Timely Topics in Nutrition

The carnivore connection to nutrition in cats

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In another time long ago, Leonardo da Vinci said, "The smallest feline is a masterpiece."[1] And for those of us who marvel at the wonder that is a cat, there is no doubt that his statement was remarkable for its simplicity as well as its truth. Cats are amazing creatures, unique and interesting in almost every way imaginable. Despite this, it has been common for veterinarians to consider cats and dogs as similar beings for anesthesia protocols, clinical diseases, and treatments. However, it is quite clear that cats are unique in all conceivable ways, particularly in their nutritional biochemistry. Cats are strict carnivores that rely on nutrients in animal tissues to meet their specific and unique nutritional requirements. This statement is news to few, yet the importance of these nutritional differences is often underestimated, especially during periods when cats are ill or have prolonged anorexia. In their natural habitat, cats consume prey high in protein with moderate amounts of fat and minimal amounts of **carbohydrate (CHO)**; thus, they are metabolically adapted for higher metabolism of proteins and lower utilization of CHOs (starch, not soluble or insoluble fiber) than dogs or other omnivores. Although cats can use CHOs as a source of metabolic energy, they have limited ability to spare protein utilization by using CHOs instead. Nevertheless, commercial diets are formulated with a mixture of animal- and plant-derived nutrients, most commonly in dry kibble form that requires CHOs for the expansion and cooking process, to provide easy-to-use food for domestic cats. And although cats have adjusted to most manufactured diets, the limitations of substituting animal-origin nutrients with plant-origin nutrients in foods formulated for cats are being increasingly realized.

The information reported here is an attempt to describe what it means metabolically and nutritionally to be a strict carnivore, with a focus on differences in nutritional biochemistry of cats. In addition, information is included on possible roles of nutrition in the development of obesity, **idiopathic hepatic lipidosis (IHL)**, inflammatory bowel disease, and diabetes mellitus in cats.

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Protein

The natural diet of cats in the wild is a meat-based regimen (eg, rodents, birds) that contains little CHO; thus, cats are metabolically adapted to preferentially use protein and fat as energy sources (**Appendix 1**). This evolutionary difference in energy metabolism mandates cats to use protein for maintenance of blood glucose concentrations even when sources of protein in the diet are limiting.[2] The substantial difference in protein requirements between cats and omnivores, such as dogs, serves to illustrate this important metabolic distinction. For example, whereas the protein requirement of kittens is 1.5 times that of the young of other species, adult cats require 2 to 3 times more protein in their diet than adults of omnivorous species.[2,4] The fact that cats have such a greater dietary protein requirement, compared to dogs, necessitates that cats must have a higher basal requirement for nitrogen (protein) or an increased requirement for essential amino acids. In the case of adult cats, the increased protein requirement is attributable to both; however, the requirement for essential amino acids in kittens is similar to that of the young of other species,[5] so a higher basal requirement for nitrogen is suggested to play the largest role in kittens.

Several possible reasons exist for the increased need for protein, but the fact that cats depend on protein for energy as well as structural and synthetic purposes is a major component. When fed a low-protein diet, most omnivores conserve amino acids by reducing the activities of aminotransferases and other enzymes involved in protein catabolism.[6,7] However, in a classic study,[8] cats were fed diets low (170 g/kg [77 g/lb] of body weight) and high (700 g/kg [318 g/lb] of body weight) in protein to determine whether they responded to low-protein conditions in a manner similar to that of omnivorous species. Regardless of whether cats were fed low or high amounts of dietary protein, there was little adaptation in the activities of the aminotransferases or urea cycle enzymes.[8] In another study,[9] it was suggested that cats have a limited ability to adjust protein utilization to the amount of protein in their diets; however, the primary finding in that study was that protein oxidation increased in cats

fed high-protein diets. Protein oxidation did not decrease in cats fed diets with moderate amounts of protein (low-protein diets were not evaluated).[9] Nevertheless, those studies document that cats continue to use protein (eg, dispensable nitrogen in the form of gluconeogenic amino acids) for production of energy and in other metabolic pathways (eg, urea cycle), even in the face of low availability of proteins. These increased protein requirements are an important reason why protein malnutrition can occur more quickly in sick, injured, or anorectic cats.

In addition to their increased need for dispensable protein, cats also have need for increased amounts of specific amino acids in their diet: taurine, arginine, methionine, and cysteine.[2] These specific amino acid requirements of cats have likely been determined on the basis that their natural diet contains an abundance of each of these specific amino acids (in addition to 11 essential amino acids; **Appendix 2**). The likely reason that synthetic pathways for these amino acids, which are found in omnivorous species, are not found in cats is that they are redundant and, thus, energy inefficient. Furthermore, even though cats do not have the ability to synthesize these amino acids, the amino acids are not conserved. In fact, utilization of these amino acids (taurine, arginine, methionine, and cysteine) is higher in cats than in dogs or other animals.

Taurine is a sulfur-containing β amino acid that is not incorporated into proteins or degraded by mammalian tissues; however, it is essential for vision, cardiac muscle function, and proper function of the nervous, reproductive, and immune systems.[2] Taurine is essential in cats because they cannot synthesize adequate quantities from the typical precursors (ie, methionine or cysteine). Enzymes required for synthesis of taurine (eg, cysteine dioxygenase and cysteine sulfinic acid decarboxylase) are only minimally active in cats.[10] Furthermore, cats have a constant and obligate loss of taurine into bile, because they conjugate bile acids only with taurine.[10] Complicating matters, the requirement for taurine in cats is influenced by many factors including, but not limited to, the source of protein (ie, taurine is found in animal-source proteins but must be supplemented when plant-source proteins are used in the diet), commercial processing (heat processing reduces taurine bioavailability[11]), content of sulfur-containing amino acids in the diet (taurine is synthesized from sulfur-containing amino acids [methionine and cysteine], although cats cannot meet their needs via this pathway[4]), and amount of dietary fiber (diets high in fiber increase the need for taurine[12]). Prolonged (ie, a period of several months) deficiency of taurine is required before clinical signs appear in most cats. The most common signs of deficiency are blindness (central retinal degeneration), reproductive failure or neonatal loss, and development of dilated cardiomyopathy.[2,10] Diagnosis of taurine deficiency in cats is confirmed by measurement of taurine concentrations in blood. Taurine concentrations in the blood reflect tissue taurine status better than do taurine concentrations in plasma, which can be affected by release of cellular taurine (especially from platelets).[2] The reference range for concentrations of taurine in healthy cats is > 300 nmol/mL, with concentrations < 160 nmol/mL consistent with deficiency.[2]

