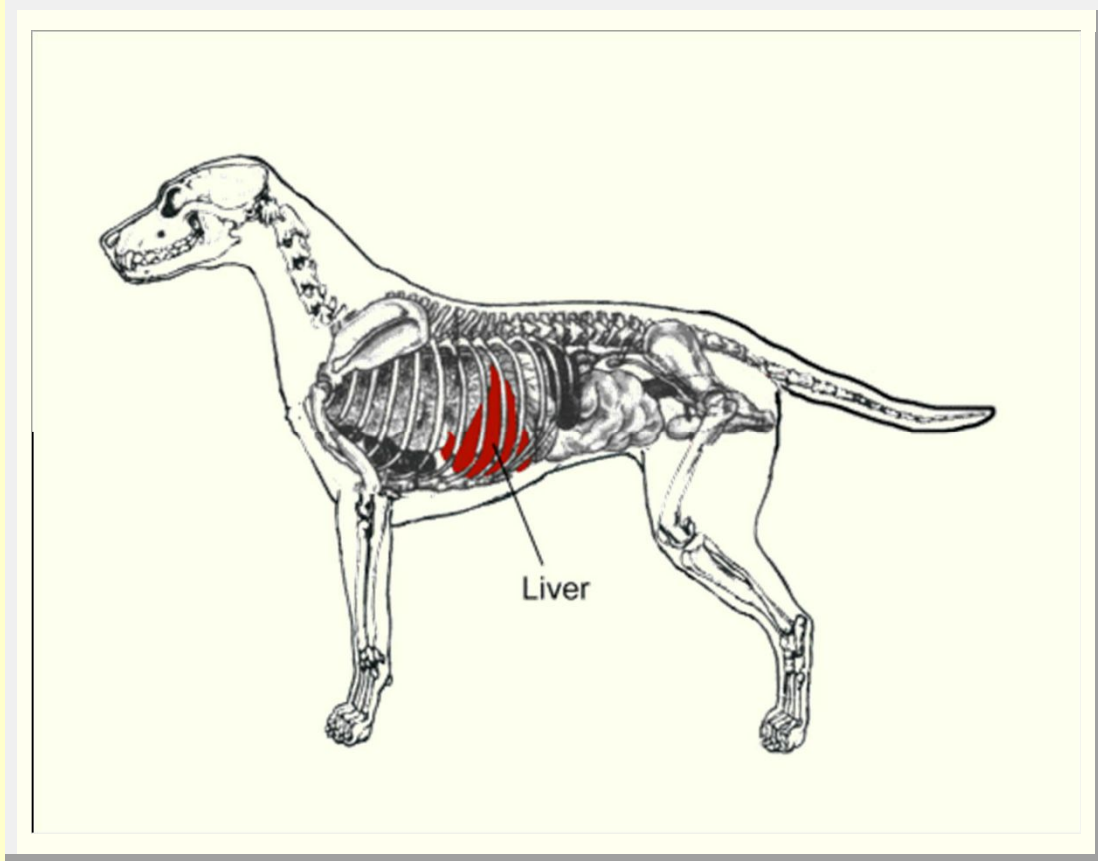


The Dalmatian Club of America Liver Disorders



Liver Disorders (A Synoptic Review)

**Study Group on Kidney & Liver Disorders
Health & Research Committee
Dalmatian Club of America**

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This site is intended to be informative only. If your dog is suffering from a health problem, diagnosis and treatment should be based upon consultation with your veterinarian.

Because the liver is one of the most important and complex organs having a multitude of functions and subject to diverse disorders, any attempt at completeness in a brief discussion is futile. The following information, gleaned from the articles listed in the [References](#), can only serve as an outline; the reader will need to consult the material in the [Informational Links](#) for more details.

