The liver is the central metabolic organ of the body. It is involved in the digestion, metabolism, and storage of many nutrients. The liver is also the site of synthesis and detoxification of numerous substances. Because of this organ's substantial functional reserve capacity and because of the ability of hepatic tissue to regenerate after an injury, significant hepatocellular damage must occur before clinical signs of liver disease become evident. Accordingly, the objective of nutritional management of liver disease is twofold. The first intention is to avoid overwhelming the limited remaining metabolic capabilities of the damaged organ. This will aid in preventing the accumulation of toxic substances that may cause further hepatocellular injury or may injure other tissues or organ systems. The second aim of nutritional management of liver disease is to provide sufficient nutrients, in particular, protein to allow the organ to regenerate itself as rapidly as possible.

This article will first review the role of the liver in the metabolism of different classes of nutrients and the impact of deranged hepatic function on that metabolism. Next, the general dietary considerations for dogs and cats with liver dysfunction will be discussed. Finally, the nutritional management of several specific disease entities will be addressed.

CARBOHYDRATE METABOLISM

The liver is the primary site of gluconeogenesis, which is the synthesis of glucose from three-carbon units (e.g., amino acids, glycerol, and
lactate) and a major site of glycogen synthesis and storage. In the absorptive state, glucose is taken up by the liver and stored as glycogen, used for the synthesis of fatty acids, or oxidized for the production of energy. In dogs, approximately 40% to 70% of the glucose ingested in a meal is taken up by the liver from the portal circulation. The amount of glucose extracted by the feline liver is less because cats lack the hepatic enzyme glucokinase. Glucokinase is active only in the presence of a high glucose concentration, and the lack of this enzyme in cats is thought to reflect the low direct contribution of dietary carbohydrate to the maintenance of serum glucose levels in this species.

In the fasting state, the liver maintains serum glucose levels by releasing glucose that was stored as glycogen or synthesized by way of the gluconeogenic pathway. Once again, cats differ from most other mammals because the gluconeogenic pathway in the feline liver is active in both the fed and fasting states. Most species are capable of down regulating many of the hepatic enzymes involved in protein catabolism after feeding or when protein intake is low. Cats lack this capability and consequently have a dietary protein requirement in excess of the amounts necessary for protein synthesis. They are metabolically programmed to meet their glucose needs through gluconeogenesis using dietary amino acids, or endogenous amino acids when dietary intake is insufficient.

In summary, the liver occupies a key role in the regulation of carbohydrate homeostasis and serum glucose levels through its ability to remove glucose from and release glucose into the circulation, although the relative significance of these mechanisms varies among species.

Extensive liver dysfunction could lead to abnormal regulation of serum glucose levels resulting either in hypoglycemia or hyperglycemia. Clinically evident fasting hypoglycemia has been reported in dogs with various types of hepatic disease including dogs with chronic hepatitis and approximately one third of dogs presenting with portacaval vascular anomalies. Fasting hypoglycemia is presumably the result of the inability of the diseased liver to store sufficient glycogen or synthesize sufficient glucose from amino acids.

Abnormal glucose tolerance has been reported in humans with cirrhosis, dogs with portacaval vascular anomalies, and cats with idiopathic hepatic lipidosis (IHL). The true underlying mechanism in any of these species remains unknown. For humans and dogs, the pathogenesis is thought to be the result of insulin resistance and poor assimilation of glucose by the damaged liver. Cats with IHL, on the other hand, show little insulin response in intravenous glucose tolerance tests.

**FAT METABOLISM**

The liver plays a central role not only in the synthesis and transportation of lipids, but also in the digestion and absorption of dietary fat through the synthesis of bile salts and the secretion of bile. It is also a
major site of cholesterol synthesis and the only site of ketogenesis in dogs and cats.\textsuperscript{9}

Normally, some of the glucose taken up by the liver in the absorptive state is used for the synthesis of long-chain fatty acids. These fatty acids are then packaged into lipoproteins and released into the systemic circulation. The liver also takes up free-fatty acids absorbed from the intestinal tract or released from adipose tissue in the fasting state. These fatty acids are transported into mitochondria to undergo oxidation for energy production, re-esterified into triglycerides, and released into the circulation or metabolized into ketone bodies. Ketone bodies are also released into the systemic circulation and can be used by many tissues in lieu of glucose as a source of metabolic fuel.