Arginine is an essential amino acid in dogs and cats; however, in contrast to dogs, cats are unable to synthesize sufficient amounts of ornithine or citrulline for conversion to arginine. Thus, it must be available in their diet.[13,14] In addition, cats continually use large amounts of arginine in the urea cycle, because this cycle is not down-regulated in cats during periods when food is withheld or in cats consuming low-protein diets.[4,7] Cats and kittens fed a diet devoid of arginine have clinical signs of hyperammonemia (eg, salivation, neurologic abnormalities, hyperesthesia, emesis, tetany, and coma) within hours, and the condition may progress to death.[13,14] Fortunately, arginine and citrulline are abundant in animal tissues; thus, arginine deficiency is rare in cats consuming appropriate foods. However, arginine supplementation must be used to avoid a deficiency in cats fed diets with plant-origin protein sources. Arginine supplements should also be considered in anorectic cats with IHL, because a deficiency of arginine may be responsible for some of the clinical signs observed in cats with this disease. The dose of arginine that will benefit cats with IHL is unknown, but 250 mg of arginine/d is recommended.

Cats also have a higher requirement for methionine and cysteine in their diet than dogs or other omnivores.[2,15] Although there are numerous explanations for this increased requirement, 1 major reason is that methionine and cysteine are gluconeogenic amino acids in cats that are catabolized to pyruvate and then subsequently oxidized to provide energy (Appendix 2). In dogs and other animals, methionine and cysteine have many uses but are primarily converted to taurine, homocysteine, and S-adenosyl-methionine and its metabolites (eg, glutathione), which are important antioxidants and scavengers of free radicals (**Fig 1**).[2,4,16,17] In addition to the aforementioned pathways, the requirement for cysteine is high in cats for production of hair and felinine, a sulfur-containing amino acid found in the urine of cats.[18] The highest concentrations of felinine are found in sexually intact male cats (95 mg of felinine excreted/24 h), with significantly lower concentrations in neutered males (29 mg/24 h), sexually intact females (19 mg/24 h), and spayed females (13 mg/24 h).[18] Thus, dietary requirements for cysteine in sexually intact male cats is substantially higher than in neutered male cats or female cats. The function of felinine is largely unknown, but it may be important in territorial marking. Additionally, the high rate of felinine excretion in male cats creates another protein sink.[18] Methionine and cysteine are found in large quantities in animal tissues, so deficiency is uncommon in cats consuming an appropriate diet. However, deficiencies may develop in anorectic cats, cats fed diets that contain plant-origin proteins, or cats fed enteral formulations created for use in humans, which are deficient in amino acids required by cats. Methionine or cysteine deficiencies are often initially seen clinically as poor growth in kittens or crusting dermatoses and poor pelage in adult cats.[2]

Tyrosine, an amino acid that is not essential for other species, is considered to be conditionally essen-

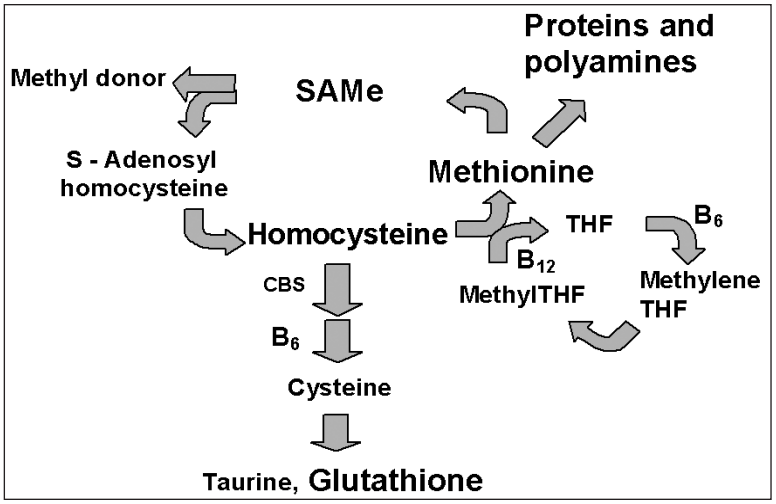

Figure 1—Schematic illustration of the multiple pathways for metabolism of methionine and cysteine, including production of S-adenosyl-methionine (SAMe) and taurine. Notice the important contributions of vitamins B_6 and B_{12} in these pathways. THF = Tetrahydrofolate. CBS = Cystathionine β synthase.

tial for cats. It has an important role in the synthesis and homeostasis of melanin, which is found in black hair and skin pigment. Tyrosine is synthesized from phenylalanine, an amino acid contained in many proteins, but diets of cats may not contain quantities sufficient to support tyrosine and, subsequently, melanin synthesis. As a result, tyrosine deficiency is most commonly observed in black cats whose hair becomes reddish-brown.[19] This effect can be reversed in cats fed diets that contain increased concentrations of tyrosine, which include diets high in animal-source proteins.[19] Tyrosine is an excellent example of a nonessential amino acid that may become deficient in cats because of an increase in the use of tyrosine for production of hair or an increase in the use of its precursor, phenylalanine, for nonessential (degradative) functions.

Carnitine metabolism in cats has received a lot of attention for its potential role in treating IHL[20] and enhancing weight loss.[21] Carnitine is an amino-group-containing, vitamin-like substance that is increasingly being considered as conditionally essential. However, there have not been any recommendations from the **Association of American Feed Control Officials (AAFCO)** or the National Research Council concerning carnitine in the diet of cats. Prior to 2002, carnitine was not an AAFCO-approved ingredient in foods formulated for pets. Thus, prior to this time, foods formulated for pets could not legally be fortified with carnitine. One major role for carnitine is transport of fatty acyl CoA compounds from the mitochondrial cytosol into the nucleus, thus making them available for β oxidation.[22,23] Cats are able to synthesize carnitine from lysine and methionine; the major dietary source of lysine and methionine is meat and dairy proteins.[23] Carnitine is synthesized in the kidneys of cats, whereas it is synthesized in the liver of dogs and other animals. Carnitine synthesis requires several B vitamins and iron; thus, synthesis may be limited in sick, anorectic cats.[23] In humans, carnitine deficiency (relative or absolute) causes hepatic lipid accumulation and liver dysfunction.[24] A similar connection is being investigated in cats with IHL, with current evidence suggesting that use of supplemental carnitine hastens recovery and improves survival in affected cats.[20] Carnitine also increases lean muscle mass and enhances weight loss in obese cats.[21] Although additional investigations are necessary to elucidate its entire role, supplemental carnitine (250 to 500 mg of carnitine/d) is recommended for obese cats and cats with IHL.[23]