Normal Liver Function

The liver, the largest organ in the body, is essential in keeping the body functioning properly. It removes or neutralizes poisons from the blood, produces immune agents to control infection, and removes germs and bacteria from the blood. It makes proteins that regulate blood clotting and produces bile to help absorb fats and fat-soluble vitamins. This organ is the main industrial center of the body, and it has the enormous task of maintaining the body's metabolic equilibrium (homeostasis). The liver:

- Processes raw materials,
- Manufactures the building blocks of the body,
- Recycles the old to make new,
- Detoxifies the waste of the body.
- Is involved in just about every biochemical process required to run the body.

The liver has a double-edged nature which, while being life preserving, makes diagnoses and treatment of liver disease extremely difficult. The liver has a tremendous reserve capacity, which means that it can easily perform its duties with up to 70 to 80 per cent of the liver mass affected by disease. While it certainly is a benefit that the liver can maintain life despite an overwhelming infection or a massive tumor, it also means that a disease can be well advanced and possibly untreatable before any symptoms are noted. Liver disease is most easily conquered early, but the very nature of the liver makes this a difficult task. However, the liver is the only organ in the body which is capable of complete regeneration and thus if it is possible to successfully treat the disease, there is a chance of complete recovery.

The Liver in Disease

As a result of these many functions, liver disease can affect just about any other part of the body and thus the symptoms of liver disease are not always specific. That is, signs of liver disease are similar to signs of malfunction of other organs or systems. Furthermore, because the liver acts as a "biochemical cross roads" for the body, it is affected by a wide range of diseases, including viral and bacterial infections, degenerative disease, cancer, and toxic insults. Because the liver has a large reserve, signs are not evident until much of it is

damaged. While it is important to consider the liver when examining any sick animal, liver disease is one of the more difficult challenges for the veterinarian.

Because of its many functions and its position in the digestive tract, the liver is vulnerable to a wide variety of metabolic, toxic, microbial, circulatory, and cancer insults. Blood flows through the liver before it returns to the heart which enables the liver to remove nutrients for processing and storage and to remove bacteria, toxins, and other harmful substances before they gain entrance to the body's circulation. Bile is a bitter greenish-brown fluid that aids digestion and is secreted by the liver and stored in the gall bladder.

Because bile formation is one of the most sophisticated functions of the liver, it is also one of the most readily disrupted.

Symptoms: If a dog is suffering from a liver disorder, one or more of the following signs may be present.

- Intermittent recurrent abdominal or gastrointestinal upsets. loss of appetite, vomiting, diarrhea, constipation.
- Lack of energy or depression.
- Build up of fluid in the abdomen (ascites).
- Pale gray feces. Bile pigments are what gives feces its characteristic brown color.
- Orange urine. The improper processing of bile results in the excretion of bilirubin in the urine in high amounts, thus orange urine.
- Jaundice (yellowing of the gums, whites of the eyes or skin).
- Rarely: bleeding problems. Many of the proteins required for proper blood clotting are created in the liver.
- Severe neurological signs (hepatic encephalopathy), behavioral changes, seizures, aimless pacing or circling, head pressing.
- Pain associated with the abdomen.
- Chronic weight loss or wasting.
- Increased water consumption and urination.

Notes on symptoms:

1. Bile pigment processing:

Bile is a complex mixture of organic and inorganic compounds. It is primarily responsible for alkalizing the intestinal contents (acidic from the stomach), emulsifying the dietary fat, and prevention of putrefaction of digestive material.

Bilirubin, one of the bile pigments, is derived from the break down of hemoglobin, the oxygen carrying molecule carried in our red blood cell. Bilirubin is quite toxic, but it usually binds to a protein called albumin, which harmlessly carries it to the liver for detoxification and excretion. Albumin is made in the liver. Liver failure results in poor bilirubin processing and decreased albumin manufacturing, which results in a dangerously high level of free floating bilirubin.

The liver excretes the bilirubin after binding it to an amino acid in the bile duct system. Eventually this bound bilirubin enters the digestive tract, where the intestinal bacteria break it down to a harmless product called urobilinogen. Urobilinogen, after complete digestion in the intestines, is brown, therefore the feces tend to be brown.

