In cooperation with

Timely Topics in Nutrition

Effects of nutrition choices and lifestyle changes on the well-being of cats, a carnivore that has moved indoors

Debra L. Zoran, DVM, PhD, DACVIM, and C. A. Tony Buffington, DVM, PhD, DACVN

Cats (*Felis catus*) are complicated creatures that have fascinated, frustrated, and even evoked fear in humans for millennia. Although many factors influence these emotions, most are certainly tied to the fact that humans have attempted to tame one of the world's greatest hunters, with only modest success. Cats have lived at the periphery of human society, cohabiting with humans but still retaining their independence, with diet options that have included small animals or birds they captured. Cats in this role were often included as members of the family, but they only interacted with humans at times of their choosing and, in the process, maintained strong ties to their feral background.

Today, of all companion animals, domestic cats retain the most anatomic, metabolic, and behavioral features of their predecessors. Domestication has changed cats relatively little.[1] However, cats have surpassed dogs as the most common household pet in American households, and even though they have been brought indoors and domesticated, their relationship with humans and their nutritional, physical, and emotional needs remain unique.[1–3] Cats have come to fill a niche that the current urban environment demands because of their ability to live in small spaces, function on little input from their human caregivers, and coexist with humans in a busy society.

Cats in confinement live under the authority of their owners, who control what, when, where, and how they eat and eliminate, and determine their opportunities to engage in species-typical activities. Animal-owner relationships also are dyadic, so the actions of the owner influence the actions of the animal, which in turn influence subsequent actions of the owner on the basis of attitudes and beliefs that arise in the mind of the owner as a result of the animal's actions.[4–6] Moreover, relationships change over time and are further influenced by other events in the owner's and cat's lives.

Fortunately for cats, their current preeminence as pets has resulted in substantial improvements in their general health and life expectancy. Protecting them from their natural predators (larger carnivores and primates) and providing preventative medical care to decrease their risk of illness from infectious diseases has increased the average lifespan of cats from 4.5 years (which is typical of an outdoor cat) to nearly 15 years.[7] However, despite these benefits, this crepuscular carnivore has been removed from a free-roaming, active existence to a captive, indoor, sedentary one. Cats have gone from frequent consumption of small meals that consisted of animals they could catch and kill to consumption of prepared diets of human choosing, which are often available in excessive amounts and consist of less protein and a wider variety of protein, fat, and carbohydrates than is found in wild birds, insects, and small rodents. Cats are one of the few true carnivores humans have attempted to domesticate. People also have attempted to get cats to adapt to human lifestyles and preferences, which sometimes leads to a failure to recognize or understand the perils of domestication and its effects on feline behavior, well-being, and health. As a result, there is increasing evidence that many of the chronic health problems of domestic cats are directly or indirectly related to nutrition or lifestyle changes that have been imposed on them by their owners (**Table 1**).[8]

The information reported here will provide a review of the importance of diet, feeding behaviors, and environmental influences that may affect the health of cats. Various associations between some chronic diseases of cats and their diet and confined environment will be reviewed. Our objective was to help veterinarians, cat owners, and people who love cats provide optimal nutrition and a healthy environment for this wild carnivore that has been moved indoors.

Abbreviations

BW	Body weight
ME	Metabolizable energy
NRC	National Research Council
PRSL	Potential renal solute load

Protein Nutrition and Metabolism

The natural diet of cats in the wild is based on consumption of small mammals, birds, and insects (ie,

From the Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843 (Zoran); and the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210 (Buffington).

Address correspondence to Dr. Zoran (dzoran@cvm.tamu.edu).

meat- or protein-based diets). Such diets contain little carbohydrate[9–13] (**Table 2**).

Cats are one of the few species that are strictly carnivorous, which explains their unusual requirement for specific nutrients, such as arachidonic acid, vitamins A and D and many B vitamins (particularly niacin), taurine, and arginine, which cannot be endogenously synthesized in sufficient amounts to meet their needs.[14,15] However, it is their unique need for large amounts of dietary protein (specifically, dispensable nitrogen) that separates them from noncarnivorous species.[14,15] Many of the dietary requirements for specific amino acids, fatty acids, and vitamins that have been observed in cats are suggested to be a result of their evolutionary adaptation for food availability from animal sources.[14] Several reviews[14–16] of feline nutrition provide details of the specific needs that dictate their diet composition. Although healthy animals of many species can accommodate large amounts of dietary protein, cats are particularly adapted both physiologically and metabolically for high protein intake (diets containing 70% protein are acceptable for cats[17]) as a result of the high, fixed rate of activity of the enzymes of protein degradation and disposal (including aminotransferases and urea cycle enzymes) in cats.[18,19] This unique aspect of feline enzyme function was clearly evident in a study[19] in which investigators found that the activity of some hepatic aminotransferases and urea cycle enzymes did not differ when cats were fed diets high (54% ME) or low (14% ME) in protein. Conversely, in noncarnivorous species, the same changes in diet resulted in multiple-fold decreases in enzyme activity when the low-protein diets were fed.[20–22] Furthermore, this lack of enzyme adaptability to dietary protein intake in cats was found to be most relevant in cats fed diets that were inadequate in protein (contained less than the NRC minimum of 16% ME or < 1.6 g of protein/d).[23] Thus, this lack of metabolic flexibility becomes critically important when cats are inappetent (as a result of disease or other health conditions, including gastrointestinal tract disturbances or hepatic lipidosis), are consuming diets containing poor-quality protein, or are not consuming a sufficient amount of protein in the diet to meet their needs (eg, inadequate amounts of protein in a diet that is fed to induce weight loss).