Hepatic dysfunction can result in an imbalance in fatty acid uptake, synthesis, utilization, and release, resulting in lipid accumulation in hepatocytes. Documented causes of fatty liver in different species include decreased triglyceride release secondary to inadequate lipoprotein synthesis and deficiencies of nutrients specifically involved in lipid metabolism.\textsuperscript{2,18}

Although the regulation of serum lipid concentrations is not under as stringent control as serum glucose concentration, the liver influences the concentrations of triglycerides, fatty acids, cholesterol, and phospholipids in the serum. As previously discussed, factors involved in the uptake of fatty acids and the release of triglycerides by the liver will obviously also affect serum levels of these substances.

Serum cholesterol levels are affected by liver function in two ways. First, the liver is a source of cholesterol through de novo synthesis. Second, the only way cholesterol is excreted from the body is by serving as a substrate for the synthesis of bile acids, which are then secreted into the gastrointestinal tract. Phospholipids are also a component of bile and excreted in this manner. Most of what is known about changes in serum lipids in dogs is based on experimental canine models of liver disease, although clinical reports exist of hyperlipidemia, hypercholesterolemia, and hypocholesterolemia in small animals with hepatic dysfunction.\textsuperscript{11,48} In dogs with experimental bile duct obstruction, the primary findings are increased serum concentrations of phospholipids and cholesterol.\textsuperscript{41}

Parenchymal liver damage or biliary obstruction can result in decreased secretion of bile salts into the small bowel. Because bile salts facilitate the absorption of long-chain fatty acids, one might think that decreased secretion of these would result in fat malabsorption. Actually, micelle formation is not essential for long-chain fatty acid absorption, and 30\% to 40\% of dietary triglyceride can still be absorbed in the complete absence of bile salts.\textsuperscript{21} Cholesterol and fat soluble vitamin (A, D, K, and E) absorption still depends on micellinization.\textsuperscript{14} A lack of bile salt secretion, therefore, can result in malabsorption of these nutrients.

**PROTEIN METABOLISM**

The liver also plays a key role in protein synthesis and degradation. It is the source of many of the serum proteins, including transport
proteins, clotting factors, and other acute phase reactants (Table 1). The liver is also the site of ammonia detoxification in the body through the synthesis of urea. As a major site of amino acid metabolism, the liver has an impact on serum amino acid concentrations. Hepatic amino acid synthesis, transamination, and deamination are regulated by host nutritional status, hormonal balance, and the ability of hepatocytes to take up and release various amino acids through specific membrane transport systems.

The ammonia that is converted to urea in the liver comes from several sources. One major source is the gastrointestinal tract. The enterocytes of the small intestine use the nonessential amino acid glutamine as a metabolic fuel. The ammonia resulting from the deamination of this amino acid is partly transferred to pyruvate to form alanine and is partly released directly into the portal circulation. The colon is also a significant site of ammonia production. Here the resident microflora are responsible. Some of the ammonia is produced by bacteria using proteins entering the colon, but most of it is generated by urease-producing bacteria. The small intestine is highly permeable to urea, and it is estimated that 20% to 30% of the urea produced by the liver diffuses into the intestinal lumen where it can become a substrate for urease-producing bacteria on reaching the colon. The resulting ammonia can diffuse back across the colonic mucosa and into the portal blood.

Ammonia is also generated from glutamine metabolism in the kidney for acid-base homeostasis. Skeletal muscle and hepatic tissues produce ammonia during the catabolism of amino acids for energy.

The normal liver has a remarkable capacity to remove ammonia from the blood. Only in the face of severe hepatic dysfunction does hyperammonemia occur, when impaired ureagenesis cannot keep pace with ammoniagenesis. Normal rates of ammonia production can be compounded if there is increased use of amino acids as metabolic fuel; a situation more likely to arise in a metabolically stressed individual as a result of the release of catabolic hormones such as glucagon, catecholamines, and glucocorticoids.