Carbohydrates and Fats

It is clear that cats have a greater need than dogs or other omnivores for protein in their diet. Cats also have several physiologic adaptations that reflect their expected low CHO intake. The first of these is that cats lack salivary amylase, the enzyme responsible for initiating CHO digestion.[25] In addition, cats also have low activities of intestinal and pancreatic amylase and reduced activities of intestinal disaccharidases that break down CHOs in the small intestines.[25,26] These specific differences do not mean cats cannot use starch. In fact, cats are extremely efficient in their use of simple sugars. However, it does underscore their development as carnivores and the expected low amounts of grain in their typical diet. These digestive differences may mean that high amounts of CHO in diets may have untoward effects on cats. For example, high amounts of CHO in diets decrease protein digestibility in cats because of a combination of factors, including increased passage rate.[27] Increased amounts of CHO in diets also causes a reduction in fecal pH in cats, which is caused by incomplete CHO fermentation in the small intestines that results in increased microbial fermentation in the colon and increased production of organic acids.[27]

In cats, the liver also has several distinct features that influence disaccharide metabolism. In most animals, hepatic hexokinase (a constitutive enzyme) and glucokinase (an inducible enzyme) are active and responsible for phosphorylation of glucose for storage or oxidation. Cats differ in that they have minimal

function of hepatic glucokinase, and the activity is not adaptive (ie, activity cannot be up-regulated when the diet contains large amounts of CHO).[28,29] In addition, cats also have minimal activity of hepatic glycogen synthetase (the enzyme responsible for converting glucose to glycogen for storage in the liver).[2] Again, the likely reason for low hepatic glucokinase and glycogen synthetase activity in cats is a metabolic program that uses gluconeogenic amino acids and fat, rather than starch, in their diet for energy. As a result, cats have limited ability to rapidly minimize hyperglycemia from a large dietary glucose load. In carnivores, blood glucose concentrations are more consistent (eg, less postprandial fluctuations), because glucose is released in small continuous boluses over a longer time frame as a result of gluconeogenic catabolism of proteins. Thus, additional starch in the diet that is not stored as muscle glycogen or used for energy is stored as fat. The liver in cats also does not contain fructokinase, an enzyme necessary for metabolism of simple sugars. Lack of this enzyme was documented in a study[30] in which cats that consumed diets high in simple sugars became hyperglycemic and fructosuric. Finally, most cats are not attracted to foods with a sweet taste, which is in contrast to taste preferences of dogs and people. Cats apparently prefer foods flavored with animal products (eg, fats, meats). This difference in food preference is especially important when choosing a food to stimulate appetite in anorectic cats.

In the diet of carnivores, fat typically provides most of the fuel for energy, but it is also important for increasing the palatability and acceptance of food.[4,31] Meat-based diets, which also contain animal fat, supply essential fatty acids to cats, including linoleic, linolenic, arachidonic acid, and some eicosotrienoic acid.[31] Most species can convert linoleic acid to arachidonic acid, the primary precursor for the 2-series prostaglandins, leukotrienes, and thromboxanes. They also can convert α-linolenic acid to eicosapentaenoic and docosahexaenoic acids through desaturation and elongation pathways. Cats lack adequate hepatic Δ-6-desaturase activity and other hepatic desaturases, all of which are required for synthesis of arachidonic acid and eicosapentaenoate and docosahexaenoate.[31,32] Similar to the situation for many other nutrients, cats do not have the enzymatic machinery to synthesize derivatives of arachidonic acid, probably because the end products are plentiful in the natural diet of cats (ie, consumption of animal tissues).

Vitamins

The vitamin needs of cats are also unique, compared with requirements of dogs and other omnivores. Cats require increased amounts of many dietary water-soluble B vitamins, including thiamin, niacin, pyridoxine (ie, B_6), and, in certain circumstances, cobalamin (ie, B_{12}). Pyridoxine is especially important, because it is an essential cofactor in all transaminase reactions, which are constantly active in cats.[2] Cats can synthesize niacin, but their dietary requirement is 4 times higher than that of dogs because of the fact that they have a much higher rate of catabolism of vitamin precursors.[33] Thiamin deficiency can occur in anorectic cats and cats consuming diets high in thiaminase (high in seafood), and it is clinically evident as severe muscle weakness. Because most water-soluble B vitamins are not stored (the exception is cobalamin, which is stored in the liver), a continually available dietary source is required to prevent deficiency. In anorectic or ill cats, daily supplementation with a solution containing multiple B complex vitamins (1 mL of multiple B complex/d) or IV administration of supplemented fluids (2 to 4 mL of multiple B complex/500 mL of fluid) will help prevent deficiency.[34] Deficiency is rare in cats consuming appropriate diets, because each of the B vitamins are found in high concentrations in animal tissues and are added to commercial diets formulated for cats.[2]

Vitamins A, D, E, and K are fat-soluble vitamins. Of these, cats have special needs for vitamins A and D. Vitamin A is found naturally only in animal tissues, and it must be provided as the biologically active form in diets formulated for cats because of the fact that cats cannot convert β-carotene (which is plentiful in plants) to retinol (the active form of vitamin A); this conversion is not possible, because cats lack the necessary intestinal enzyme.[35] Vitamin A has a number of vital roles in physiologic processes and clinical health, including maintenance of vision, bone and muscle growth, reproduction, and healthy epithelial tissues.[2] Deficiency of Vitamin A is rare in cats fed commercially available foods and develops slowly with deficient diets, because it is stored in the liver. In fact, deficiencies are rare and only develop in cats with severe liver failure or disease of the gastrointestinal tract that results in fat malabsorption. Caution is strongly advised in supplementation of vitamin A, because toxicosis can easily develop, resulting in hepatotoxic effects or steatitis.[2,35] The recommended dose for oral administration of supplemental vitamin A in deficient cats is 400 U/kg (182 U/lb) of body weight/d.[34]

