Hepatic Encephalopathy – Canine

David C. Twedt, DVM, DACVIM

Definition

Hepatic encephalopathy (HE) may be defined as a disturbance in central nervous system function resulting from nitrogenous substances derived from the gastrointestinal tract that gain access to the brain from decreased hepatic function or portal-systemic shunting of blood. HE can occur in dogs secondary to congenital portal systemic vascular shunts (PSS) or acute or chronic liver failure.

Key Diagnostic Tools and Measures

Diagnosis of HE is based on history, clinical signs, and elevated blood ammonia concentrations. Laboratory and imaging testing is required to determine if HE is the result of liver failure or PSS. Precipitating factors that can promote HE (see below) should also be investigated. The body condition score (BCS) and body weight (BW) should be noted and the energy requirements for the patient should be calculated based on ideal BW.

Pathophysiology

HE results from nitrogenous substances absorbed from the intestine that without adequate liver metabolism enter the brain and produce alterations of neurotransmission affecting consciousness and behavior. Ammonia is a key factor but other gut-derived toxins include benzodiazepine-like substances, short- and medium-chain fatty acids, phenols, and mercaptans. Alterations in the ratios of aromatic amino acids (AAA) to branched-chain amino acids (BCAA) in the brain may also contribute to HE as increased concentrations of AAA are thought to promote the formation of false neurotransmitters.

Signalment

Congenital PSS are usually identified in young, small-breed dogs. Acute liver disease can occur at any age or in any breed. Chronic liver disease is most often identified in older dogs. Certain breeds are at risk including the Bedlington terrier, Doberman pinscher, West Highland white terrier, Skye terrier, Dalmatian, Labrador retriever, standard poodle, and cocker spaniel.

Key Nutrient Modifications

Diet is key to the management of HE and should be selected to reduce the nitrogenous load in the gut by protein restriction. Severe protein restriction should be avoided but rather a moderate dietary protein content diet should be fed. Protracted nitrogen restriction contributes to malnutrition and is detrimental. A positive nitrogen balance can often be achieved in conjunction with adjunct HE therapy. A high quality highly digestible protein source contributing 15 to 20% of dry matter basis (DM). Vegetable and dairy sources are preferable to animal protein as they provide a higher calorie to nitrogen ratio and tend to be higher in BCAA than AAA. Further protein restriction should only be instituted in the patient that has clinical evidence of protein intolerance despite adequate HE therapy. Diets containing or supplemented with soluble fiber, a substrate for colonic bacteria, and subsequent colonic acidification may also be of benefit.

Recommended Ranges of Key Nutrients

Nutrient	% DM	g/100 kcal	% DM	g/100 kcal
	Recommended dietary level		Minimum dietary requirement*	
Protein	15–20	3.5–6.0	18	5.1
Carbohydrate	50–65	10–15	n/a	n/a
Fat	15–30	3–7	5	1.4
Fiber#	2–4	0.3–2.0	n/a	n/a
	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

#Soluble fibers are preferred. The crude fiber analysis includes most insoluble fibers, but does not include soluble fibers. Therefore, crude fiber has limited usefulness when evaluating the total fiber content of foods. The ingredient list should be evaluated for sources of soluble fiber.

**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 nutritional recommendation for the patient suffering from HE involves modification of the diet to limit production of nitrogenous byproducts that when absorbed fail to be metabolized by the liver and contribute to HE. First, it is important to assure that the dog is consuming adequate calories as this will minimize catabolism and promote recovery of hepatic function, regeneration and adequate protein synthesis. Next the protein content should be considered. Protein restriction is generally always initiated with clinical evidence of HE. The protein fed should be highly digestible and 15% to 20% of the DM fed. Diets high in aromatic amino acids (AAA) that promote the formation of false neurotransmitters should be avoided. 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 can lessen HE. Soluble fiber undergoes colonic bacterial fermentation producing organic acids. Fermentation promotes the conversion of luminal ammonia (NH_3) to ammonium (NH_4^+), which, by virtue of its net charge, is less readily absorbed into the bloodstream. Fiber also functions as an osmotic laxative reducing absorption of ammonia and related nitrogenous derived encephalopathic factors from the GI tract. Fermentable fiber such as psyllium (1–3 teaspoons per meal) can be supplemented if fermentable fiber is not present in the diet fed.