Protein is the primary macronutrient responsible for maintenance of muscle mass (more specifically, indispensable amino acids and nitrogen).[24–29] The preservation of muscle mass is a function of 2 processes: consumption of a sufficient amount of high-quality protein (with adequate indispensable amino acid content) and adequate neuromuscular activity to promote maintenance of the tissue mass.[24,29] Furthermore, lean body mass is a primary determinant of a cat's resting energy requirement[28]; thus, dietary protein intake (on an energy basis) and the amount of activity are 2 key variables that must be considered because the loss of lean muscle tissue is a potentially important contributor to energy imbalances in neutered, sedentary indoor cats.

Dietary protein requirements for cats traditionally have been based on minimum requirements for short-term nitrogen balance (ie, the state at which nitrogen intake equals nitrogen excretion) in the presence of adequate energy intake. For the nitrogen-balance method, subjects are fed varying amounts of protein and the requirement is deemed to be at the level of intake that maintains a neutral or slightly positive nitrogen balance.[14] This state can be difficult to define for cats because there is not always a definitive plateau.[14,18] In 2 studies[23,30] conducted to estimate protein needs for adult cats, investigators of both studies found that 2.5 to 2.7 g of protein/kg of BW (1.14 to 1.23 g of protein/lb of BW) were sufficient to maintain nitrogen balance for the short duration of those studies (approx 3 weeks). In the longer term, the 2006 NRC publication[17] indicated that for evaluation of commercial dry, expanded diets that have provided sustained maintenance for months to years, none were found with < 265 g of crude protein/kg of diet (< 120.5 g of crude protein/lb of diet) that contained 4.0 kcal ME/g. For example, an active 4-kg (8.8-lb) cat consuming 65 kcal/kg of BW/d (29.5 kcal/lb of BW/d), which was derived from the NRC recommended intake[17] of $100 \times (BW_{kg}^{0.67})$, translates to 4.3 g of protein/kg of BW/d (1.95 g of protein/lb of BW/d). However for an inactive, neutered 4-kg cat consuming fewer calories (eg, 45 kcal/kg of BW/d [20.5 kcal/lb of BW/d]), feeding the same diet would translate into a protein intake of 3.0 g of protein/kg of BW/d (1.4 g of protein/lb of BW/d). This recommended reduction in intake is based on results of several reports[31–33] in which

Table 1—Effect of housing* on disease risk in cats.

Variable	Outdoors	Indoors
Life expectancy	Shorter	Longer
Trauma and identity risk†	Higher	Lower
Perception of control (by the cat)	Higher	Lower
Risk of illness attributable to environment‡	High	High
Efforts for food acquisition	High	Low

*Housing refers to owned cats housed only indoors or to owned cats housed indoors that are permitted to go outdoors. †Identity risk is defined as the risk of a cat being lost, trapped, or harmed by humans who believe that the cat is unowned. ‡It is recognized that indoor cats permitted to go outdoors into environments with a high cat density also may have risks similar to those of cats confined exclusively indoors.

Table 2—Approximate body composition of cat prey species.

Prey	Weight (g)	Water (%)	Dry matter (%)	Fat-free mass (%)*	Fat (%)*	Reference
Sparrow	23	65	35	35–50	20	9
Mouse	16	75	25	43–65	4–18	10,11
Lizard	10	72	28	63–67	4	12
Cricket	0.3	70	30	45–55	20–25	13

*Dry-matter basis.

investigators detected a significant reduction in the energy intake required to maintain moderate body condition after neutering and a meta-analysis of the energy requirements of cats.[34] Thus, the protein intake of cats housed indoors that are consuming fewer calories in a typical feline diet will be reduced. Maintenance of adequate long-term protein intake is difficult to assess, but detection of a serum albumin concentration within the reference range, preservation of lean body mass, and maintenance of plasma amino acid concentrations have been used for assessment. In research settings, scanning with dual-energy x-ray absorptiometry permits accurate, repeatable assessment of muscle mass, but it requires that an animal be anesthetized and is not universally available; thus, it is impractical for clinical use. Unfortunately, none of these variables were reported in the NRC for adult cats, and authors of 1 study[30] concluded that dietary protein concentration and dietary ingredients were not directly associated with plasma amino acid or whole blood taurine concentrations.