The response to an acute injury, whether it is hepatic damage or another type of insult, is the reprioritization of host protein. Because there is no storage form of protein or amino acids in the body similar to the storage forms of fat (adipose tissue) and carbohydrate (glycogen), functional proteins must be catabolized to meet the demands for the synthesis of host defense proteins, granulation tissue, and acute phase reactants. Proteins in skeletal muscle and other tissues are broken down,

Table 1. PROTEINS SYNTHESIZED BY THE LIVER

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Fibrinogen and other β-globulins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin</td>
<td>Apolipoproteins</td>
</tr>
<tr>
<td>Retinol-binding protein</td>
<td>Prothrombin</td>
</tr>
<tr>
<td>Pre-albumin</td>
<td>Clotting factors (V, VII, VIII, IX, X)</td>
</tr>
<tr>
<td>Ceruloplasmin and other α-globulins</td>
<td>Numerous serum enzymes</td>
</tr>
</tbody>
</table>
and the resulting amino acids are, for the most part, released into the systemic circulation. These amino acids can be taken up by hepatocytes and used for protein synthesis and energy production. The branched chain amino acids (BCAA), leucine, isoleucine, and valine, are the exception. These amino acids are used principally by the peripheral tissues as metabolic fuel. In the face of hepatic injury, this acute injury response can be hindered. Numerous studies using canine models of liver disease show that loss of hepatic function, whether from resection of tissue or portosystemic shunts, results in decreased serum levels of the BCAA and increased serum levels of all other amino acids.\(^1\) This is notably the case with the aromatic amino acids (AAA), phenylalanine, tyrosine, and tryptophan, which are not degraded outside of the liver. As with other aspects of hepatic metabolism, derangements of serum amino acid concentrations and hepatic protein synthesis are not seen until severe loss of hepatocellular mass has occurred.

It should be clear from this discussion that the protein requirement of animals with liver dysfunction is at least as great as that of normal healthy individuals. A recent investigation involving clinically stable dogs with surgically produced portosystemic shunts found no change in the protein requirement of these animals before and after shunt production (2.07 g crude protein/kg body weight/day versus 2.11 g crude protein/kg body weight/day).\(^2\) These dogs were capable of adapting to a lower protein intake in a manner similar to normal dogs; however, they ultimately had lower serum total protein and albumin concentrations than dogs with portosystemic shunts who consumed a higher protein diet. Reduced serum protein concentrations seen in the dogs in this study were suggestive that protein malnutrition and depletion of host proteins had occurred during the consumption of the low protein diet.

MICRONUTRIENT METABOLISM

The liver is also involved directly and indirectly in the absorption, metabolism, transport, and storage of many micronutrients.

Fat soluble vitamins must be packaged into micelles for absorption from the gastrointestinal tract, and bile acids are required in this process. The liver is indirectly involved in the absorption of calcium because the first step in the activation of vitamin D occurs there.\(^3\) With the exception of vitamin K (discussed later), fat soluble vitamin deficiency secondary to liver disease is not commonly recognized in dogs and cats.\(^4\) This is probably partly due to the abundant stores of these vitamins that exist in most adult animals.

Aside from the hydroxylation of vitamin D, the liver is the principal site of the synthesis or activation of numerous other vitamins. Pyrophosphorylation of thiamine (B\(_1\)) occurs in the liver and in the kidney.\(^5\) Conversion of folic acid to the active form, 5-methyl tetrahydrofolate, occurs principally in the liver, as does the transformation of pyridoxine.
(B6) into coenzyme pyridoxal-5'-phosphate. The liver is also a major site of vitamin C synthesis in dogs and cats and decreased serum levels of vitamin C have been reported in dogs with experimentally induced hepatic disease. Finally, the recycling of vitamin K epoxide, formed during the carboxylation of clotting factor precursors, back to the active form, occurs solely in hepatic tissue.

Clinically, vitamin K deficiency is the most rapidly developing and readily detectable vitamin deficiency seen in liver disease. Prolonged prothrombin time and clinical bleeding has been reported in dogs and cats with various types of hepatic dysfunction, including cholestatic disease and hepatic lipidosis. Because clinical signs and abnormal clotting function often resolve with vitamin K administration, it seems that the problem is due more to impaired vitamin K absorption or recycling than to impaired clotting factor synthesis.

