Hepatic Disease – Canine

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Definition

Primary liver disease in dogs is generally either acute or chronic. ***Acute hepatopathies*** are often the result of various drugs, toxins, or secondary to metabolic diseases. If severe, acute hepatopathies can result in liver failure; if less severe, they may be reversible. The most common chronic liver disease in dogs is ***chronic hepatitis*** (CH), which in some cases can progress to cirrhosis. Abnormal copper accumulation has been implicated in many cases of CH. Congenital ***portal systemic vascular shunt*** (PSS) anomalies are common in dogs and result in a number of metabolic derangements and ***hepatic encephalopathy*** (HE).

Key Diagnostic Tools and Measures

The dietary history should be taken and energy requirements for the patient calculated based on ideal body weight (BW). The body condition score (BCS) and BW should be noted. Changes in laboratory tests that reflect liver function (e.g., glucose, albumin, BUN, cholesterol, and serum bile acids) may indicate significant hepatic dysfunction. Diagnosis of HE is based on clinical signs, disease condition, and elevated blood ammonia concentrations.

Pathophysiology

The liver performs a multitude of metabolic processes including the removal of toxic products, storage of nutrients, and the metabolism and regulation of carbohydrates, fats, and proteins. When there is abnormal hepatic metabolism of intestinal nitrogenous byproducts, HE will result. Coagulopathies occur due to a failure of the liver to produce clotting factors and hypoglycemia from altered carbohydrate metabolism. Hypoalbuminemia from decreased liver production will contribute to ascites formation and gastrointestinal ulceration in some patients. Alterations in copper and vitamin metabolism may also occur with various types of liver dysfunction.

Signalment

Liver disease can occur in any breed of dog. Congenital PSS are identified in young, most often small-breed dogs. Acute liver disease from drugs or toxins can occur at any age in any breed. CH is most often seen in middle-aged female dogs (generally from 3 to 10 years of age). Certain breeds of dogs are reported to have metabolic defects in copper metabolism causing a copper-associated CH, including the Bedlington terrier, Doberman pinscher, West Highland white terrier, Skye terrier, Dalmatian, and Labrador retriever.

Key Nutrient Modifications

It is important to ensure there is adequate caloric intake in the dog with liver disease. Diets should be selected for palatability and lipid restriction is not necessary. Carbohydrates should make up no more than 45% of total calories. When hypoglycemia is a concern (i.e., liver failure or PSS) multiple small frequent meals a day may help maintain glucose concentrations and lessen the metabolic impact on the liver. Restricting protein could be detrimental if the dog is in a negative nitrogen balance (i.e., weight loss and hypoalbuminemia). Provide a high quality and highly digestible protein source contributing 15% to 20% on a dry matter basis (DM). Protein restriction should only be instituted in the patient that has clinical evidence of protein intolerance (most often PSS or advanced liver failure). Proteins of milk or plant sources rather than meat-based proteins are suggested. When HE is present dietary protein restriction should be implemented.

In dogs with copper-associated CH, diets containing a high copper content should be avoided (ideally copper should be <5 mg/kg on a dry matter basis). Adequate vitamin supplementation is important because of the important metabolic roles of vitamins in the liver. Animals unwilling to eat often require enteral feeding tubes or parenteral feeding.

Recommended Ranges of Key Nutrients

Nutrient	% DM	g/100 kcal	% DM	g/100 kcal
	Recommended dietary level		Minimum dietary requirement*	
Protein	15–30#	3.5–8.0	18	5.1
Carbohydrate	35–50	5–13	n/a	n/a
Fat	10–25	3–6	5	1.4
	mg/kg diet		mg/kg diet	
Copper**	<5.0		7.3	

Modified intake of these nutrients may help address metabolic alterations induced by disease states. The recommended dietary composition is shown as percent of dietary DM and as g or mg per 100 kcal metabolizable energy. All other essential nutrients should meet normal requirements adjusted for life stage, lifestyle and energy intake.

*Nutrient requirement for adult animals as determined by the Association of American Feed Control Officials

#When protein restriction is needed due to hepatic encephalopathy, meat proteins should be avoided and total protein limited to 15 to 20% of the diet dry matter.

**For dogs with copper-storage associated liver disease, copper should be restricted. Ideally, in these dogs, copper should be <5 mg/kg on a dry matter basis.

Therapeutic Feeding Principles

The goal of nutritional management of liver disease is basically supportive and requires a fine balance between promoting hepatocellular regeneration and providing nutrients to maintain homeostasis without exceeding the metabolic capacity that will lead to accumulation of toxic metabolites. It is vital that the animal with liver disease has adequate caloric intake in order to minimize catabolism and promote recovery of hepatic function, regeneration, and adequate protein synthesis. If necessary enteral tube feeding or parenteral feeding may be required to meet the patient's caloric requirements.

Next the protein content should be considered and protein restriction initiated only with clinical evidence of protein intolerance (i.e., hepatic encephalopathy). The digestibility of the protein and type of amino acids fed also appear to be important. Diets that are high in aromatic amino acids (AAA) promote the formation of false neurotransmitters and subsequent HE. In general, meat-based proteins are higher in AAA content and should be avoided while dairy- and vegetable-based proteins are higher sources of branched-chain amino acids (BCAA) and lessen the risk of HE.