Prolonged inadequate protein intake can result in various abnormalities, including loss of muscle mass, abnormal energy metabolism, reduced or poor immune function, reduced protein availability for structural repair, and abnormal function of critical metabolic pathways, such as those for glutathione or nitric oxide.[35–38] Whereas the roles of protein in preservation of muscle mass, immune function, and structural repair are easy to grasp, it may not be as easy to appreciate the importance of protein to other critical metabolic pathways and oxidative processes. The problem with identification of protein deficiency is that in many cases, the effects are not immediate (except for arginine deficiency, which can be acutely fatal for cats[39]) and many of the outward effects are associated with specific deficiencies in amino acids that result when the protein source is inadequate, poorly digestible, or fed in quantities too low to meet needs. The most famous example of an amino acid deficiency in veterinary medicine is that of cats fed taurine-deficient diets for up to 3 years before the effects of taurine deficiency on cardiac muscle function resulted in development of cardiomyopathy.[40] This example was all the more remarkable because while it was believed that adequate taurine was included in the diets during the study, dietary processing, diet ingredients, and other factors resulted in the fact that the amount of taurine actually available to the cats was inadequate. The key point is that protein deficiency, unless it is extreme or causes specific, measurable illness, can develop insidiously.

One of the areas for which protein intake in cats has received the most attention is in composition of diets fed to achieve weight loss. In several studies,[28,41–44] investigators found a relationship between protein intake and preservation of lean body tissue in obese cats during weight loss (**Table 3**). Intakes of > 3.3 g of protein/kg of initial BW (> 1.5 g of protein/lb of initial BW) resulted in greater reductions in fat mass (and hence preservation of lean mass) than did lower protein intakes. The amount of 3.3 g of protein/kg is slightly higher than the current NRC-recommended allowances for cats of this size (2.7 g of protein/kg of BW/d [1.23 g of protein/lb of BW/d]).[17] To ensure that sufficient protein is consumed, multiply the cat's current BW (kg × 3.3 [lb × 1.5]) to estimate the total protein intake needed per day. This can be compared to the protein in the diet by multiplying the number of grams of food to be fed by the percentage dietary protein (which is a minimum). Of course, these calculations are estimates because without knowing the exact metabolic rate of an animal (and thus the correct calculation for energy requirement), the digestibility of a diet (protein digestibility can vary considerably in commercial diets), or the adequacy of gastrointestinal tract function (and thus the ability to digest and absorb nutrients properly), it is impossible to accurately determine the needs of a specific cat. Nevertheless, an example calculation of the estimation of the amount of protein needed, compared with the amount of protein available in the diet, may be helpful. For example, a 6-kg (13.2-lb) obese cat would need 6 × 3.3 = 20 g of protein/d. To cause a weight loss of 20% (to a final weight of 4.8 kg [10.6 lb]), the cat could be fed at 35 kcal/kg of target BW (15.9 kcal/lb of target BW), which is 168 kcal/d. If the weight-loss diet contains 3.5 kcal ME/g, this amount of energy would be contained in approximately 50 g of food. To provide 20 g of protein, the food would need to contain 40% protein (50 g × 40% = 20), which is 11.4 g/100 kcal of diet. Alternatively, a 4.5-kg (9.9-lb) cat in moderate body condition that is housed exclusively indoors might consume approximately 45 kcal/kg of BW/d (ie, 4.5 × 45 = 202 kcal/d). To provide 3.3 g of protein/kg of BW/d

Table 3—Effects of dietary protein content on BW and fat mass loss in cats.

Cats	Age (y)*	Diet	Protein intake (g/kg of BW/d)†	BW			Body fat (%)			Reference
				Initial (kg)	Final (kg)	Change (%)‡	Initial	Final	Change‡	
8 F and 8 M (Lab)	5.1 ± 1.2	Dry CP	1.7	6.4	3.7	42	58	52	10	41
		Dry HP	2.7	6.3	3.5	44	57	41	28	
8 F and 8 M (Lab)	4–8	Dry CP	2.5	4.9	3.8	22	39	29	26	28
		Dry HP	3.8	5.2	4.0	23	38	24	37	
1 F and 6 M (Lab)	3.2–8.6	Dry CP	5.6	6.8	5.2	24	41	26	37	42
		Dry HP	5.3	6.3	4.5	29	46	30	35	
16 F (Lab)	NR	Dry CP	3.3	5.4	4.3	20	47	36	23	43
		Dry HP	4.4	5.4	4.3	20	48	32	33	
7 F and 5 M (CO)	6.5–13	Dry or canned	4.9–5.0	6.9	5.0	28	36	18	50	44

*Value reported is mean ± SD or range. †To convert to g/lb of BW/d, divide by 2.2. ‡Calculated as ([initial value – final value]/initial value) × 100.