Severe liver disease may result in impaired metabolism of the other vitamins previously discussed, and this in turn may have repercussions on energy and protein metabolism and on the ability of the liver to regenerate. The extent to which these deficiencies actually occur is unknown, and if they do occur, the extent to which they contribute to the clinical picture of liver disease is similarly unclear.

Several of the proteins listed in Table 1 are involved in the transport of vitamins and minerals. Impaired synthesis of one or more of these proteins can lead to decreased serum levels of the nutrients to which they normally bind, and in turn, affect the availability of the nutrients to peripheral tissues. For example, decreased serum concentrations of vitamin A in the face of abundant liver stores have been detected in human patients with acute and long-term liver disease secondary to decreased synthesis of retinol binding-prealbumin complex. These patients often have clinical signs of vitamin A deficiency, such as abnormal dark adaptation.

In some cases, such as with copper, impaired hepatic protein synthesis may result in decreased excretion. Copper is highly toxic when not bound to protein. It is normally stored in the liver in the protein-bound state and is either excreted in the bile as such or secreted into the serum bound to ceruloplasmin for uptake by other tissues. Accumulation of copper in hepatic tissues has been documented in humans and dogs with long-term hepatitis.

Finally, the liver acts as a storage site for virtually all of the vitamins, both fat and water soluble. Hepatocytes also store iron, copper, zinc, manganese, and magnesium. In the face of liver disease, hepatic reserves can be decreased, normal, or increased, depending on the nutrient in question and the underlying etiology of the disease.

DETOXIFICATION AND EXCRETION OF METABOLITES

Although the detoxification and excretion of metabolites are not directly related to nutrition, these functions deserve consideration be-
Because the liver is the primary site of detoxification both of the endogenous by-products of the intermediary metabolism (e.g., ammonia) and of exogenous substances absorbed from the gastrointestinal tract. These exogenous substances may be constituents of foods, food additives, or metabolites of bacterial action on dietary components. It has been postulated that this is the origin of some of the toxins implicated in the pathogenesis of hepatic encephalopathy (e.g., mercaptans from methionine and short chain fatty acids from carbohydrates). Some investigators have suggested that consumption of commercial pet foods in the face of liver disease should be avoided because intestinal microflora can metabolize food additives into potent hepatotoxins, which, because they are not readily inactivated by the impaired liver, may cause further hepatic injury.49

GENERAL DIETARY RECOMMENDATIONS

From the preceding discussion, it should be clear that no single diet will best suit the nutritional and clinical needs of all patients with liver disease or even those with one specific type of hepatic dysfunction. With a few exceptions, the nutrient requirements of dogs or cats with liver disease will be at least as great as those of a clinically normal animal. In fact, the requirements for protein and various micronutrients may be greater in liver disease than in the normal state, although very little information regarding specific nutrient requirements of injured or ill dogs and cats is currently available.

Whether an animal with hepatic dysfunction can tolerate a normal diet without the induction of metabolic disturbances is another question. The ideal diet would be one that exactly met a patient's energy, protein, and micronutrient requirements, so that no synthetic or metabolic pathway would be compromised by nutrient deficiencies, while at the same time the potential for overwhelming the remaining functional tissue with the work of metabolizing nutrient excesses would be avoided. Even if such a diet could be formulated, it is probable that a patient with severe hepatic dysfunction would still exhibit some metabolic derangement.

The real challenge facing the practitioner is judging the nutritional adequacy of a diet for a given patient when the clinically available methods for that kind of evaluation are crude at best.

Energy Requirement

The energy requirement of an individual reflects the energy consumed in its basal metabolic processes plus the energy expended in physical exertion. Although basal metabolic energy expenditure is often elevated in acute illness because of increased protein turnover, fever, and other energy consuming processes, physical exertion is usually
significantly curtailed. If one of the goals in feeding animals with liver disease is to match energy intake as closely as possible to energy expenditure, then it is important to be conservative when estimating caloric requirements. Currently, the only means for clinically evaluating the caloric adequacy of a diet is determining whether it prevents weight loss or gain. This criterion can be difficult to use in an acutely ill patient with significant fluid shifts. Obviously, changes in body weight can also be misleading in patients with ascites.