Jaundice results from the accumulation of bilirubin in the body tissues. This becomes visible to the veterinarian, especially around the whites of the eyes and on the pale areas of the gums.

2. Important biological functions:

a. hormone metabolism. The liver is both the target organ for many of the body's hormones and the recycling center for most of the hormones. Some of the symptoms stemming from liver failure may mimic a major hormonal imbalance.

b. vitamin metabolism. Practically all the vitamins consumed in our diets are either directly involved in liver function or require liver aided transformation to be used in the body. This includes Vitamin C, the B vitamins, Vitamins A, D, E and K. Vitamin K is important to maintain blood clotting and requires hepatic transformation from the inactive form to the active form.

c. Red blood cell maintenance. In the mature dog the liver plays an active role in the removal of aged or damaged red blood cells from circulation. Anemia may be present in chronic liver disease.

d. Blood clotting ability. Most of the proteins involved in the creation of a blood clot are made in the liver.

e. Carbohydrate and fat metabolism: Sugars, or carbohydrates are the basic fuel of the body. The liver is the primary center for processing of the sugars into the form immediately required. The liver is also responsible for the destruction of insulin, the hormone directly involved with the cellular absorption of blood sugars. Alterations in liver function often do not affect blood sugar levels until much of the liver has been destroyed.

Fat metabolism is very complex due to the vast number of functions fat carries out in the body. The liver is central to those many functions.

Cholesterol is probably the most common fat based product in the body, being the major component in the cell wall, the basis for the steroid hormones and bile pigments, and the precursor of vitamin D. Any disease in fat metabolism can adversely affect the liver, and any disease in the liver can result in problems in fat metabolism.

f. Protein synthesis: The liver manufactures many of the proteins involved in the body functions. The major protein is albumin, which is required for transport of many nutrients and toxins (i.e. bilirubin). Albumin is also responsible for keeping the serum concentration constant, which is important with regards to serum fluid and salt balance. Also synthesized

in the liver is the globulin series, which are responsible for numerous biochemical reactions throughout the body. Elevations of select globulins may indicate a particular liver pathology.

The building blocks of proteins are the amino acids. The liver is also primarily involved in processing of dietary amino acids to modify them into required or useful forms.

Specific Diseases of the Liver

Listed below are several liver diseases of dogs:

Portosystemic Shunts

A portosystemic shunt is a blood vessel that bypasses liver tissue, carrying blood from the intestines, stomach, spleen, and pancreas to the heart before it can be filtered and cleansed of proteins, sugars, bacteria, and toxins. Shunts are present in all fetal mammals and usually close down shortly before or after birth so that the baby's liver takes over the functions of filtration, storage, and production. In some individuals the shunt doesn't close down or develops in an abnormal place, and the animal's liver doesn't get enough blood supply to grow or function properly.

Shunts may be congenital (found at birth) or acquired (developing after birth). Dogs with acquired shunts usually have cirrhosis, or "hardening" of the liver, secondary to severe liver disease. These dogs develop multiple shunting blood vessels to relieve high blood pressure in the liver. There is no effective surgical treatment for these patients, short of a liver transplantation.

Diagnosis is usually based on finding high levels of fasting and post-prandial bile acids, increased blood ammonia levels, and variable changes in laboratory parameters such as increased SGPT and SAP, decreased BUN, and mild anemia, hypoalbuminemia and hypoglycemia. Confirmatory tests include ultrasonography, portography or scintigraphy. Some single or large multiple shunts can be corrected surgically, while others can only be managed medically. Prognosis varies but is generally guarded to poor.

Copper Storage Disease (Copper Toxicosis)

Several breeds of dogs are prone to a genetic disease caused by accumulation of copper in the liver. Breeds most often affected include the Bedlington, West Highland, Kerry Blue and Skye Terriers, Doberman Pinscher, Cocker Spaniel, Labrador Retriever, German Shepherd Dog, Miniature Schnauzer, Bulldog and Pekingese. Although the disease is not believed to be commonplace in Dalmatians, several cases have been reported. Copper is found in all foods then absorbed by the intestines, stored in the liver and excreted through the bile system. Affected dogs genetically have the inability to eliminate copper from the liver.

