CHAPTER

15

The Unique Nutritional Requirements of the Cat: A Strict Carnivore

Beth Hamper, Joe Bartges, Claudia Kirk, Angela L. Witzel, Maryanne Murphy, and Donna Raditic

OUTLINE

The domestic cat is believed to have evolved from the African wild cat *Felis sylvestris libyca* between 4000 and 10,000 years ago.[4,20] Cats belong to the order Carnivora, meaning "flesh eating," and the family Felidae. The felids diverged from the other carnivorous groups early in the evolutionary tree.[16] Other members of the order Carnivora include canids/canines, bears, pandas, weasels, raccoons, and hyenas. There is a wide diversity of feeding patterns within the order Carnivora. Canids and bears are considered omnivores, whereas pandas are strict herbivores. All felids are meat eaters, or strict carnivores. This specialized and exclusive meat diet has led to unique metabolic and nutritional adaptations not seen in canids/canines or other members of the order Carnivora. A great deal of knowledge has been gained regarding the cat's unique metabolic and nutritional requirements over the past 60 years, thanks to the work of Dr. James Morris and Dr. Quinton Rodgers, along with many other nutritionists and researchers around the world. The goal of this chapter is to review these findings and provide a review of the unique requirements of the cat.[16,18] Some highlights of this research in feline nutrition and metabolism include:

- A limited ability to downregulate enzymes of nitrogen catabolism and urea cycle enzymes
- A strict requirement for the amino acid arginine, which, if lacking in the diet for longer than 24 hours, can lead to life-threatening consequences
- An inability to synthesize taurine from cysteine
- Limited capabilities in handling carbohydrates in the diet
- An inability to synthesize vitamin A from beta carotenes
- An inability to synthesize niacin from the amino acid tryptophan

Arginine, taurine, niacin, and vitamin A are abundant in an all-flesh diet, along with high levels of protein and amino acids and very limited carbohydrates.

ANATOMY AND PHYSIOLOGY

Cats have fewer teeth than dogs. They have the same number of incisors, canine, and carnassial teeth but fewer premolar and molar teeth with fissured surfaces. Their dentition is more specialized for shearing flesh rather than grinding it. Cats lack salivary amylase, the enzyme that is involved in early starch digestion.[19] Because cats evolved to eat small, frequent meals throughout the day, their stomach capacity is smaller than that of dogs. The cat's maximum stomach capacity is between 45 and 60 mL/kg of body weight, compared with 90 mL/kg in the dog.

Relative intestinal length is determined by the ratio of intestinal length to body length. Intestinal length is one of the factors that influence the amount of time for digestion and absorption to occur. Cats have a shorter intestinal length than dogs and other omnivores and

herbivores. In the cat, this ratio is 4:1 compared with 6:1 in dogs.[19] In herbivorous species this ratio is much higher due to the lower digestibility of their foodstuffs: 12:1 in the horse, 20:1 in the ox, and 27:1 in the sheep.[19]

Cobalamin, or vitamin B_{12}, requires binding to intrinsic factor for its absorption and uptake in the ileum. Most mammals manufacture and secrete intrinsic factor from both the stomach and pancreas. In the cat, intrinsic factor is produced only in the pancreas.[7]

Very little is known about companion animals' microbiome. The effect of small intestinal microbes on nutrient requirements in dogs and cats has yet to be established. The human microbiome contains approximately 10^{14} microorganisms, ten times the number of human cells.[28] The metabolic functions of the microbiota within the gastrointestinal tract include production of metabolites such as short-chain fatty acids used as an energy source for colonocytes, degradation of potentially toxic compounds, enhanced metabolism of amino acids and nondigestible carbohydrates, and synthesis of vitamins and lipids.[29] A study in clinically healthy cats demonstrated that cats have large numbers of bacteria in their proximal small intestine compared to dogs. Cats show unique numbers of microbes within the intestinal tract. The total bacterial counts from duodenal cultures in cats ranged from 10^5 to 10^8 colony-forming units (CFU)/mL, compared with a maximum of 10^4 CFU/mL in dogs.[10] Higher bacterial levels in the gut may be another adaption to a carnivorous diet. Relying on culturing methods alone has greatly limited identification of microbial species. Newer molecular techniques show promise in evaluating these ecosystems in both the cat and dog and their effect on diet, and vice versa.[27]