CO = Client-owned cats in homes. CP = Control protein. F = Female. HP = High protein. Lab = Laboratory cats. M = Male. NR = Not recorded.

(3.3 × 4.5 = 14.85 g of protein/d) would require a diet containing at least 7.3 g of protein/100 kcal of diet. Information on macronutrient content of some commercial diets (compared on a 100-kcal basis) is available[a] for use in matching nutrient content to food intake.

Protein requirements for optimal nutrition in older humans currently are being reevaluated in light of the fact that protein deficiency and sarcopenia (the degenerative loss of muscle mass and strength associated with aging) are now recognized as major problems associated with increased morbidity in aging humans.[45,46] Veterinary clinicians commonly observe loss of muscle mass in geriatric cats, although few studies have documented this problem by objective means. Aging cats sometimes are fed diets that contain lower amounts of protein (even in cats without kidney disease), but conversely, these older cats are less able to digest the protein efficiently.[47,48] This was particularly evident in a study[49] in which there was an age-related decrease in the apparent digestibility of protein ($P = 0.08$), fat ($P = 0.025$), and energy ($P < 0.001$) in cats that were 10 to 14 years old. That age-related decrease, in combination with the decrease in activity that often is evident in aging animals, may combine to cause age-related reductions in muscle mass in cats that could be clinically and physiologically relevant. There currently is a paucity of information on the effects of dietary protein on sarcopenia in cats, protein needs in geriatric cats, and aging-related illnesses that may be influenced by nutrition in cats. Nevertheless, because of the use of protein for gluconeogenesis and protein oxidation in cats, many middle-aged and geriatric cats consuming typical diets have been observed by clinical practitioners to develop substantial sarcopenia. These cats presumably may also be affected by concurrent conditions, such as lower metabolism, muscle weakness, lameness, and reduced mobility. Although the appropriate amount of protein in diets for healthy older cats has not been studied to any extent, data from humans have revealed that increased amounts of protein (particularly certain amino acids, such as leucine) in the diet help reduce the loss of muscle.[45] It is reasonable to believe that greater intake of high-quality protein, in combination with increases in the activity of indoor cats, may help decrease loss of muscle mass and the potential debilitation in some middle-aged and older cats, although it must be recognized that the causes of sarcopenia are multifactorial and include disuse, altered endocrine function, chronic disease, inflammation, insulin resistance, and nutritional deficiencies. As with all general recommendations for dietary interventions, it is incumbent on practitioners to assess the situation for each specific animal and ensure that increasing the protein intake is appropriate for that particular cat (ie, no abnormalities in liver and kidney function and no contraindications for a higher protein intake).

Ultimately, this information should prompt reconsideration of the definition of adequate protein intake for cats of all life stages, with a particular emphasis on a better understanding of the specific protein needs for cats in a broad range of living and health conditions. This reevaluation is necessary because many cats are not permitted to obtain supplemental food (ie, prey) other than the diet they are fed and because humans have assumed the responsibility of providing optimal nutrition for cats through control of food choices.

Intermediary Metabolism

The role of protein in maintenance of body fat and physiologic intermediary metabolism, which may be one of the key components of optimal nutrition in cats, has been examined. Some metabolic effects of feeding diets higher (39% ME) or lower (24% ME) in protein to obese (before and after weight loss) and lean laboratory-housed cats were evaluated.[41] For the lower-protein diet, protein was replaced with carbohydrate. Neither diet affected differences in glucose effectiveness or insulin sensitivity between the lean and obese cats, and baseline heat production (a measure of resting energy expenditure) was higher in lean cats fed the higher-protein–low-carbohydrate diet than in obese cats fed either diet before or after weight loss.[41] For those same cats, effects of feeding a diet containing 28% ME on heat production, fat, and glucose metabolism were reported for simultaneous application of the euglycemic hyperinsulinemic clamp and indirect calorimetry.[50] In the lean cats, glucose oxidation predominated during food deprivation, whereas lipid oxidation predominated in obese cats; glucose oxidation was significantly lower in obese female cats than in any other group. Additionally, insulin suppressed plasma concentrations of nonesterified fatty acids to a greater extent in obese cats than in lean cats, which suggested greater clearance of fatty acids in obese cats than in lean cats. In addition, heat production per metabolic size was lower in obese cats than in lean cats, as determined by use of indirect calorimetry.[50] Analysis of the results of these studies suggests that the obese state, and to a certain extent sex, modify responses of cats to the macronutrient constituents of their diets.

Obesity

Obesity is currently recognized as the number one nutritional disorder of domestic cats and is associated with a number of other health issues, including osteoarthritis, diabetes mellitus, and other disorders that increase the morbidity and mortality rates of affected cats.[51] Obesity often has been attributed to excess energy intake, decreased energy expenditure, or both, but evidence increasingly suggests that while these aspects are important, they do not explain the entire depth or breadth of the problem.[52,53] It is clear that the decrease in energy expenditure that often results after gonadectomy in cats,[31,32,54,55] when promoted by environments with reduced opportunities for physical activity and mental stimulation, also may increase the risk for development of obesity. When these events are combined with the ready availability of highly palatable, energy-dense diets and free-choice feeding, obesity in a large number of indoor cats is the predictable result.