Although the temptation to try to put weight back on a debilitated animal is great, if that patient is currently experiencing severe hepatic dysfunction, the excess calories will only be a potential burden on the remaining functional hepatocytes. The goal should be to prevent further weight loss until the patient’s clinical situation has stabilized and at least some hepatic regeneration has occurred.

The form that the calories should take depends on the extent to which the patient is experiencing cholestatic liver disease. Normally, high fat foods are useful for dogs and cats who are sick and have reduced appetites. This is because increased fat content not only makes a food more palatable, it also increases the amount of energy contained per gram of food. Mild or even moderate cholestatic disease will probably not result in significant steatorrhea because bile acids are not strictly necessary for long-chain fatty acid absorption. Patients experiencing a severe reduction in bile secretion, however, may require moderation of fat intake. The practitioner should be cautious about using low-fat, reducing type diets for this purpose. These diets are purposely designed to be calorically restricted and to promote early satiety. Because most clinically ill patients already have a reduced appetite, diets of this type will only make the task of providing adequate calories more difficult.

**Protein Requirement**

Estimating the protein requirement of a patient with liver disease is also a challenge. Most veterinarians focus on reducing dietary protein as a means of managing hyperammonemia. This maneuver, however, becomes counterproductive if either total protein intake or the intake of one or more of the essential amino acids is insufficient to meet the patient’s protein requirements. Recall that the hormonal milieu of sick or injured animals is very different from that of healthy animals. While the healthy animal can adapt to some extent to a lower protein intake by limiting protein turnover, this adaptive mechanism is opposed by the need for increased synthesis of host defense proteins in the sick animal. If protein intake is inadequate, endogenous protein will be catabolized and some of the amino acids released will be deaminated. This response is compounded when a protein-deficient diet is fed to a sick animal who is already in a catabolic state. The provision of adequate protein will not completely shut down this catabolic response, particularly in critically ill patients, but there is evidence in human patients
that the response can be blunted.\textsuperscript{45} It is important to recognize that the protein must be given with adequate nonprotein calories; otherwise it partly will be used to meet the patient’s energy needs (although there is no way of avoiding this in feline patients, given their metabolic predisposition to use amino acids for gluconeogenesis).\textsuperscript{30} To summarize, feeding inadequate amounts of protein to a patient with liver disease can result in increased breakdown of endogenous protein, some of which will be deaminated with the consequence of ammonia production.

On the other hand, feeding protein in excess of a patient's requirement will insure that the excess amino acids will be used for energy metabolism, with the production of ammonia as a by-product. The amount of excess protein that can be metabolized by an animal with liver disease without the development of hyperammonemia depends on the severity of hepatic dysfunction and varies significantly among patients. A practitioner faced with a patient with liver disease must not only evaluate the patient for clinical signs of neurologic disturbance and, if possible, blood ammonia levels, but also take a dietary history before deciding on the level of protein intake to recommend. A dietary history may show a patient that is being fed a very high protein diet (e.g., a meat-based, canned food). Neurologic signs associated with feeding this diet may be abolished simply by feeding a diet with a more moderate protein content, without recourse to drastic protein restriction.

A key point to be made is that protein quality, in addition to protein quantity, will vary from food to food. Protein quality refers to the digestibility and the amino acid content of the protein. The more digestible the protein is, and the better the amino acid content of the protein reflects the amino acid requirements of the animal consuming the protein, the less of the protein the animal will require to meet its protein needs. Generally, proteins of animal origin are of higher quality than proteins of plant origin. Traditionally, diets made with cottage cheese or egg have been advocated for patients with liver disease largely for this reason. The evaluation of a diet for a patient with liver disease, therefore, should include assessing the quality as well as the quantity of the protein in the diet.

The practitioner must use the clinical evaluation of each patient coupled with a dietary history to select an appropriate level of protein intake. Once the patient is eating the diet, the practitioner can re-evaluate the situation in light of the patient’s tolerance of the diet and clinical response to therapy and can increase or decrease the level of protein intake accordingly.

**Micronutrient Requirements**

Unfortunately, the practitioner has virtually no means of gauging a patient’s micronutrient status short of detecting signs of extreme deficiency, as in abnormal prothrombin time caused by vitamin K deficiency. Serum concentrations of vitamins or minerals often do not reflect total
body stores. 