FEEDING BEHAVIOR

In the wild cats hunt small prey such as mice, rats, rabbits, birds, frogs, reptiles, and insects. Mice are the most common prey for the cat, with a caloric density of approximately 30 kcal per mouse. The small size and low kcal of their prey dictate that cats need to eat many small meals throughout the day to meet their energy and nutritional requirements. Cats prefer to ingest freshly killed prey rather than carrion. Domestic cats will have 7 to 20 small meals a day if given free access to food. Predatory behavior is a strong drive in the cat and will even take precedence over feeding. Cats will stop eating a meal to kill prey and then go back to eating the original meal rather than the freshly killed rat.[1]

Food preferences are influenced by the diet of the queen during pregnancy and lactation. Particularly important to later food preferences and choices are the flavors kittens experience between 1 and 6 months of age.[32] Owners should be encouraged to feed kittens a variety of flavors and textures at this stage with the hope that it will lead to more flexibility in the adult.

Smell, taste, and texture all play important roles in the cat's dietary preferences. The most abundant taste receptors (neurons of the facial nerve) are those for amino acids, particularly those amino acids that are described as sweet.[3] These include proline, cysteine, ornithine, lysine, histidine, and alanine. Cats reject bitter-tasting amino acids such as arginine, isoleucine, phenylalanine, and tryptophan. The second most abundant taste receptors are for acidic foods. These receptors are stimulated by phosphoric acid, carboxylic acids, and nucleotide dipeptides and tripeptides.[3] Cats will avoid monophosphate nucleotides, which accumulate in tissues after death. This may be why cats dislike carrion. Cats have no taste receptors for sucrose/sugar.[3,14] Temperature is also important, with cats preferring food at body or room temperature. Cats will generally reject foods at temperatures colder than 15° C or greater than 50° C.[32] Food preferences are strongly correlated with the amount of protein in the diet, particularly animal protein. Liver, blood, and red meat are highly palatable to cats. Besides protein, fat has been shown to have positive palatability in cat. Fats applied to the outside of dry kibble are positive flavor enhancers, but it is believed that the positive influence of fat is more related to textural changes rather than flavor. Despite this, cats do show a strong aversion to medium-chain fatty acids.[16] Cats will generally select moist foods similar in water content to animal tissue, compared to dry, extruded diets. Cats that have been fed exclusively dry foods for an extended period of time can develop a strong preference for only dry foods.

Stressful situations can result in learned aversions to new or novel foods; therefore starting a new therapeutic diet in hospitalized cats is inadvisable. Cats are intermediate in their ability to avoid foods that can result in deficiencies over a long period of time; for example, cats will consistently eat taurine-free diets despite development of cardiac, reproductive, and retinal diseases. Similar to other species, cats will learn to avoid foods that are toxic.

The cat is believed to have evolved as a desert animal because of its ability to highly concentrate its urine (specific gravity up to 1.080 to 1.085). Cats will drink less water than dogs under the same conditions. Cats on canned or moist diets may not drink any additional water, although it should always be available. Besides the water content of the food, the protein and mineral content of the diet may affect water intake. High-protein diets increase the solute load, with increased water production and urination. The weak thirst drive in the cat has been implicated in some aspects of lower urinary tract health, particularly in cats fed dry foods, because of the propensity of minerals to crystallize in concentrated solutions.

SPECIFIC NUTRIENTS

Protein and Amino Acids

Protein

Dietary protein is required for two reasons. The first is for amino acids (AAs) the cat cannot synthesize, called the essential amino acids. The second is for nitrogen and carbon skeletons for the synthesis of nonessential AAs and other necessary compounds containing nitrogen (i.e., purines, pyrimidines, heme, hormones, and neurotransmitters). Both essential and nonessential AAs become part of the AA pool for protein synthesis in the tissues. The essential AAs for both dogs and cats are arginine (Arg), histidine (His), isoleucine (Ile), leucine (Leu), lysine (Lys), methionine (Met), phenylalanine (Phe), threonine (Thr), tryptophan (Trp), and valine (Val).[19] Cats have an additional requirement for taurine, which they cannot synthesize from cysteine compared to dogs.