Investigators in several studies[31,32,34,54,55] have found that neutering can alter food intake and energy expenditure; however, this information apparently has not been used to resolve the obesity epidemic in cats. Moreover, not all neutered cats gain weight, which suggests that factors in addition to food intake and energy expendi-

ture may mediate the final outcome. Evidence also suggests that the historical perspective on obesity as an input-output problem may not be sufficient to explain the biology of the problem,[53] and it certainly has not prevented a worldwide epidemic of obesity and related disorders, such as type 2 diabetes mellitus.[56] Current models of obesity and related diseases suggest that these disorders may result from a variety of gene-environment interactions. Various combinations of malnutrition and environmental stressors during gestation can promote obesity in offspring.[57] The risk appears to depend on complex interactions between the genetic background of the dam and her offspring, epigenetic modulation of gene expression, and the nature of the environment into which the offspring are born.[58] Although appropriate nutritional and environmental management may reduce the adverse effects of some of these prenatal factors,[59,60] inappropriate management (eg, free-choice feeding and unhealthy indoor environment) may exacerbate the risk for development of obesity. Despite the likelihood that many variables affect domestic cats, given the challenging conditions faced during gestation by many cats, future work is needed to better understand the role of early environmental experience on obesity.[61,62]

Thus, although it is impossible to point to any 1 factor when discussing the problem of obesity in cats, it is clear that the current approach to diet and feeding management of cats is not optimal. New feeding approaches (diet composition as well as feeding strategies) may help stop the epidemic of obesity, but such new approaches currently are unknown. For example, changes in postprandial hormone concentrations in response to diets differing in protein, fat, and carbohydrate content were evaluated in cats.[63] Investigators in that study[63] found that obesity, rather than any diet, was the main factor responsible for the observed changes in hormones involved in glucose metabolism, food intake, and control of BW. In fact, the highest postprandial glucose concentrations were found in cats fed a high-fat diet, and postprandial insulin concentrations were highest in cats fed a high-protein diet. Whether these findings reveal beneficial or detrimental effects indicates the limited utility of attempting to extrapolate a single measurement of a circulating concentration of a metabolite. Furthermore, to address obvious difficulties in extrapolating results from laboratory-housed to client-owned cats, novel dietary and feeding strategies also are being explored in clinical populations. In 1 study,[64] changes in both macronutrient content of the diet and feeding strategies resulted in improvements in weight loss, although the investigators were not able to parse these effects. Additionally, the goal of obesity treatment is not weight loss but maintenance of weight loss[65]; thus, long-term studies are needed.

Urolithiasis

Water is an essential nutrient with numerous vital functions in the body, but it often is not considered in discussions of diet and nutrient requirements. Although it has been thought that the water requirements of cats reflected their early status as desert-dwelling animals[66] that obtained most of their water requirements from prey and that concentrated their urine intensely to reduce water loss, an alternative explanation exists. With regard to a classification as desert animals, some may have confused the evolution of cats with their domestication history.[67–69] On the basis of results of molecular investigations, it has been determined that all modern cats descended from one of several *Pseudaelurus* spp that lived in Asia approximately 11 million years ago.[70] Domestic cats appear to have been domesticated in the region of the Fertile Crescent of the Middle East.[71] Although some of this region is now a desert, it was quite different 12,000 years ago. The ability of domestic cats to concentrate their urine intensely is not unique. In addition, it was pointed out in 1 study[72] that there was nothing special about the urine-concentrating ability of cats; this observation was confirmed in a review[73] of the urine-concentrating ability of several species.

Cats can maintain water balance when fed dry or canned foods,[74] but they adjust their water intake to the dry-matter content of their diet, rather than to the moisture content of their diet. Unfortunately, the composition of the diets fed was not reported in that study[74]—an omission that affects the study's impact; these data are essential for interpretation of the effects of diet on the volume of water voluntarily ingested by cats because consumption depends on both the composition and quantity of the diet ingested. This is because the PRSL of the diet influences the volume of water ingested. The PRSL consists of urea (an end product of protein metabolism) and the ions sodium, potassium, calcium, magnesium, phosphate, chloride, and sulfate.[75] For most practical purposes, PRSL (in mmol) may be estimated as urea concentration + (2 × [sodium concentration + potassium concentration]).[76,77] The urea concentration may be estimated by dividing the amount of dietary nitrogen by 28 (there are 28 mg of nitrogen/mmol urea). For adult animals in nutritional balance, all the PRSL ingested must be excreted via the gastrointestinal tract or urinary system. Thus, estimation of the PRSL permits a more complete interpretation of the effects of diet on water intake and excretion. Because increasing the protein content of the diet will increase the PRSL, diets higher in protein are naturally associated with higher total water intake.[78] Increasing the percentage of salt in foods also is associated with increased water intake in cats,[79] and this principle has been exploited to increase voluntary water consumption in cats that are at risk for developing urolithiasis.[80]