Similar to vitamin A, vitamin D (eg, calcitriol) is also required in the diets of cats. Cats are unable to meet their metabolic needs for vitamin D via dermal photosynthesis because they lack 7-dehydrocholesterol, which is required for synthesis.[36] Vitamin D is found in high amounts in the liver and fatty tissue of animals, so cats normally meet their needs for this vitamin via their carnivorous diet. The primary function of vitamin D is calcium and phosphorus homeostasis, with particular emphasis on intestinal absorption, retention, and bone deposition of calcium. Similar to the situation for vitamin A, deficiency of calcitriol is rare and develops slowly; thus, supplementation should be approached cautiously and only for cats with severe hypocalcemia, because excess amounts of vitamin D can cause hypercalcemia. The recommended dose of vitamin D_3 (calcitriol) in cats is 0.03 to 0.06 μg/kg (0.015 to 0.03 μg/lb) of body weight/d, PO.[34] Cats administered calcitriol should be monitored by measuring serum ionized calcium concentrations, because they are more accurate and more rapidly reflect potential overdoses than serum calcium concentrations.

The other 2 fat-soluble vitamins (vitamins E and K) are also important and may become deficient in cats that have prolonged anorexia, hepatic disease, or severe intestinal disease with fat malabsorption.

However, dietary deficiency is unlikely because of the fact that commercial foods formulated for cats are fortified with these vitamins.

Water

The water needs of cats reflect their early status as desert-dwelling animals and their development as strict carnivores that obtain most of their water requirements from consumption of prey. Cats have a less sensitive response to thirst and dehydration than dogs or other omnivores, and they adjust their water intake to the dry-matter content of their diet rather than the moisture content.[37] This means that cats eating commercial dry foods will consume approximately half the amount of water (in their diet and through drinking), compared with cats eating canned foods.[2] Feeding canned foods increases water intake and urine volume; thus, it will decrease the concentration of urolith-forming minerals in the urine. In older cats that tend to produce urine with a lower concentration, an increase in water consumption becomes even more important to avoid dehydration and development of prerenal azotemia. However, feeding canned foods or moistened dry foods will increase accumulation of dental tartar and the resulting periodontal disease.

Obesity in Cats

Although figures vary, it is estimated that 25 to 33% of cats are overweight or substantially obese.[38] In fact, obesity is the most common nutritional disorder in dogs and cats in the United States. There are a large number of factors that contribute to this problem, including sex (sexually intact vs neutered; male vs female), age, activity (indoor vs outdoor), and feeding style (meal feeding vs free choice).[39] Neutered male and female animals require fewer calories (estimates of 25 to 30%) for maintenance than sexually intact animals.[40] It has also been suggested that neutering may increase food intake, especially in male cats, and result in disordered leptin control of body fat mass.[c] Furthermore, many people prefer to feed their cats dry food that is available free choice. Active cats with a thin body condition that effectively self-regulate their intake may be fed food free choice. However, many inactive cats cannot be fed this way, because they tend to overeat as a result of the increased amount of fat and palatability of commercially available foods. There are a variety of possible explanations for obesity in pet cats, including hormonal changes (eg, neutering), boredom (eg, indoor cats), type of diet (eg, dry CHO-based food), inactivity (eg, decreased energy expenditure), or simple overfeeding. However, although a combination of these factors is likely to be important in the development of obesity, the role of diet in this problem is increasingly being scrutinized. Regardless of the cause, obese cats have many health issues, such as development of diabetes mellitus, joint disturbances or lameness, development of feline lower urinary tract disease, IHL, and nonallergic skin conditions.

One dietary factor that is receiving increased attention in obese cats is the role of CHO-dense diets. Cats housed exclusively indoors and consuming energy-dense, high-starch, dry foods are provided with more energy than they can effectively use. Any dietary CHO not used for energy is converted and stored as fat. Diets that are severely restricted for energy (eg, traditional low-fat, high-fiber, weight-loss diets) may result in weight loss, but it is often to the detriment of lean body mass.[41,d] Many of these diets contain high concentrations (> 15%) of insoluble fiber, which increases fecal bulk and volume, potentially increases fecal water loss (eg, increase risk of dehydration in cats not consuming an adequate quantity of water), and has detrimental effects on nutrient (eg, protein) digestibility.[42,43] Ultimately, successful weight loss requires maintenance of lean body mass, because lean body mass is the major determinant of basal energy metabolism and is a major influence on whether weight is regained.[44]

Several investigators have evaluated the use of a high-protein, low-CHO diet (protein, 45% or higher; **nitrogen free extract [NFE]**, < 10%; energy, 3,030 kcal of **metabolizable energy [ME]**/kg of food on an as-fed basis) for weight loss in cats. In 1 study,[d] weight reduction in cats on a high-protein, low-CHO diet was compared with that for cats fed a commercial hypoenergetic diet (protein, 34%; NFE, 45%; energy, 2,600 kcal of ME/kg of food on an as-fed basis). Cats in both groups lost weight, but cats consuming the high-protein, low-CHO diet maintained lean body mass during weight loss. Additional studies are necessary, but this approach to inducing weight loss in cats makes metabolic and nutritional sense providing that they are fed appropriate amounts of food (ie, food is not available free choice).

Canned foods generally are best to provide a high-protein, low-CHO dietary combination. Most dry foods are energy dense and have greater CHO concentrations (CHO > 25% on a **dry-matter [DM]** basis), because starch is necessary to make the kibble. The typical nutrient characteristics of canned foods formulated for kittens are 45 to 55% protein (DM basis), 8 to 15% starch (DM basis), and 15 to 25% fat (DM basis) with little dietary fiber (< 1% [DM basis]). These characteristics are not far removed from that of the natural diet of cats (Appendix 1).

One aspect of weight loss that has received a great deal of attention in recent years is the use of carnitine supplementation in an attempt to enhance weight loss. In 1 study,[20] investigators revealed that supplemental amounts of carnitine in diets formulated for cats increased lipid metabolism despite an apparent lack of evidence of a carnitine deficiency in those cats. Furthermore, it decreased the amount of time required to achieve safe weight loss in those cats. Oral administration of carnitine (250 mg/d) is recommended for obese cats undergoing weight loss.[20,21,23] Underscoring the increased interest in the use of carnitine for weight loss, pet food companies are adding carnitine to their weight-reduction diet formulas, and this should be taken into account when considering the provision of additional amounts of carnitine.