Tissue levels are sometimes more reliable indicators of micronutrient status, but normal reference values for dogs and cats are largely unavailable. The dilemma is compounded by the lack of knowledge of the specific requirements of animals with impaired hepatic function. It is probably safe to provide micronutrients to animals with liver disease in the quantities currently recommended for normal dogs and cats. Supplementation of commercial foods that already contain balanced amounts of vitamins and minerals should be approached with care to avoid overconsumption of potentially toxic micronutrients (e.g., fat-soluble vitamins, copper). Mineral supplementation can also impair the absorption of the minerals already existing in the diet.

If cholestatic disease is severe, it may be necessary to provide parenteral vitamin K. Parenteral supplementation of vitamins A and D should not be necessary unless the pathologic condition becomes long-term. The potential for the development of vitamin E deficiency in dogs and cats due to reduced bile secretion and the clinical consequences of such a deficiency is currently unknown.

**Feeding Management**

The preceding discussion has not addressed the issue of anorexia and the acceptability of diets prescribed for liver disease. Many animals with hepatic dysfunction will be anorectic or will object to a change from their usual diet. Anorexia is the hallmark of IHL in cats, and force-feeding, using nasogastric or gastrostomy tubes, is the accepted therapeutic approach to these patients.

Every effort should be made to encourage patients with liver disease to eat voluntarily. Food should be made as palatable as possible, served fresh, possibly warmed, and given in many small portions throughout the day. Benzodiazepine appetite stimulants should be avoided because they may exacerbate the signs of hepatic encephalopathy. There is evidence that the stimulation of the gamma-aminobutyric acid (GABA) neurotransmission system in the brain may be involved in the development of hepatic encephalopathy. Benzodiazepine drugs bind to a receptor complex that includes the GABA receptor and can potentiate the effects of GABA binding. There are clinical reports of successful use of benzodiazepine antagonists to treat hepatic coma and other manifestations of hepatic encephalopathy in humans and dogs (Lesley G. King, MVB, personal communication, 1994).

Once the practitioner managing a dog or a cat with liver disease has decided on an appropriate diet for that patient, it is essential that he or she set a caloric goal for voluntary intake. If a patient does not meet that goal after 2 to 3 days, the practitioner should seriously consider some form of force-feeding. The reader should refer to one of the numerous reviews of nutritional support of small animals for a detailed discussion of the special issues involved.

Aside from its use as a strategy for dealing with anorexia, there is
Table 2. RECIPES FOR HOMEMADE DIETS USEFUL FOR DOGS WITH LIVER DISEASE

<table>
<thead>
<tr>
<th>Basic Canine Recipe*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 large eggs</td>
</tr>
<tr>
<td>1 cup rice (uncooked)</td>
</tr>
<tr>
<td>2 tsp corn oil</td>
</tr>
<tr>
<td>5 g dicalcium phosphate</td>
</tr>
<tr>
<td>⅛ tsp iodized KCI (salt substitute)</td>
</tr>
</tbody>
</table>

Cooking directions: All ingredients except the eggs can be combined and cooked with the rice. The eggs can be stirred into the rice during the last few minutes of cooking or hard boiled and added to the cooked rice mixture.

Give one multiple vitamin/mineral supplement per recipe portion fed per day.

The protein content of the Basic Recipe can be adjusted upwards by adding 2 eggs and subtracting 1/4 cup uncooked rice and downwards by subtracting 2 eggs and adding 1/4 cup uncooked rice. These adjustments will not affect the total calories in one recipe portion.

*The Basic Recipe contains approximately 1000 Kcal, 13% protein, 25% fat, and 62% carbohydrate on an energy basis.

another excellent reason for offering patients with liver disease many small meals throughout the course of a day. Dividing a patient’s daily ration into several portions in effect decreases the dose of protein and other nutrients that the liver is required to metabolize at any given time. An animal may be able to tolerate a higher protein intake without developing hyperammonemia, if the protein is fed in four or more portions a day rather than in one or two large meals.