The effect of PRSL on water intake helps explain the reason that cats consuming foods that are higher in carbohydrate and lower in protein (characteristic of dry foods) consume less water (both in the diet and by drinking), compared with the water consumption for cats eating diets containing less carbohydrate and more protein (eg, canned foods).[74,80] Thus, feeding diets that contain a higher PRSL will increase water intake, which may be beneficial for cats that tend to develop uroliths. However, the assumption that increasing water intake will increase urine volume (and thus decrease the risk of urolith formation) is not always accurate. For example, investigators in 1 study[78] reported a significant diet-related increase in water intake but without a significant increase in urine volume in 4 female cats fed

4 diets with increasing amounts of protein, whereas both diet-related water intake and urine volume increased significantly in 4 male cats fed 2 diets with increasing amounts of protein. Interestingly, this relationship was not observed in 8 (4 female and 4 male) cats fed those 2 diets in a subsequent study.[80] In addition to the issues of variability within and between studies, most studies conducted to investigate relationships between diet and water intake have not provided sufficient information to parse the roles of PRSL and its individual components (eg, protein and sodium) on relevant outcome variables.[81,82]

Other approaches for use in evaluating relationships between diet and urine variables have been subject to other issues. The urine composition of 85 adult feral cats that were trapped and subsequently euthanized was evaluated in 1 study.[83] Investigators of that study[83] reported that the range of urine pH was 5.73 to 7.39 (mean, 6.10) in male cats, which was significantly higher than the range of 5.54 to 6.57 (mean, 5.80) found in female cats, and that specific gravity ranged from 1.016 to 1.065 (mean, 1.048 in males and 1.045 in females). Unfortunately, results of evaluation of gastrointestinal contents were not reported, so effects of diet composition and timing of food intake relative to sample collection could not be determined. Moreover, because the metabolic response to stressors increases urine pH,[81] the effect of trapping on the resulting data confound the interpretation of those results. Nevertheless, stress-induced increases in urine pH notwithstanding, the mean urine pH of these cats (which were presumably consuming a diet of wild prey) was substantially acidic, as would be expected from consumption of a high-protein–low-carbohydrate diet.

Because of the concern related to diet-induced struvite urolithiasis, pet food manufacturers have added urinary acidifiers (eg, ammonium chloride, methionine, or calcium chloride) to counteract the typically positive cation-anion balance (as determined by concentrations of the cations calcium, magnesium, sodium, and potassium and the anions phosphorus, methionine, cysteine, cystine, and chloride) of their diets.[80,82] Increasing dietary protein intake also influences urine pH of cats, depending on the amino acid content of the diet. In 1 study,[80] 2 experiments were conducted to investigate the effects of dietary protein, sodium chloride, and ammonium chloride on urine pH and struvite-related variables in healthy cats. In the first experiment, urine pH was significantly lower in cats fed a 55% protein diet than in cats fed a 29% protein diet (mean ± SD urine pH, 6.63 ± 0.11 and 7.25 ± 0.18, respectively), whereas no differences in food intake, water intake, or urine volume were detected.[80] In contrast in the second experiment, addition of 1.5% ammonium chloride to the 29% protein diet resulted in a mean urine pH of 6.13 ± 0.08, whereas addition of sodium chloride did not affect urine pH. Curiously, food intake of the diets in the second experiment were approximately half that reported for the first experiment. These experiments revealed that consumption of high-protein diets and diets containing ammonium chloride urinary acidifiers resulted in significant reductions in urine pH and that the magnitude of the effect was greater for ammonium chloride. Unfortunately, effects on systemic acid-base balance were not reported; excessive acidification of diets may result in chronic metabolic acidosis in cats that consume such diets.[84–86]