Diabetes Mellitus in Cats

Approximately 65% of all diabetic cats have type-II (non–insulin-dependent) diabetes.[45] However, these cats may be transiently, or permanently, insulin-depen-

dent at the time when the condition is diagnosed. This is in sharp contrast to dogs, the overwhelming majority of which have type-I (insulin-dependent) diabetes.[46] Dietary recommendations extrapolated from recommendations for humans and dogs are to feed affected cats diets high in insoluble or mixed fiber.[47] However, with the increased understanding of unique protein and CHO metabolism in cats, these recommendations have been challenged. High-protein, low-CHO diets and low-fiber diets are highly beneficial in the management of cats with diabetes, resulting in a reduction of > 50% in the amount of insulin required in 8 of 9 cats in 1 study.[48] In another study,[e] complete cessation of insulin administration was reported for one-third of the cats. In another study,[49] researchers reported that contrary to what is observed in dogs, cats fed diets containing soluble or insoluble fiber had altered glucose tolerance. Another study reported that feeding typical adult maintenance diets to cats resulted in development of greater postprandial hyperinsulinemia, even in cats with normal body weights, compared to cats consuming a high-protein diet.[50] Persistent hyperinsulinemia may lead to decreased mobilization of nonesterified fatty acids (or possibly re-esterification of fatty acids); thus, it could potentially lead to weight gain or obesity in cats consuming typical maintenance (high-CHO) diets.[50] In obese diabetic cats, high-protein, low-CHO diets reduce postprandial hyperglycemia but also decrease the overall insulin requirement. Furthermore, canned high-protein, low-CHO diets result in weight loss that will ultimately reduce obesity-induced insulin resistance. Unfortunately, not all diabetic cats have adequate function of β cells, especially when the hyperglycemia (which causes down-regulation of β cells through glucose toxicity) or insulin resistance (attributable to obesity or other causes) has been a longstanding condition.[45] Nevertheless, a reduction in dietary starch will substantially reduce the insulin requirement (endogenous and exogenous) in affected cats. Thus, the earlier that obesity and hyperglycemia are recognized and corrected, the more likely that the injury to (or down-regulation of) β cells will not be permanent. Several reviews have been published on management of diabetes in cats, including use of insulin therapy, oral hypoglycemic therapy, and other aspects of management of this common endocrine problem in cats.[45,51]

IHL in Cats

Idiopathic hepatic lipidosis is a common hepatobiliary problem in cats, especially cats that are obese or stressed. It is the most common metabolic hepatic disease of cats.[52] Despite the concerted efforts of many clinicians and researchers, the etiopathogenesis of IHL is still incompletely understood. It has been suggested that IHL is the result of a combination of factors, including excessive peripheral lipid mobilization (as a result of cortisol and catecholamine release attributable to stress or illness) and subsequent development of nutritional deficiencies in the formation of lipoproteins and the mobilization of triglycerides.[20,52,53] Various nutrients may be involved in the pathogenesis of IHL, including (but not limited to or proven) taurine, carnitine, arginine, threonine, citrulline, choline, nonesterified fatty acids, and B vitamins. Additional studies are required to elucidate which, if any, of these nutrients may be critical to development of the lipid and lipoprotein derangements that characterize IHL. Nonetheless, successful treatment of IHL is based on early intervention and, in most cases, placement of a feeding tube so that adequate nutritional support can be provided.[54] In cats that receive early aggressive nutritional support, the prognosis for survival approaches 90%, but in cats not receiving such treatment, the chance of survival is only 10 to 15%.[55] The best diet for treatment of cats with IHL is unknown, but evidence clearly suggests that dietary protein reduces hepatic lipid accumulation and maintains nitrogen and energy balance in cats with IHL.[56] Furthermore, although ingestion of CHO reduces hepatic lipid accumulation, it is ineffective in preventing clinical manifestations of IHL, which are likely attributable to the need for protein and other nutrients that cats derive from a meat-based diet (eg, carnitine, arginine, vitamin A, and certain B vitamins).

Carnitine improves hepatic lipid oxidation, arginine is essential for proper function of the urea cycle and metabolism of dietary proteins, and B vitamins are essential cofactors that are necessary for multiple pathways of protein and lipid metabolism. Supplemental amounts of these components most commonly recommended for cats with IHL have been identified (**Appendix 3**). In general, the keys to prevention and treatment of IHL are to recognize at-risk cats, develop plans for management of obesity, aggressively treat anorectic cats regardless of the cause or the cat's body condition, and remember that cats are true carnivores and that even those in severe hepatic failure need protein. Cats with signs of hepatoencephalopathy may require diets containing a lower percentage of protein than is found in maintenance or recovery diets to reduce ammoniagenesis (30 to 35% protein on a DM basis), or they need diets with other types of protein to reduce formation of false neurotransmitters (eg, less aromatic amino acids). Several reviews have been published that provide information on the diagnosis of IHL or specific medical treatment of cats with this condition.[54,55]

Dietary Intolerance and Inflammatory Bowel Disease (IBD) in Cats

Dietary intolerance is a non–immune-mediated, clinically important cause of gastrointestinal tract disease (eg, vomiting and diarrhea) in cats. It can be caused by a number of substances found in diets formulated for cats, including protein and CHO source, flavorings, and preservatives and additives such as colors or extenders. Despite the wide array of potential causes of food intolerance, removal of the offending substance from the diet will cure the problem. Conversely, IBD in cats is an idiopathic, inflammatory, immune-mediated disease of the intestinal tract that dietary and immunosuppressive or anti-inflammatory treatments may control, but we do not have a clear understanding of the cause of IBD.[57,58] It is likely that IBD is triggered by an antigenic response to food, bacterial, or parasitic antigens in the intestinal lumen by

immune cells of the gastrointestinal tract. The mechanism by which this normal inflammatory response becomes aberrant and persistent, ultimately resulting in chronic severe inflammation (ie, IBD), loss of normal gastrointestinal function (eg, vomiting or diarrhea), and, possibly, the development of neoplasia (eg, lymphoma) in the gastrointestinal tract of some cats, is unknown.