The protein requirement for the kitten is approximately 1.5 times the protein requirement for the puppy. Adult cats require 2 to 3 times as much protein as adult dogs.[19] The increased protein requirement in the cat is not for increased levels of essential AAs but rather for a dietary source of nitrogen. Excess nitrogen from proteins and other sources is removed by way of the urea cycle in the liver. Most omnivorous species, when given a low-protein diet, will conserve AAs by decreasing enzyme levels involved in AA catabolism. Omnivorous species can also conserve AAs and nitrogen when given low-protein diets by altering the activity of the urea cycle enzymes. In cats given low-protein diets, enzymes for both AA catabolism and the urea cycle are not downregulated.[23] Therefore cats cannot conserve nitrogen when given low-protein diets and will begin to catabolize protein sources within the body (i.e., muscle) to supply tissue needs. Endogenous urinary nitrogen losses in animals fed protein-free diets have been found to be 360 mg N/kg in cats, compared with 210 mg N/kg in dogs, 128 mg N/kg in rats, and 62 mg N/kg in humans, indicating lack of enzyme adaptation in the cat.[19] Protein is also being continually utilized for gluconeogenesis in the cat. Because of the very limited number of carbohydrates they ingest in their wild diet, cats are very efficient at synthesizing glucose from proteins by gluconeogenesis. In other species, gluconeogenesis occurs several hours after a meal, whereas in cats it occurs immediately after a meal and is permanently "switched on" to maintain blood glucose levels. The benefit of these adaptations is the immediate ability to catabolize high levels of protein without developing hyperammonemia and the rapid ability to make glucose from protein for energy through gluconeogensis.[18]

Arginine

Arginine is a key intermediate in the urea cycle involved in the excretion of nitrogen via urea. A single meal without the AA arginine can result in life-threatening events in the cat. Arginine-deficient cats develop emesis, hypersalivation, hyperactivity, and hyperesthesia eventually leading to death as a result of ammonia intoxication. This is due to the cat's inability to synthesize arginine from other dietary precursors. Arginine can be produced from ornithine and citrulline in the intestine in humans and rats and to some degree in dogs. The cat has lost this ability because of the lack of two enzymes in the pathway, pyrroline-5-carboxylate synthase and ornithine aminotransferase. Overnight food deprivation results in a low concentration of plasma arginine and urea cycle intermediates. When the cat eats a meal with protein that includes arginine, the arginine replenishes the level in the liver for urea cycle function with subsequent disposal of nitrogen and ammonia. If arginine is missing from the meal, the cat cannot replenish its urea cycle intermediates and severe hyperammonemia develops.[17] Animal tissue is high in arginine content, making its de novo synthesis redundant in carnivores on all meat diets. Also, depletion of urea cycle intermediates after a meal results in conserving nitrogen needed for synthesis of disposable AAs.

Methionine and Cysteine

The dietary requirement for the sulfur AAs, methionine, and cysteine is higher in cats than in other mammals.[19] Methionine can be converted to cysteine; therefore the sulfur AA requirement can be met with either methionine alone or methionine and cysteine. Methionine is a methyl group donor important for DNA and RNA synthesis and is a component of many proteins. Cysteine is a component of many proteins and is an important component of hair/fur. Cysteine is also the precursor for glutathione, a major antioxidant in mammalian systems, and a precursor for the synthesis of felinine. Felinine is a branched-chain AA found in the urine of domestic cats. The biological function of felinine is not fully known, although it is believed to function as a pheromone and is important in territorial marking. It can be found in the urine of cats as young as 2 months of age, with levels being quite high in intact male cats (0.4 to 8 grams/L of urine).[8] Felinine concentrations in females are only 20% to 25% of that in intact males. The high requirement for sulfur AAs in cats has been attributed to their dense hair and the need to synthesize felinine.[16]

Taurine

Taurine is a beta-sulfonic AA that is not used in protein synthesis but is found as a free AA in tissues. The highest concentrations of taurine are found in the heart, muscle, brain, and retina. Taurine serves numerous important

functions, including osmoregulation, calcium channel modulation, as an antioxidant, and bile acid conjugation.[9] Many mammals are able to use either glycine or taurine for bile acid conjugation. Cats and dogs are only able to utilize taurine to conjugate bile acids. Dogs are able to synthesize sufficient taurine from cysteine. Cats are also able to synthesize taurine from cysteine, but the activity of two enzymes in the pathway is so low that taurine synthesis is negligible and therefore taurine must be provided in the diet.[18] Taurine deficiency can be due to:

- Inadequate dietary supply
- Loss of taurine in the enterohepatic circulation associated with increases in bacterial flora that degrade taurine or processing effects

Taurine deficiency in the cat is well documented as being associated with dilated cardiomyopathy (see Chapter 20), feline central retinal degeneration (see Chapter 29, Figures 29-61 and 29-62), and reproductive failure. Insofar as taurine is abundant in animal tissue, the need to synthesize taurine would be redundant in the cat's normal metabolic pathways.