Hepatic Lipidosis (Fatty Liver)

A severe accumulation of fat in the liver, termed hepatic lipidosis, occurs in cats and dogs and is idiopathic in the cat. Underlying causes include primary liver disease, shunts, diabetes, intestinal disease, pancreatitis, cancer, and other illnesses causing loss of

appetite. It may be secondary to diabetes mellitus, malnutrition or exposure to drugs or toxins. Diagnosis is based on finding very high SAP (up to 20 times elevated) and SGPT (up to 10 times elevated), and high bilirubin and fasting bile acids. Ultrasonography and liver biopsy are used for confirmation.

Chronic Active Hepatitis

Chronic active hepatitis is a progressive inflammatory condition believed to have an autoimmune or infectious cause. It has been associated with infectious canine hepatitis, leptospirosis and copper toxicosis. The condition progresses to liver failure.

Hepatic Encephalopathy

A metabolic disorder affecting the CNS (central nervous system) that develops as a result of liver disease causing seizures. The end result is the accumulation of ammonia in the blood stream due to prolonged circulation of toxins in the blood stream from portal shunts, cirrhosis, or end stage liver disease.

Clinical signs include: behavior changes, visual defects (blindness), circling, pacing, anxiety, stupor, and seizures. These signs are more prevalent after eating due to the increased amount of ammonia in the blood stream affecting the brain.

Causes include portal shunts, infectious hepatitis, cirrhosis.

Acute Hepatic Failure

A rapid loss of liver function due to death of liver cells.

Causes include drugs, toxins, infectious diseases, and lack of oxygen.

Clinical signs: acute depression and illness-vomiting, icterus, diarrhea, seizures, hemorrhage

Diagnosis: abnormal laboratory values, abnormal x-rays and ultrasounds, and biopsy

Infectious Hepatitis

A viral disease targeting the liver, kidneys, eyes, and blood stream.

Clinical signs: fever, loss of appetite, vomiting, diarrhea, abdominal pain,

Diagnosis: Blood tests, x-rays, ultrasound, liver biopsy.

Leptospirosis Hepatitis

Leptospirosis, a contagious disease affecting both animals and humans and spread by infection with a bacterial pathogen called *Leptospira*, may result in chronic liver and kidney disease and fatality in the dog.

Clinical signs: Depression, loss of appetite, signs of kidney disease, respiratory disease.

Diagnosis: Blood tests, serum testing for leptospirosis, urine culturing.

Cirrhosis

End-stage liver disease from a variety of causes produces cirrhosis (widespread fibrosis of the liver).

Clinical signs: In addition to the laboratory biochemical changes typical of liver dysfunction, excessive bleeding may be seen clinically from decreased platelet numbers and/or increased coagulation times.

Neoplasia (Cancer)

Various neoplasms can involve the liver. Primary neoplasms are usually hepatocellular (hepatoma, hepatic carcinoma), bile duct carcinoma, or multicentric lymphosarcoma. Metastatic liver cancer usually arises from mammary gland adenocarcinoma, splenic hemangiosarcoma or pancreatic carcinoma.

Drug-Induced Liver Disease

Only a handful of commonly prescribed drugs are intrinsically harmful, causing predictable liver damage at identified doses.

High doses of acetaminophen are toxic to a dog's liver - although cats are far more sensitive to acetaminophen than dogs.

A fair number of dogs have livers that are idiosyncratically sensitive to anticonvulsants used to control epileptic seizures. Phenobarbital is more liver-friendly than other anticonvulsants used in the past, but its long-term use can cause liver problems. For this reason, some veterinarians prescribe potassium bromide for their epileptic patients. Potassium bromide coupled with lower doses of phenobarbital often allows the practitioner to effectively manage seizures.