Several possible causes have been investigated in humans with IBD, with a great deal of research focused on the role of bacteria in the development and persistence of the aberrant immune response.[59] Direct supportive evidence for a specific role of bacteria in the development of IBD in cats is lacking, but several aspects of digestive physiologic and intestinal microbiologic characteristics of cats suggest a possible role for bacteria in the disease. First, cats have higher concentrations of bacteria in their small intestine (approx 10^9 organisms), compared to dogs and people (< 10^5 organisms).[60,61] The reason for the increased number of bacteria in the small intestines of cats is not known, but it may be attributable to their expected carnivorous diet and shorter (relative to dogs on the basis of body size) gastrointestinal tract. It has been suggested that increased numbers of bacteria in the intestines serve to enhance digestion of proteins and fats in diets typically fed to cats.[55] Conversely, diets higher in CHO or fiber may influence bacterial numbers or species, altering bacterial flora in ways that may include overgrowth of nonbeneficial or pathogenic species. To the author's knowledge, there have not been any studies to evaluate the effects of a moderate- to high-CHO maintenance diet, compared with effects for a high-protein, low-CHO diet, on the numbers or species of enteric microflora in cats. Nevertheless, because the natural diet of cats is a high-protein, moderate-fat, low-CHO diet, it seems reasonable to assume that enteric flora and anatomy of the gastrointestinal tract of cats would be designed to accommodate these diets more readily. Because IBD and dietary intolerance are common causes of clinical gastrointestinal tract disease in cats, this is an area of investigation that requires further concentrated effort.

Conclusion

Although a simple change in diet will not solve all of the ills of affected cats, it is reasonable to believe that their lives are influenced by the foods they consume. There is no question that nutrition plays a key role in obesity, diabetes mellitus, IHL, and, probably, IBD in cats. However, these problems are clearly complex and involve multiple factors, including genetic and environmental influences as well as the nutritional factors described previously. Nevertheless, veterinarians cannot ignore the unique nutritional needs of cats, because unlike omnivorous dogs, cats are cats and true carnivores.

[a]Science Diet Feline Maintenance Beef, Hill's Pet Nutrition Inc, Topeka, Kan.

[b]Science Diet Growth, Hill's Pet Nutrition Inc, Topeka, Kan.

[c]Kanchuck ML, Backus RC, Calvert CC, et al. The effect of neutering on food intake, body weight, plasma leptin, and insulin concentrations in normal and lipoprotein lipase deficient male cats, in *Proceedings*. Waltham Int Symp Small Anim Nutr 2001:34.

[d]Nguyen P, Martin L, Siliart B, et al. Weight loss in obese cats: evaluation of a high protein diet, in *Proceedings*. Waltham Int Symp Small Anim Nutr 2001;28.

[e]Bennett N, Greco DS, Peterson ME. Comparison of a low carbohydrate versus high fiber diet in cats with diabetes mellitus (abstr). *J Vet Intern Med* 2001:15;297.

References

1. Dratfield J, Coughlin P. *The quotable feline*. New York: Alfred A. Knopf Inc, 1996;6–7.
2. Kirk CA, Debraekeleer J, Armstrong PJ. Normal cats. In: Hand MS, Thatcher CD, Remillard RL, et al, eds. *Small animal clinical nutrition*. 4th ed. Philadelphia: WB Saunders Co, 2000;291–351.
3. Vondruska JF. The effect of a rat carcass diet on the urinary pH of the cat. *Comp Anim Pract* 1987;1:5–9.
4. Morris JG. Idiosyncratic nutrient requirements of cats appear to be diet-induced evolutionary adaptations. *Nutr Res Rev* 2002;15:153–168.
5. Rogers QR, Morris JG. Essentiality of amino acids for the growing kitten. *J Nutr* 1979;109:718–723.
6. Harper AE. Effect of variations in protein intake on enzymes of amino acid metabolism. *Can J Biochem* 1965;43: 1589–1603.
7. Das TK, Waterlow JC. The rate of adaptation of the urea cycle enzymes, aminotransferase, and glutamic dehydrogenase to changes in dietary protein. *Br J Nutr* 1974;32:353–373.
8. Rogers QR, Morris JG, Freedland RA. Lack of hepatic enzymatic adaptation to low and high levels of dietary protein in the adult cat. *Enzyme* 1977;22:348–356.
9. Russell K, Murgtroyd PR, Batt RM. Net protein oxidation is adapted to dietary protein intake in domestic cats (*Felis silvestris catus*). *J Nutr* 2002;132:456–460.
10. Knopf K, Sturman JA, Armstrong M, et al. Taurine: an essential nutrient for the cat. *J Nutr* 1978;108:773–778.
11. Hickman MA, Rogers QR, Morris JG. Effect of processing on the fate of dietary [^{14}C] taurine in cats. *J Nutr* 1990;120:995–1000.
12. Morris JG, Rogers QR, Kim SW, et al. Dietary requirement of taurine of cats is determined by microbial degradation of taurine in the gut. *Adv Exp Med Biol* 1994;359:59–70.
13. Morris JG, Rogers QR, Winterrowd DL, et al. The utilization of ornithine and citrulline by the growing kitten. *J Nutr* 1979;109:724–729.
14. Morris JG, Rogers QR. Ammonia intoxication in the near adult cat as a result of a dietary deficiency of arginine. *Science* 1978;199:431–432.
15. National Research Council. Nutrient requirements of cats. Washington, DC: National Academy Press, 1986.
16. Stipanuk MH, Bagley PJ, Hou YC, et al. Hepatic regulation of cysteine utilization for taurine synthesis. *Adv Exp Med Biol* 1994;359:79–89.
17. Center SA. S-Adenosyl-methionine (SAMe): an antioxidant and anti-inflammatory nutriceutical, in *Proceedings*. 18th Annu Meet Am Coll Vet Int Med Forum 2000;550–552.
18. Hendriks WH, Moughan PJ, Tartlelin MF, et al. Felinine: a urinary amino acid of Felidae. *Comp Biochem Physiol B Biochem Mol Biol* 1995;112B:581–588.
19. Morris JG, Rogers QR. Cats require more dietary phenylalanine or tyrosine for melanin deposition in hair than for maximal growth. *J Nutr* 2002;132:2037–2042.
20. Blanchard G, Paragon BM, Milliat F, et al. Dietary L-carnitine supplementation in obese cats alters carnitine metabolism and decreases ketosis during fasting and induced hepatic lipidosis. *J Nutr* 2002;132:204–210.
21. Center SA, Harte J, Watrous D, et al. The clinical and metabolic effects of rapid weight loss in obese pet cats and the influence of supplemental oral L-carnitine. *J Vet Intern Med* 2000;14:598–608.
22. Rebouche CJ, Seim H. Carnitine metabolism and its regulation in microorganisms and mammals. *Ann Rev Nutr* 1998;8:39–61.
23. Carroll MC, Cote E. Carnitine: a review. *Compend Contin Educ Pract Vet* 2001;23:45–52.
24. Hoppel CL, Genuth SM. Carnitine metabolism in normal

weight and obese human subjects during fasting. *Am J Physiol* 1980;238:E409–E415.