Fat and Fatty Acids

Fats and fatty acids have four major physiologic roles[26]:

1. As a concentrated source of energy for storage and utilization
2. As structural components of cell membranes
3. As lubricants
4. As important signaling molecules (i.e., eicosanoids, cholesterol-derived hormones)

Cats are able to tolerate high levels of fat in their diet.

Dietary fats are fatty acids linked to either a glycerol backbone as triglycerides or fatty acids linked to cholesterol or retinol as cholesterol or retinyl esters. Free fatty acids are long-chain hydrocarbons with (unsaturated) or without (saturated) double bonds. Fatty acids can be classified in either of two ways on the basis of the position of these double bonds in comparison to the carboxyl end or the methyl end of the hydrocarbon chain. The delta system utilizes counting from the carboxyl end. The 18 carbon linoleic acid with two double bonds is notated as 18:2 Δ9,12 in the delta system. If counted from the methyl end as in the omega system, linoleic acid is 18:2 n-6.

Cats are able to synthesize nonessential saturated and monounsaturated fatty acids from glucose or AAs. However, cats, like other mammals, are unable to introduce double bonds between carbon 12-13 and carbon 15-16 via Δ12 and carbon Δ15 desaturase enzymes. This is the basis for the essential nature of the fatty acids linoleic (18:2n-6), and linolenic (18:3n-3).[2] Most mammals can subsequently convert linoleic (n-6) and linolenic (n-3) to their respective longer-chain derivatives, arachidonic and eicosapentaenoic acid/docosahexaenoic acid (EPA/DHA), through a Δ6 desaturase. Arachidonic acid is a precursor for eicosanoid synthesis and is an abundant component of cell membranes. Cats are unique in that they have low Δ6 desaturase activity. Initially, it was believed that cats lacked any Δ6 desaturase activity and thus had an absolute requirement for arachidonic acid as well as linoleic acid. Further studies have shown that cats may have an alternative pathway for arachidonic acid synthesis,[2] and studies have shown that they are able to synthesize sufficient quantities for maintenance but have an absolute requirement for arachidonic acid during reproduction and early growth.[2] Similarly, for the n-3 or omega 3 fatty acids EPA/DHA, cats have limited synthesis from the precursor alpha-linolenic acid. High levels of DHA are required for neural and retinal tissue development in kittens, so DHA becomes conditionally essential for cats at this life stage. Flaxseed oil is an 18 carbon n-3 fatty acid typically added to foods to increased EPA/DHA levels. This 18 carbon n-3 fatty acid is not significantly converted to EPA/DHA in dogs or cats and should not be considered as a source.[19]

Carbohydrates

Cats that eat only animal flesh have a diet low in carbohydrates. As with protein, cats have evolved several unique adaptations to metabolism of carbohydrates compared with omnivores or herbivores. These include:

- An absence of glucokinase activity in the liver
- Lower levels of amylase and the disaccharidases sucrase and lactase in the pancreas and intestine
- Little adaptation in amylase activity with increased carbohydrate diets
- High levels of gluconeogenesis from proteins and fats

Cats have no dietary requirement for carbohydrates but do have a dietary requirement for energy. As long as their diet contains fats and gluconeogenic proteins, they are able to synthesize glucose and energy sufficient for maintenance. A study in dogs demonstrated that lactating dogs given a carbohydrate-free diet became hypoglycemic, with a low survival rate among the puppies.[24] It is probable that although cats have no absolute carbohydrate requirement, queens with some carbohydrate in the diet are better able to support lactation and nursing kittens.