Adequate vitamin supplementation, given as a B-complex product, is suggested due to their important metabolic roles vitamins play in the liver. Many types of liver disease may benefit from support in the form of nutritional antioxidants. Nutritional supplements given for antioxidant function include vitamin E, zinc, and glutathione precursors such as S-adenosylmethionine (SAMe) and may be beneficial. Zinc, a cofactor of urea cycle enzymes, is often deficient in humans with HE and supplementation could prove beneficial although this has not been documented in dogs. Feeding multiple small frequent meals a day may help maintain glucose concentrations and lessen the metabolic impact on the liver at one time. If the animal is anorexic enteral tube feeding or parenteral feeding may be required to meet the patient's nutritional requirements.

■ **Treats** – Treats generally are not recommended. Giving low-protein

treats or predominantly carbohydrate-based treats such as raw vegetables would be acceptable. Treats or vitamin-mineral supplements containing copper should be avoided. Rawhide or other chews should be avoided in most cases as they provide minimal nutritional benefit.

■ **Tips for Increasing Palatability** – Palatability of the diet is extremely important. First, one should investigate for liver-associated conditions that could contribute to anorexia such as gastrointestinal ulceration or electrolyte abnormalities and if identified they should be corrected. Dietary fat improves palatability and there is no need to restrict fat content in the patient having liver disease and HE. Fat not only improves the palpability but also is an important source of energy density. Warming the food or adding flavorings also may also be helpful.

■ **Diet Recommendations** – Recommended diets to feed the patient suffering from HE include the specialty liver or renal diets. Both contain highly digestible moderate-protein diets. Some geriatric diets or the hydrolyzed diets may also meet nutritional goals in HE therapy. The caloric requirements should be calculated to determine the patient's needs and the amount divided into four to six small meals a day. Animals exhibiting protein intolerance and worsening clinical signs will require lower-protein diets and additional therapy for HE. Resources are also available on home-cooked diets to use for dogs with liver disease and HE.

Client Education Points

- For dogs with congenital PSS that have clinical signs of HE, the general recommendation is surgery to correct the anomaly. Dogs that do not have surgery must be treated medically, which includes feeding a modified-protein diet, oral lactulose, and if necessary intestinal antibiotics to control the signs. The long-term prognosis is quite variable.
- Acute liver disease that causes HE is generally severe and has a guarded prognosis. Acute liver disease has the potential to be reversible, however, if vital metabolic functions can be maintained until the liver has time to regenerate. Therapy involves providing basic liver support and treating complications as they occur.
- The prognosis for chronic liver disease is grave. When HE occurs in chronic liver disease, cirrhosis generally is present. In this situation therapy is only supportive, treating complications of chronic liver disease. With appropriate HE therapy the patient may improve in the short term.

Common Comorbidities

Dogs having congenital PSS often have concurrent urate renal or cystic calculi as a result of elevated blood ammonia concentrations. Removal of current cystic calculi, surgical correction of the PSS, and using measures to control elevated ammonia concentrations prevents further calculi formation. Occasionally dogs having one congenital anomaly will have additional anomalies.

Both acute and chronic liver disease can result in HE, GI ulceration, or a 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 as 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

The medical management of HE usually always involves additional therapy beyond dietary manipulation using protein-restricted diets and a soluble fiber source. With acute HE, bowel cleansing is a mainstay of therapy because colonic evacuation enemas remove intestinal nitrogenous substrates. Chronic management of HE usually requires the use of oral lactulose and intestinal antibiotics. Precipitating factors in HE, including hypoglycemia, hypokalemia, alkalosis and gastrointestinal ulceration, should be avoided or prevented.

There is evidence in human cirrhotic patients with HE that zinc, a cofactor of urea cycle enzymes, may be deficient especially if associated with concurrent malnutrition. Zinc supplementation may be beneficial in chronic liver disease in dogs but this has not been documented.

Monitoring

The patient should be consuming adequate calories and specific therapies for the primary disease condition should be instituted. The clinical and neurologic status should be improved with appropriate diet and lactulose therapy. If these measures fail to improve the patient's status then intestinal antibiotics should be initiated. Precipitating factors in HE should be excluded with a biochemical profile including electrolytes and with a fecal occult blood analysis. If abnormalities are identified they should be treated.

Algorithm – Nutritional Management of Canine Hepatic Encephalopathy (HE)