25. Kienzle E. Carbohydrate metabolism of the cat. 1. Activity of amylase in the gastrointestinal tract of the cat. *J Anim Physiol Anim Nutr* 1993;69:92–101.

26. Kienzle E. Carbohydrate metabolism of the cat. 2. Digestion of starch. *J Anim Physiol Anim Nutr* 1993;69:102–114.

27. Kienzle E. Effects of carbohydrate on digestion in the cat. *J Nutr* 1994;124:2568S–2571S.

28. Ballard FJ. Glucose utilization in the mammalian liver. *Comp Biochem Physiol* 1965;14:437–443.

29. Ureta T. Comparative isoenzymology of vertebrate hexokinases. *Comp Biochem Physiol* 1982;71:549–555.

30. Kienzle E. Blood sugar levels and renal sugar excretion after intake of high carbohydrate diets in cats. *J Nutr* 1994;124:2563S–2567S.

31. MacDonald ML, Rogers QR, Morris JG. Role of linoleate as an essential fatty acid for the cat independent of arachidonate synthesis. *J Nutr* 1983;113:1422–1433.

32. Bauer JE. Fatty acid metabolism in domestic cats (*Felis catus*) and cheetahs (*Acinonyx jubatas*), in *Proceedings*. Nutr Soc 1997;56:1013–1024.

33. MacDonald ML, Rogers QR, Morris JG. Nutrition of the domestic cat, a mammalian carnivore. *Annu Rev Nutr* 1984;4:521–562.

34. Boothe DM. Small animal formulary. In: *Boothe's small animal formulary*. 5th ed. Lakewood, Colo: AAHA Press, 2000;1–139.

35. Gershoff SN, Andrus SB, Hegsted DM, et al. Vitamin A deficiency in cats. *Lab Invest* 1957;6:227–240.

36. How KL, Hazewinkel HA, Mol JA. Dietary vitamin D dependence of cat and dog due to inadequate cutaneous synthesis of vitamin D. *Gen Comp Endocrinol* 1994;96:12–18.

37. Anderson RS. Water balance in the dog and cat. *J Small Anim Pract* 1982;23:588–598.

38. Scarlett JM, Donoghue S, Daidla J, et al. Overweight cats: prevalence and risk factors. *Int J Obes* 1994;18:S22–S28.

39. Donoghue S, Scarlett JM. Diet and feline obesity. *J Nutr* 1998;128:S2776–S2778.

40. Flynn MF, Hardie EM, Armstrong PJ. Effect of ovariohysterectomy on maintenance energy requirement in cats. *J Am Vet Med Assoc* 1996;209:1572–1581.

41. McIntosh MK. Nutrients and compounds affecting body composition and metabolism, in *Proceedings*. Purina Nutr Forum 2000;18–28.

42. Hannah S. Role of dietary protein in weight management. *Compend Contin Educ Pract Vet* 1999;21:32–33.

43. Fahey GC Jr, Merchen NR, Corbin JE, et al. Dietary fiber for dogs. I. Effects of graded levels of dietary beet pulp on nutrient intake, digestibility, metabolizable energy and digesta mean retention time. *J Anim Sci* 1990;68:4221–4228.

44. Butterwick RF, Markwell PJ. Body composition changes in cats during weight reduction by controlled calorie restriction. *Vet Rec* 1996;138:354–357.

45. Rand JS, Martin GJ. Management of feline diabetes mellitus. *Vet Clin North Am Small Anim Pract* 2001;31:881–913.

46. Freeman LM. Understanding canine diabetes and its management—part I, in *Proceedings*. 20th Annu Am Coll Vet Intern Med Forum, 2002;35–40.

47. Nelson RW, Scott-Moncrieff JC, Feldman EC, et al. Effect of dietary insoluble fiber on control of glycemia in cats with naturally acquired diabetes mellitus. *J Am Vet Med Assoc* 2000;216:1082–1088.

48. Frank G, Anderson W, Pazak H, et al. Use of a high-protein diet in the management of feline diabetes mellitus. *Vet Ther* 2001;2:238–246.

49. Hoenig M, Laflamme DP. Effect of fiber on glucose metabolism and lipids in the cat. *Compend Contin Educ Pract Vet* 2001;23:77–78.

50. Hoenig M, Alexander S, Pazak H. Effect of a high- and low-protein diet on glucose metabolism and lipids in the cat, in *Proceedings*. Purina Nutr Forum 2000;98–99.

51. Behrend EN, Greco DS. Treatment of feline diabetes mellitus: overview and therapy. *Compend Contin Educ Pract Vet* 2000;22:423–438.

52. Griffin B. Feline hepatic lipidosis: pathophysiology, clinical signs, and diagnosis. *Compend Contin Educ Pract Vet* 2000;22:847–858.

53. Brown B, Mauldin GE, Armstrong J, et al. Metabolic and hormonal alterations in cats with hepatic lipidosis. *J Vet Intern Med* 2000;14:20–26.

54. Griffin B. Feline hepatic lipidosis: treatment recommendations. *Compend Contin Educ Pract Vet* 2000;22:910–922.

55. Center SA, Warner K. Feline hepatic lipidosis: better defining the syndrome and its management, in *Proceedings*. 16th Am Coll Vet Intern Med Forum, 1998;56–58.

56. Biourge V, Massat B, Groff JM, et al. Effects of protein, lipid, or carbohydrate supplementation on hepatic lipid accumulation during rapid weight loss in obese cats. *Am J Vet Res* 1994;55:1406–1415.