Mammals have up to four isoenzymes in the liver that catalyze the conversion of glucose to glucose-6-phosphate, the first step in glucose utilization. The hexokinase responsible for operating under high glucose loads is hexokinase D, or glucokinase. The cat does not have glucokinase activity, in line with a diet

containing low levels of carbohydrates.[30] In contrast, dogs do possess glucokinase activity and are able to handle larger carbohydrate loads. In contrast, enzymes involved in gluconeogenesis such as pyruvate carboxylase, fructose 1,6-bisphosphate, and glucose-6-phosphatase are much higher in feline than canine liver.[30] It was previously believed that cats do not express fructokinase activity as high-sucrose diets resulted in fructosuria and fructosemia. A recent study found that cats do have fructokinase enzyme activity in their liver producing frucose-1-phosphate.[25] Fructose-1-phosphate is then catalyzed into dihydroxyacetone and glyceraldehyde by way of the enzyme aldolase. It is believed that fructose intolerance in humans is due to a defect in this enzyme. The level of aldose activity has not been analyzed in the cat but low levels would support their low tolerance for elevated levels of fructose with resulting fructosuria.

Amylase activity, the enzyme responsible for hydrolysis of starch to glucose, is low in cats compared with dogs. The cat lacks salivary amylase,[19] with pancreatic amylase levels only 5% of those found in dogs, and intestinal values only 10% of those found in dogs.[11] The activity of the sugar transporters in the intestine is also not adaptable to higher levels of carbohydrate in the diet, compared with the dog. Compared with other species, cats have much lower levels of maltase, isomaltase, and sucrase activity in the small intestinal mucosa.[12] Lactase activity is high in newborn kittens but rapidly declines at weaning, as has been found in other mammals. Compared with puppies, however, kittens exhibit a more rapid decrease in lactase.[12] Despite limited enzymatic breakdown of sugars, once absorbed, the digestibility of all the sugars, with the exception of lactose is high, between 98% and 100%.[12] Apparent protein digestibility was found to be reduced in the diets containing lactose or sucrose by 4% to 5% compared with the carbohydrate-free diet.[13] This was believed to be due to the accelerated rate of passage of the food resulting from the osmotic effects of the soluble sugars and increased bacterial carbohydrate fermentation with increased bacterial nitrogen fixation.

There has been much speculation recently regarding high-carbohydrate diets and the increasing incidence of obesity and diabetes mellitus in cats. Dry foods can contain up to 40% carbohydrate on a dry matter basis. Although this seems feasible given the cat's unique metabolic pathways, long-term studies are needed to fully evaluate long term carbohydrate feeding effects in the cat.

Vitamins

The cat has several unique vitamin requirements, both quantitatively and qualitatively different from those of other mammals, including the following:

- An absolute requirement for preformed vitamin A
- An increased tolerance for high levels of vitamin A in the diet
- An absolute requirement for niacin
- A higher level of requirement for thiamine (four times higher that of the dog), pyridoxine (four times that of the dog), and folate (four times higher than that of the dog)

Vitamin A

Cats are able to absorb carotenoids but cannot convert these to the active form of vitamin A because of the lack the enzyme 15,15′-dioxygenase.[18] Carotenoids are vitamin A precursors synthesized in plant lipids. Preformed vitamin A occurs naturally only in animal tissues where high levels occur within the viscera. It would therefore be redundant to convert carotenoids when the preformed vitamin is already present in the diet. Vitamin A, being lipid soluble, can become toxic if given in large doses. Vitamin A toxicity occurs in cats given mainly all liver diets or given high dosages of vitamin A supplements. Chronic hypervitaminosis A in cats is characterized by the formation of exostoses on the cervical vertebrae causing ankylosis, deformity, and crippling.[21] Cats are believed to be more tolerant of high vitamin A levels than are rodents or humans. In a study comparing effects of high levels of vitamin A given during gestation in cats and rats, the incidence of malformations in the rat offspring was 80% compared with 2.9% in the kittens.[6] Unlike rodents and humans, cats transport vitamin A primarily as retinyl esters rather than retinol and are able to excrete large amounts of retinyl esters in the urine.[22] Cats are also able to store higher concentrations of vitamin A in their livers compared with humans, rats, and dogs. A smaller amount is also stored in the kidneys. As animal viscera can be high in vitamin A content, increased storage and the ability to excrete large amounts in the urine would be protective mechanisms for minimizing vitamin A toxicity.

Vitamin D

Vitamin D is conditionally essential for most mammals dependent on their exposure to sunlight. Both cats and dogs are unable to convert the precursor of vitamin D in the skin, 7-dehydrocholesterol to pre-vitamin D via ultraviolet radiation. This is not due to their thick hair coat, but rather to high levels of an enzyme in an alternative pathway that converts 7-dehydrocholesterol to cholesterol rather than pre-vitamin D.[19] Insofar as a carnivorous diet has adequate amounts of vitamin D, pathways for synthesis would be unnecessary.