Inflammatory Bowel Disease

In addition to effects on energy metabolism, muscle mass, water intake, and acidification of the urine, protein intake also appears to play an important role in gastrointestinal tract disease. Development of gastrointestinal disease in cats attributable to food intolerance or food allergy has been reported, and dietary protein appears to be a common culprit.[87,88] However, the situation appears to be far more complex. For example, analysis of evidence suggests that inflammatory bowel disease, which is one of the most common causes of chronic vomiting and diarrhea in cats, results from an immune-mediated disorder initiated by alterations in the intestinal microbiota.[87–90] Furthermore, evidence from studies[89–93] of the intestinal microbiota of cats has identified a significant influence of diet (specific nutrients) on the number and species of bacteria present in the gastrointestinal tract and that these are altered in inflammatory bowel disease. Unfortunately, inadequate evidence currently prevents formation of conclusions about the specific effects of protein or carbohydrate on the intestinal microbiota or the component or components of the diet that might be beneficial in maintenance of the normal flora. Whereas it has been suggested that routine feeding of commercially available dry diets with moderate amounts of protein and moderate to high amounts of carbohydrate to cats may be associated with promotion of a less-than-ideal microbiota in the feline gastrointestinal tract, it has also been suggested that canning may result in an increase and a qualitative difference in the immunogenicity for certain proteins, compared with those of unprocessed proteins. Investigators also concluded that canned diets may not be ideal for management of cats with enteritis.[94] However, a study[95] conducted to compare the effectiveness of a canned high-protein, highly digestible diet with that of a canned moderate-protein, high-carbohydrate, highly digestible diet for reduction of nonspecific diarrhea in adult cats revealed that the cats fed the high-protein, highly digestible diet had a significantly better response than did cats fed the moderate-protein, high-carbohydrate, highly digestible diet (reduction in episodes of nonspecific diarrhea of 65% and 28%, respectively). However, because the diets differed in more than just their protein and carbohydrate concentration, it is possible that other dietary effects were responsible for the differences in response.

These aforementioned studies may be confounded by differences in nutrient digestibility. Simple improvement of the nutrient digestibility of a diet can decrease or even resolve diarrhea in a large number of cats with chronic diarrhea.[87,88] Clearly, additional research is needed in this area, but the digestibility of the nutrients (and particularly protein and carbohydrate) in the diet may be a key issue because undigested foods can become nutrients for pathogenic bacteria in the gastrointestinal tract as well as serving as antigens.

Moreover, the role of the environment does not appear to have been considered in studies of diet-gastrointestinal interactions in cats, although there is evidence that there are environmental influences on the gastrointestinal tract[96,97] and that gastrointestinal conditions are responsive to environmental enrichment.[98] Human gastroenterologists have recognized the complexity of these interactions in patients with irritable bowel syndrome and inflammatory bowel disease,[99] and the current unifying model includes a background of genetic and epigenetic variables triggered by altered bacterial flora associated with life stressors that results in immune dysfunction and mucosal inflammation of variable severity, which is further exacerbated by environmental distress.[100] It is easy to imagine that typically benign dietary proteins may become antigens that exacerbate these underlying abnormalities, which suggests that in addition to dietary treatment,[101] environmental enrichment may offer beneficial adjunctive effects for some cats with gastrointestinal disease, similar to the beneficial effect for some humans.[102]

Diabetes Mellitus

The incidence of type 2 diabetes mellitus in domestic cats appears to be rapidly increasing, and this increase reflects the increase in obesity as well as the popularity of cats as pets.[103] Similar to many other chronic diseases, diabetes mellitus in cats is a complex problem that is likely the result of a variety of interacting genetic, environmental, and nutritional factors.[103] However, because diabetes mellitus in cats is a disease of insulin resistance and loss of beta cell function, nutritional treatment plays an important role in the overall management of the disease. However, the exact role remains a matter of some controversy. Control of type 2 diabetes mellitus in cats via diets containing moderate to high amounts of carbohydrate and added dietary fiber[104,105] and via high-protein–low-carbohydrate diets[106–109] has been reported. Results of studies of healthy, laboratory-housed cats are conflicting. For example, investigators in 1 study[110] compared 3 commercial diets fed to 5 healthy adult domestic cats (2 males and 3 females); they found that the diet containing the most protein reduced glucose concentrations and increased insulin concentrations to a greater extent than did the other 2 diets. In contrast, investigators in another study[111] compared 3 homemade diets fed to 9 healthy adult domestic cats (4 males and 5 females); they reported that in contrast to other studies in which energy sources were increased instead of being reduced, their results contradicted the often-suggested negative impact of carbohydrates on insulin sensitivity in carnivores and indicated that reducing the dietary carbohydrate content below amounts commonly found in commercial foods evoked an insulin-resistant state, which can be explained by the strictly carnivorous nature of cats. Results for that study[111] even pointed to a negative effect of protein on insulin sensitivity, a finding that corresponded with the highly gluconeogenic nature of amino acids in animals that are strictly carnivorous. The many differences between these 2 studies, including the number of cats, type of diet, form of diet, and food intake, all complicate interpretation of the results. Additionally, the relevance of short-term studies in healthy, normal-weight, laboratory-housed cats to long-term clinical management of diabetic cats is not obvious.