57. Krecic MR. Feline inflammatory bowel disease: pathogenesis, diagnosis, and relationship to lymphosarcoma. *Compend Contin Educ Pract Vet* 2001;23:951–960.

58. Jergens AE. Feline inflammatory bowel disease. *Vet Clin North Am Small Anim Pract* 1999;29:501–521.

59. Sartor RB. Pathogenesis and immune mechanisms of chronic inflammatory bowel diseases. *Am J Gastroenterol* 1997;92:S5–S11.

60. Gruffydd-Jones TJ, Papasouliotis K, Sparkes AH. Characterization of the intestinal flora of the cat and its potential for modification. In: Reinhart GA, Carey DP, eds. *Recent advances in canine and feline nutrition*. Vol II. Wilmington, Del: Orange Frazier Press, 1998;473–483.

61. Johnston KL, Swift NC, Forster-van Hijfte M, et al. Comparison of the bacterial flora of the duodenum in healthy cats and cats with signs of gastrointestinal tract disease. *J Am Vet Med Assoc* 2001;218:48–51.

Appendix 1

Comparison of nutrients in selected diets[2] consumed by cats

Nutrient	Rat carcass[3]	Canned maintenance diet*,[a]	Canned growth diet*,[b]	AAFCO*
Protein (%)	55	45.2	49	26
Fat (%)	38.1	25.4	36.2	9.0
Carbohydrate (%)	9.1	19.9	6.9	–
Fiber (%)	1.2	2.9	0.6	–
Moisture (%)	63.6	75.6	69.6	–
Calcium (%)	1.15	0.94	1.09	0.6
Phosphorus (%)	0.98	0.78	0.95	0.5
Vitamin A (U/kg)	84,800	–	–	5,000
Vitamin E (U/kg)	33	–	–	30
Thiamin (mg/kg)	5.8	–	–	5.0
Riboflavin (mg/kg)	10.7	–	–	4.0
Niacin (mg/kg)	156.6	–	–	60
Folic acid (mg/kg)	2.8	–	–	0.8
Pantothenic acid (mg/kg)	54.9	–	–	5.0
Cobalamin (µg/kg)	22.5	–	–	20
Iron (mg/kg)	288	–	–	80
Zinc (mg/kg)	71.4	–	–	75

*Nutrients are expressed on a dry-matter basis.

AAFCO = Association of American Feed Control Officials. – = Not determined.

Appendix 2

Amino acids in cats[2]

Amino acid	Essentiality	Gluconeogenic (G) or ketogenic (K) status	Sources and comments
Alanine	Nonessential	G	Synthesized from pyruvate and glutamate. Used in glucose-alanine cycle.
Arginine	Essential	G	High concentrations in muscle proteins; can be synthesized, but cats synthesize low amounts because they lack enzymes for synthesis of ornithine and citrulline. Essential for function of urea cycle and formation of nitric oxide and polyamines.
Asparagine	Nonessential	G	Abundant in potatoes; synthesized from aspartate and glutamine.
Aspartate	Nonessential	G	Synthesized from glutamate and oxaloacetate. Used as a neurotransmitter and in synthesis of purine and pyrimidine nucleotides.
Cysteine	Conditionally	G	Synthesized from serine. A sulfur-containing amino acid, it can replace methionine. Important in synthesis of S-adenosyl-methionine (SAMe), and glutathione.
Glutamate	Nonessential	G	Synthesized from branched-chain amino acids. Used as a neurotransmitter and as a precursor to alanine and glutamine synthesis in muscle.
Glutamine	Conditionally	G	Abundant in potatoes; synthesized from glutamate. Used in synthesis of purine and pyrimidine nucleotides; important energy source for enterocytes; precursor to citrulline and, thus, arginine.
Glycine	Nonessential	G	Synthesized from serine or choline. Used in formation of creatine, purine, and pyrimidine.
Histidine	Essential	G	High amounts in hemoglobin. Used in formation of histamine.
Isoleucine	Essential	G and K	Branched-chain amino acid.
Leucine	Essential	K	Branched-chain amino acid.
Lysine	Essential	K	Precursor for carnitine synthesis; it is easily destroyed by heat processing.
Methionine	Essential	G	Sulfur-containing amino acid that is converted to cysteine and is important in polyamine synthesis (SAMe), carnitine synthesis, and as a methyl donor. It may be a limiting amino acid in cats.
Phenylalanine	Essential	G and K	Aromatic amino acid that is degraded in liver to form tyrosine. It may be a limiting amino acid in cats.
Proline	Nonessential	G	Synthesized from glutamate. It may be conditionally essential in cats, because they lack biosynthetic enzymes.
Serine	Nonessential	G	Synthesized from glycolytic intermediates or pyruvate.
Taurine	Essential		Synthesized from methionine and cysteine but in extremely low concentrations in cats. Used in conjugation of bile acids; essential for vision, reproduction, and muscle function (especially cardiac muscle).
Threonine	Essential	G	Used as an energy source and in muscle protein.
Tryptophan	Essential	G and K	Used as a neurotransmitter.
Tyrosine	Conditionally	G and K	Used as a neurotransmitter; important in (source of melatonin and dopamine metabolism and methionine) synthesis of thyroid hormones; increased requirements in cats with black coats.
Valine	Essential	G	Branched-chain amino acid.

Appendix 3

Supplemental dietary components for cats

Component	Dose	Comments
L-Carnitine	250 to 500 mg/d, PO	May be administered all at once or divided throughout the day. Administer with food.
Taurine	250 to 500 mg/d, PO	May be administered all at once or divided throughout the day. Administer with food.
SAMe	20 mg/kg, PO	Administer once daily. Used as an antioxidant and source of methionine for other metabolic pathways.
Vitamin E	100 to 200 U/cat, PO	Administer with food. Used as an antioxidant. May be required in severe hepatic disease or gastrointestinal malabsorption.
Vitamin K	0.5 to 1.5 mg/kg, SC	Administer once daily as needed for severe hepatic disease, fat malabsorption, or deficiency of vitamin K.
B-complex vitamins	2 or 4 mL/L of fluids, IV 0.5 mL/d, SC	Especially important in sick or anorectic cats, because B vitamins are not stored.
Cobalamin	250 µg/wk, SC, for 4 weeks, then 250 µg/mo, SC, as needed	Cats with severe gastrointestinal tract disease may become deficient and require long-term parenteral administration to prevent deficiency.