Niacin (B_3)

Niacin can be endogenously synthesized from the AA tryptophan, but the efficiency of this conversion varies

among mammals. Rats are able to do this conversion very well, whereas cats are able to synthesize only negligible amounts of niacin. This is due to the high activity of an enzyme at a branching point in the pathway. The enzyme picolinic carboxylase dominates this branching point in the cat and directs it to the production of acetyl CoA and CO_2 rather than niacin synthesis.[18] Because muscle tissue is well supplied with niacin, de novo synthesis is unnecessary, and the production of acetyl CoA for ATP production is more energetically advantageous.

Pyridoxine (B_6)

One of the major biological functions of pyridoxine is to serve as a coenzyme in transamination reactions or amino group removal from amino acids.[26] Cats have high transaminase activity because of their constant state of gluconeogenesis. Therefore they have a high pyridoxine requirement, approximately four times higher than that of the dog.

Thiamine (B_1)

Thiamine is one of the water-soluble B vitamins that is required for the formation of the coenzyme thiamin pyrophosphate (TPP). TPP serves as a coenzyme in decarboxylation reactions in both carbohydrate and AA catabolism. Cats require four times as much thiamine in their diet compared with dogs. This may be due to their higher level of AA catabolism and gluconeogenesis. TPP is a coenzyme in branched-chain keto acid dehydrogenase complex involved in the catabolism of leucine, isoleucine, and valine. These reactions result in the production of acetyl CoA, which can enter the tricarboxylic acid cycle for ATP production.

Thiamine deficiency can be seen in cats fed raw or undercooked fish diets. Certain raw fish contain enzyme thiaminases.[15] Thiaminase enzymes have also been found in certain species of the bacteria *Clostridium* spp. and *Bacillus* spp. Thiaminase bacterial production has been found in the contents of ruminant animals with resulting neurological deficits.[5] It has been documented that cats have higher numbers of bacteria within their intestinal tract compared with dogs. Whether there are thiaminase bacteria within these populations resulting in a higher requirement for thiamine is unknown at this time. Clinical signs of thiamine deficiency include anorexia, weight loss, and depression, progressing to neurological signs of dilated pupils, ataxia, weakness, seizures and eventually death.

Folate

Folate, similar to the other B vitamins, is an important coenzyme in several metabolic pathways. Folate is used in metabolic reactions involving one-carbon transfers. It is important in AA metabolism, DNA synthesis, and protein synthesis.[26] Specifically, folate is involved in histidine catabolism, thymidylate synthesis, interconversion of the AAs serine and glycine, and methionine catabolism. Cats have a fourfold higher requirement for folate compared with dogs. This is probably due to higher amino acid catabolic activity. In histidine metabolism, folate is required for the conversion of the intermediate, formiminoglutamate to glutamate. Folate deficiency has been shown to result in increased urinary formiminoglutamic acid (FIGLU) secretion in cats.[31]

CONCLUSION

The unique nutritional requirements of cats reflect their adaptation to an all-meat diet. Their high protein requirement reflects their high level of gluconeogenic activity and amino acid catabolism and their inability to downregulate the nitrogen catabolic enzyme pathways. Their unique requirement for arginine, taurine, vitamin A, vitamin D, and niacin are due to adaptations in their enzyme systems secondary to deletion or downregulation of enzymes for synthesis of nutrients found abundantly in their diet.[18]