Soluble fiber will undergo colonic bacterial fermentation producing organic acids lowering of the intraluminal colonic pH and, as a consequence, available acids convert NH_3 to the less readily absorbed NH_4^+, in essence trapping ammonia in the colon. Fiber also functions as an osmotic laxative reducing absorption of ammonia and related nitrogenous derived encephalopathic factors from the gastrointestinal tract.

Many types of liver disease may benefit from support in the form of nutritional antioxidants. Nutritional supplements given for antioxidant function including vitamin E, zinc, and glutathione precursors such as S-adenosylmethionine (SAMe) may be beneficial.

■ **Treats** – Vitamin supplementation is appropriate for dogs with liver disease because there may be either an increased demand for vitamins, altered conversion to the active form of the vitamin, or decreased hepatic storage in these patients. Treats or vitamin-mineral supplements containing copper, however, should be avoided especially for dogs having copper-associated CH. Treats containing poor-quality protein, such as rawhide chews, should be avoided in dogs having protein intolerance.

■ **Tips for Increasing Palatability** – Anorexia is often a concern in animals with liver disease. The cause could be associated with HE, gastrointestinal ulceration, or electrolyte abnormalities. Measures should be first taken to correct these conditions. Next, the palatability of the diet should be considered. There is often a misconception regarding fat content in diets for

liver disease; dogs generally have a good tolerance for fat and fat not only improves the palpability but also is an important source of energy density. Sometimes the use of specialty diets intended for liver disease may be rejected simply due to poor palatability and if so dietary flavorings should be tried.

■ **Diet Recommendations** – Without evidence of protein intolerance, premium commercial diets are recommended. The caloric requirements should be calculated to determine needs and the amount divided into four to six small meals a day. For dogs exhibiting protein intolerance or dogs with advanced liver disease, restricted-protein diets are necessary. Feeding commercial therapeutic diets for liver disease or renal disease is recommended for this purpose. Recipes for home-made diets for liver disease have also been published.

Client Education Points

- Dogs with clinical signs related to PSS that do not undergo surgery to correct the shunt should be fed a modified-protein diet, oral lactulose, and if necessary intestinal antibiotics to control the signs. The long-term prognosis is quite variable.
- CH secondary to copper accumulation should be treated with low-copper diets and copper chelation therapy. Following chelation therapy, oral zinc given at high doses can block further absorption of copper. If diagnosed early and with appropriate therapy, the prognosis is good.
- CH from other causes requires specific therapy and if the etiology is not identified an anti-inflammatory is often used. Dietary manipulation, vitamin supplementation, and antioxidant therapy are recommended for most cases. The prognosis is variable for CH.
- Acute liver toxicity is treated with general support and the prognosis is based on the reversibility of the condition. The use of antioxidants and measures to increase hepatic glutathione concentrations are indicated.

Common Comorbidities

Dogs with PSS often have concurrent urate renal or cystic calculi as a result of elevated blood ammonia concentrations. Removal of current cystic calculi, correction of the PSS, and use of measures to control elevated ammonia concentrations prevent further calculi formation. Both acute and chronic liver disease can result in HE, GI ulceration, or coagulopathy. Ascites formation can occur with chronic liver disease due to the combination of portal hypertension and hypoalbuminemia. Ascites is treated with diuretics and sodium-restricted diets, such those used for the management of cardiac failure. With advanced acute or chronic liver disease, multi-organ failure can result including renal shutdown and cardiopulmonary failure; when the latter occurs the prognosis is grave.

Interacting Medical Management Strategies

Dogs having congenital macroscopic PSS are generally treated surgically. Without surgery cases must be managed nutritionally using protein-restricted diets, soluble fiber source such as Metamucil® (Proctor & Gamble), lactulose, and intestinal antibiotics. Copper-associated CH should be treated with copper chelators such as penicillamine or trientine and diets having lower copper concentrations. With successful chelation therapy zinc supplementation at high concentrations will block intestinal copper absorption by inducing binding of copper to a specific intestinal binding protein in the enterocyte. Specific therapy for animals having CH generally involves anti-inflammatory therapy, such as corticosteroids and or immunosuppressive agents. Ursodeoxycholic acid and antioxidants such as vitamin E, SAMe, and milk thistle derivatives are often used as adjunct therapy. Acute liver toxicity involves removal of the offending agent, treating specific complications of the liver disease and providing support to promote liver regeneration. Supplementation using either SAMe or N-acetylcysteine is a means of providing glutathione, a major intracellular detoxifier. Other antioxidants, such as vitamin E and milk thistle or its derivatives, are often used as supplemental adjunct therapy.

Monitoring

The patient's daily caloric intake, in addition to BW and BCS, should be recorded. The liver enzymes and electrolytes should be evaluated periodically to observe improvement or need for modification of the treatment protocol. Repeat liver biopsies are recommended for CH and copper-associated CH to determine the effectiveness of the therapy and to direct modifications in the treatment protocol

Algorithm – Nutritional Management of Canine Hepatic Disease