Tables 2 and 3 contain examples of simple recipes for homemade diets for dogs and cats with liver disease. The basic canine recipe is formulated to provide approximately 2.1 g protein/kg body weight,

Table 3. RECIPES FOR HOMEMADE DIETS USEFUL FOR CATS WITH LIVER DISEASE

<table>
<thead>
<tr>
<th>Basic Feline Recipe*</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 large eggs</td>
</tr>
<tr>
<td>⅛ cup rice (uncooked)</td>
</tr>
<tr>
<td>⅛ tsp corn oil</td>
</tr>
<tr>
<td>3 g dicalcium phosphate</td>
</tr>
<tr>
<td>⅛ tsp iodized KCl (salt substitute)</td>
</tr>
</tbody>
</table>

Cooking directions: All ingredients except the eggs can be combined and cooked with the rice. The eggs can be stirred into the rice during the last few minutes of cooking or hard boiled and added to the cooked rice mixture.

Give one multiple vitamin/mineral supplement per recipe portion fed per day.

The protein content of the Basic Recipe can be adjusted upwards by adding 1 egg and subtracting 1/8 cup uncooked rice. This adjustment will not affect the total calories in one recipe portion.

*The Basic Recipe contains approximately 500 Kcal, 22% protein, 45% fat, and 33% carbohydrate on an energy basis.
which was found to be the requirement of dogs with surgically produced portosystemic shunts. The protein content of the basic feline recipe reflects the minimum amount of protein that has been used safely in therapeutic diets in the past. There are numerous other published recipes to which the reader can refer.

**SPECIFIC RECOMMENDATIONS**

**Hepatic Encephalopathy**

The neurologic derangement that can accompany severe liver disease or portosystemic shunts is believed to be the result of altered serum concentrations of one or more metabolites. Hyperammonemia is commonly seen in patients with hepatic dysfunction and can cause a variety of neurologic signs. It has been observed in humans and dogs, however, that serum ammonia levels often do not correlate well with the clinical severity of neurologic derangement. This observation has prompted a search for other potential toxic substances or metabolic imbalances that may be at work in patients with hepatic encephalopathy.

Various studies, often involving canine models of liver disease, have implicated metabolites generated by gastrointestinal microbes and altered serum amino acid concentrations as putative causes of hepatic encephalopathy. By-products of gut microbial metabolism include mercaptans that are synthesized from methionine and short chain fatty acids (SCFA), which principally are the result of the fermentation of fiber in the colon.

Both methionine toxicosis and abnormal serum amino acid concentrations have been observed clinically in small animals with neurologic signs. Coma has been induced in normal dogs by altering serum amino acid concentrations to reflect the concentrations observed in spontaneous hepatic encephalopathy (i.e., elevated AAA and decreased BCAA). These findings and others have prompted a number of dietary recommendations for patients with liver disease.

First is the recommendation that excess methionine consumption be avoided. Methionine is an essential amino acid and is contained in most sources of protein that are used to formulate diets for dogs and cats. It is unlikely that the amount of methionine found in most proteins would pose a problem for patients with liver disease. The provision of supplemental methionine to an animal with liver disease, however, may present a risk. Choline is important for the synthesis of lipoproteins, and choline deficiency is a reported cause of hepatic lipidosis. Choline supplementation has been advocated in some forms of liver disease. Because methionine is a synthetic precursor of choline, it has been used in lieu of, or in addition to, choline for the same purpose. Commercial "lipo-trophic" products containing methionine should be avoided in patients with a predisposition to hepatic encephalopathy.

Greater consumption of BCAA relative to consumption of AAA has
also been advocated. To date, trials of parenteral and enteral formulas in human patients with hepatic encephalopathy have shown little if any clinical benefit.\textsuperscript{19} It is also interesting to note that in one study involving dogs with surgically produced portosystemic shunts, more of the dogs consuming a diet enriched with BCAA developed neurologic signs than did the dogs consuming a diet containing the same total amount of protein but enriched with AAA.\textsuperscript{26}

Concerning SCFA, there has been some confusion in the veterinary literature as to the source of these compounds in the diet. Low-fat diets have been advocated for patients with liver disease because it was believed that SCFA resulted from incomplete oxidation of long-chain fatty acids. In fact, SCFA are a by-product of microbial fermentation in the colon. Diets high in fermentable fiber and carbohydrate, rather than fat, promote the production of these substances.\textsuperscript{13}

Therapeutic strategies aimed at modifying gastrointestinal microbial metabolism and the absorption of microbial by-products should receive as much attention as dietary manipulation in addressing the management of hepatic encephalopathy. Lactulose and antibiotic therapy should be initiated in patients with liver disease and neurologic signs. Until clinical signs of neurologic derangement resolve, the patient should be maintained without food intake. When feeding can be resumed, the diet should be selected based on the patient’s clinical condition and previous dietary history.