Several other drugs have been linked to idiosyncratic liver problems. Very high doses of anti-inflammatory corticosteroids (used occasionally to tame a dangerously overactive immune system) can harm the liver, though the low doses more commonly prescribed to treat itchy skin and other minor inflammations are not harmful to the liver. The combination of diethylcarbamazine and oxibendazole for heartworm and hookworm prevention has caused adverse liver reactions in some dogs, as have the antibacterial combination of trimethoprim and sulfadiazine and the antifungal drug ketoconazole. Most recently, veterinarians have discovered that carprofen, an anti-inflammatory used to treat the pain and stiffness of arthritis, causes liver anomalies in a few dogs.

Blood Clotting Abnormalities

Because the liver is the primary site of coagulation factor synthesis, significant hepatic disease produces prolongation of coagulation tests and may cause an overt bleeding tendency.

Tests for Liver Disorders

Among other blood chemistry tests, your veterinarian may want to check the following serum levels:

Bilirubin: Bilirubin is by-product of the breakdown of hemoglobin. Hemoglobin is the molecule within red blood cells that is responsible for carrying oxygen to the tissues. When the blood cells die or are destroyed, hemoglobin is released and quickly broken down and excreted by the liver as bilirubin. Therefore, bilirubin levels may be higher than normal when excessive numbers of red blood cells are breaking down or if the liver is diseased and unable to clear the bilirubin from the blood. If there is an obstruction within the liver or bile duct so that the bilirubin cannot be released into the intestine, blood levels will also elevate.

Alkaline Phosphatase: Serum alkaline phosphatase (**SAP**) belongs to a class of compounds called enzymes. These are protein molecules that function to assist various chemical reactions. Although the normal level of alkaline phosphatase varies in different species of animals, alkaline phosphatase in a dog is seen at higher levels in certain forms of cancer and some muscle and liver diseases.

SGPT: Serum Glutamic Pyruvic Transaminase (SGPT) is also called alanine amino transferase (**ALT**). It is an enzyme important in liver function. An elevation usually means that the liver cells are breaking down for some reason. The liver may be cancerous, have an infection within it, be congested or engorged with too much blood (as in heart failure), failing or worn out as in cirrhosis, obstructed so that the waste products and toxins it filters from the blood cannot be removed from the body via the bile duct, etc. Basically, anything that adversely affects the liver or its ability to function correctly will elevate the SGPT.

Normal levels for these tests will depend on the measurement units and reference ranges used by the testing laboratory.

Treating Liver Disease

The predisposing cause should be identified and eliminated. Identify and remove any drug or toxin which may potentially hurt the liver.

Supportive care allows time for hepatic regeneration and recovery in some patients. Rest and confinement will help divert body resources to the healing process at the liver and reduce discomfort caused by inflammation of the liver such as painful belly, nausea, malaise. In other patients, supportive care minimizes the clinical manifestations of liver disease for variable periods of time.

Dietary management is extremely important. The goal is to provide all the necessary nutrients which may be lost due to failure of liver processing without overtaxing the liver with regards to processing of dietary intake. High levels of top quality protein to provide the essential amino acids in an easily digestible carrier which will not produce high levels of ammonia during digestion. Cottage cheese is good, meat tends to produce high levels of ammonia. High level carbohydrates to drive the metabolism of the body, essential fatty acids not less than 6% of the daily intake, and a good mineral and vitamin supplement. The primary goal for dietary management of liver disorders includes maintaining metabolic balance while providing nutrients for healing and regeneration of damaged tissue. Other important objectives include:

1. correcting and preventing malnutrition,
2. reducing the need for liver "work," and

3. avoiding production of liver-toxic and nerve-toxic compounds.

Control water retention. Reduce sodium intake. Diuretics will help in resistant cases.

Control concurrent infections with antibiotics.

Deal with the concurrent medical problems as they crop up. The dog may develop bleeding problems, malabsorption problems, and neurological problems. Each separate problem has to be dealt with both individually and as a part of the whole disease entity. Neurological symptoms such as coma need to be addressed aggressively with a combination of therapies.

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