References

1. Adamec RE: The interaction of hunger and preying in the domestic cat *(Felis catus):* an adaptive hierarchy? *Behav Biol* 18:263, 1976.
2. Bauer JE: Metabolic basis for the essential nature of fatty acids and the unique dietary fatty acid requirements of cats, *J Am Vet Med Assoc* 229:1729, 2006.
3. Bradshaw JW, Goodwin D, Legrand-Defretin V et al: Food selection by the domestic cat, an obligate carnivore, *Comp Biochem Physiol A Physiol* 114:205, 1996.
4. Driscoll CA, et al: The Near Eastern origin of cat domestication, *Science* 317:519, 2007.
5. Edwin EE, Jackman R: Ruminant thiamine requirement in perspective, *Vet Res Commun* 5:237, 1982.
6. Freytag TL: *Vitamin A metabolism and toxicity in the domestic cat*, Davis, Calif, 2001, University of California.
7. Fyfe JC: Feline intrinsic factor is pancreatic in origin and mediates ileal cobalamin absorption (abstract), *J Vet Intern Med* 7:133, 1993.
8. Hendriks WH, Rutherfurd-Markwick KJ, Weidgraaf K et al: Urinary felinine excretion in intact male cats is increased by dietary cystine, *Br J Nutr* 100:801, 2008.
9. Huxtable RJ: Physiological actions of taurine, *Physiol Rev* 72:101, 1992.
10. Johnston K, Lamport A, Batt RM: An unexpected bacterial flora in the proximal small intestine of normal cats, *Vet Rec* 132:362, 1993.
11. Kienzle E: Carbohydrate metabolism of the cat 1. Activity of amylase in the gastrointestinal tract of the cat, *J Anim Physiol Anim Nutr (Berl)* 69:92, 1993.
12. Kienzle E: Carbohydrate metabolism of the cat. 3. Digestion of sugars, *J Anim Physiol Anim Nutr (Berl)* 69:203, 1993.
13. Kienzle E: Effect of carbohydrates on digestion in the cat, *J Nutr* 124:2568S, 1994.
14. Li X, Li W, Wang H et al: Cats lack a sweet taste receptor, *J Nutr* 136:1932S, 2006.
15. Lonsdale D: A review of the biochemistry, metabolism and clinical benefits of thiamin(e) and its derivatives, *Evid Based Complement Alternat Med* 3:49, 2006.

16. MacDonald ML, Rogers QR, Morris JG: Nutrition of the domestic cat, a mammalian carnivore, *Annu Rev Nutr* 4:521, 1984.
17. Morris JG: Nutritional and metabolic responses to arginine deficiency in carnivores, *J Nutr* 115:524, 1985.
18. Morris JG: Idiosyncratic nutrient requirements of cats appear to be diet-induced evolutionary adaptations, *Nutr Res Rev* 15:153, 2002.
19. National Research Council: *Nutrient requirements of dogs and cats*, Washington, DC, 2006, National Academies Press.
20. O'Brien SJ, Yuhki N: Comparative genome organization of the major histocompatibility complex: lessons from the Felidae, *Immunol Rev* 167:133, 1999.
21. Polizopoulou Z, Kazakos G, Patsikas M et al: Hypervitaminosis A in the cat: a case report and review of the literature, *J Fel Med Surg* 7:363, 2005.
22. Raila J, Mathews U, Schweigert FJ: Plasma transport and tissue distribution of beta-carotene, vitamin A and retinol-binding protein in domestic cats, *Comp Biochem Physiol A Mol Integr Physiol* 130:849, 2001.
23. 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.
24. Romsos DR, Palmer HJ, Muiruri KL et al: Influence of a low carbohydrate diet on performance of pregnant and lactating dogs, *J Nutr* 111:678, 1981.
25. Springer N, Lindbloom-Hawley S, Schermerhorn T: Tissue expression of ketohexokinase in cats, *Res Vet Sci* 87:115, 2009.
26. Stipanuk M: *Biochemical, physiological and molecular aspects of human nutrition*, ed 2, St Louis, 2006, Saunders.
27. Swanson KS: Using molecular techniques to study canine and feline gut microbial ecology, *Comp Contin Edu Pract Vet* 29:34, 2007.
28. Turnbaugh PJ, Ley RE, Hamady M et al: The human microbiome project, *Nature* 449:804, 2007.
29. Verberkmoes NC, Russell AL, Shah M et al: Shotgun metaproteomics of the human distal gut microbiota, *ISME J* 3:179, 2009.
30. Washizu T, Tanaka A, Sako T et al: Comparison of the activities of enzymes related to glycolysis and gluconeogenesis in the liver of dogs and cats, *Res Vet Sci* 67:205, 1999.
31. Yu S, Morris JG: Folate requirement of growing kittens to prevent elevated formiminoglutamic acid excretion following histidine loading, *J Nutr* 128:2606S, 1998.
32. Zaghini G, Biagi G: Nutritional peculiarities and diet palatability in the cat, *Vet Res Commun* 29(Suppl 2):39, 2005.