\textbf{Feline Idiopathic Hepatic Lipidosis}

The goal in feeding a cat with idiopathic hepatic lipidosis (IHL) is to provide a complete and balanced diet that can be force-fed until the patient resumes eating voluntarily. It is necessary to emphasize “complete and balanced” diet because these patients often require force-feeding for weeks. The ideal approach would be to use a blenderized cat food. This will work best if the cat has a large bore feeding tube in place. Small bore nasogastric tubes necessitate the use of liquid formulas. On the other hand, adapting one of the many human liquid diets for use in cats gives the practitioner more flexibility in manipulating both macronutrient (i.e., protein, fat, and carbohydrate) and micronutrient content. It is critical to remember, however, that most human enteral products contain amounts of protein, taurine, arginine, B vitamins, and various minerals that are deficient for feline maintenance. Human enteral products, therefore, must be supplemented appropriately if they are to be used for feline patients.

The treatment of cats with IHL who develop signs of hepatic encephalopathy is particularly difficult. Despite the fact that force-feeding is currently the only therapeutic option for cats with IHL, it is necessary to stop food intake in a patient with neurologic signs until those signs are resolved by medical means.
Copper Toxicosis

Liver disease secondary to excessive copper accumulation resulting from an inherited defect of copper excretion is recognized in several breeds of dogs. Hepatic copper accumulation is also thought to occur secondary to primary liver disease in dogs without any inherited defect in copper excretion. Dietary therapy (i.e., feeding low copper diets) is unlikely to have much impact on patients with copper storage disease that are showing clinical signs of hepatic dysfunction, because these dogs already have large amounts of copper in their livers. Instead, copper chelator therapy is indicated. Chelator therapy seems not only to prevent absorption of dietary copper, but also to promote the loss of endogenous copper, thus gradually reducing the amount of copper stored in the liver.

It is possible that a restricted copper diet might be useful in the management of dogs with inherited defects of copper metabolism if such a diet is initiated early in life. Because all commercial dog foods are supplemented with copper, however, this approach would necessitate the use of a homemade diet. Ingredients rich in copper, such as shellfish and organ meats and copper-containing vitamin/mineral supplements, should be avoided when formulating such diets. Feeding homemade diets to young dogs while they are still actively growing could potentially be damaging because of the greater stringency of nutritional requirements during growth. Such an approach should be undertaken with great care and caution.

SUMMARY

The provision of adequate nutrition to the patient with liver disease is a challenge. The practitioner must avoid overwhelming the remaining metabolic capabilities of the damaged organ. The ability of the liver to regenerate and the patient to recover depends on the availability of sufficient nutrients.

There is no default diet for the patient with liver disease. Each patient must be evaluated individually, with consideration given to the type and origin of the liver disease, the current extent of hepatic dysfunction, and the patient's previous dietary history. Efforts should be directed at the provision of an energy intake adequate to maintain body weight and a protein intake as close to normal as can be tolerated without precipitating signs of hepatic encephalopathy.

References


42. Rogers QR, Morris JG, Freedland RA: Lack of hepatic enzymatic adaptation to low and high levels of dietary protein in the adult cat. Enzyme 22:348, 1977
46. Silva SVPS, Mercer JR: Effect of protein intake on amino acid catabolism and gluconeogenesis by isolated hepatocytes from the cat (Felis Domestic). Comparative Biochem Physiol 80B:603, 1985

Address reprint requests to
Kathryn E. Michel, DVM, MS
Department of Clinical Studies–Philadelphia
School of Veterinary Medicine
University of Pennsylvania
3850 Spruce Street
Philadelphia, PA 19104-6010