The environment also appears to play a role in type 2 diabetes mellitus in cats.[112] For example, in 1 study,[112] indoor housing, but not diet, was found to be a significant risk factor for the development of type 2 diabetes mellitus. The sensitivity of changes in circulating glucose concentrations to environmental circumstances in cats has long been recognized. Early in the 20th century, investigators in 1 study[113] found that cats that appeared to be frightened or enraged during restraint developed glycosuria more quickly than did those that appeared to be calm. Veterinarians have observed the effects of housing on glucose tolerance curves and remission of the hyperglycemic state in cats with type 2 diabetes mellitus. Despite these observations, the role, if any, of environmental enrichment on resolution of type 2 diabetes mellitus does not appear to have been examined in cats. In contrast, addition of nutritional education or cognitive-behavioral treatment to a prescriptive diet intervention led to significantly better outcomes than did the use of diet alone in humans with type 2 diabetes mellitus.[114]

Feeding Behavior, Food Preferences, and Finicky Eaters

Food and taste preferences are learned behaviors that are acquired at an early age.[1] Food preferences of cats form early and are based possibly on genetic and probably on early experiences with maternal foods.[115,116] Initial preferences are determined by 6 to 8 weeks after birth. In addition to taste preferences, cats develop preferences for foods on the basis of shape, mouth feel, and other physical characteristics.[116,117] As kittens grow, they become more (or less) interested in a variety of foods as a result of additional learning opportunities, and providing a variety of diets to kittens after weaning and into adulthood results in expanded food preferences that will likely be important later in life when dietary changes for therapeutic purposes may be warranted.[118]

Many cats display a growing aversion toward foods that have formed a large part of their diet in the past (ie, a monotony effect[117]), although taste and texture preferences seem particularly difficult to change in some cats. This behavior has been interpreted as finicky eating, and it is doubtful that it results from an evolutionarily conserved vigilance against potentially harmful foods. In a study[8] conducted by one of the authors, cats had decreased food intake in response to environmental challenges (a behavior likely to be interpreted as finicky eating by owners), but the intake resumed with removal of the challenge condition. This suggests that external as well as internal influences may modify food intake in confined cats.

Cats, similar to other species, also are sensitive to hedonic aspects associated with their food: odor (or aroma), form (shape), texture (dry vs canned or soft-moist), and palatability.[115–117] Food odor is one of the major criteria for food selection, so a decrease in the ability to smell or breathe through the nose and perceive odors can result in food avoidance or anorexia. Learned preferences for food shape and texture also affect food choices. There

also appear to be breed preferences based on mouth size because trials with Persians identified preferences that differed from those identified for domestic shorthair cats.[115] Thus, providing a variety of foods, types, textures, and forms throughout life in cats is necessary to maintain their dietary flexibility.

An important aspect of the well-being of confined animals appears to be the perception of control over one's environment.[119] Because of the centrality of food to the lives of confined animals, consideration of the forms of food and feeding practices may be more important than generally considered. Whereas numerous forms (canned or dry) and flavors of food and feeding methods (meal feeding or free choice) can clearly meet the nutritional needs of cats, consideration of a cat's preferences, which may have been formed by experiences prior to the cat coming into the care of the current owner, may influence the cat's well-being. For this reason, owners can determine diet preferences by offering foods of various forms and flavors in a side-by-side manner so that the cat can express its preferences. Such preference testing also can be extended to preferred feeding locations (generally quiet areas where the cat will not be disturbed by other animals or other interruptions). Alternative feeding practices, such as putting food in a puzzle-type device or hiding it in different locations, encourage the cat to more actively pursue its food. In addition to the increased muscular activity, the effects on neurocognitive function may enhance the cat's well-being.[8]

Feeding Guidelines

Obesity is the most common nutritional and endocrine disorder in cats in the United States, with a reported incidence of 25% to 40%, depending on the study type and sources.[120] There are a large number of factors that contribute to BW, including neuter status, sex, age, quality of environment, activity (indoors vs outdoors), and feeding style (meal feeding vs free choice). Neutered cats, both male and female, generally need substantially fewer (eg, 25% to 30%) calories to maintain an ideal body condition score than do sexually intact cats; this fact has been proven repeatedly in several studies[31,32,54,55] conducted to evaluate the effect of neutering on food intake, body fat mass, weight gain, and metabolism. In 1 study[31] of ovariohysterectomized cats that were allowed free access to a dry food, investigators found that fat mass increased from 18% to 33% in just 4 months—a staggering increase in body fat. Effective feeding recommendations for a wide range of cats are clearly needed, but current maintenance energy equations may underestimate or overestimate the needs of individual cats by > 50%, and recommendations on labels of food containers often are quite wide, and many are based on the needs of young, sexually intact, active animals. On the basis of current NRC-recommended equations, a 4.5-kg lean adult cat should consume approximately 274 kcal/d ($100 \times 4.5^{0.67}$); the recommendation for a 4.5-kg obese adult cat would be reduced to approximately 240 kcal/d ($130 \times 4.5^{0.4}$).[17] However, based on recent studies,[31,b] female cats in laboratory housing require only 60 to 70 kcals $\times$ $(BW)^{0.67}$ to maintain a body condition score of 5 of 9 after neutering (for a 4.5-kcal cat, 60 to 70 $\times$ $4.5^{0.67}$ = 165 to 190 kcal/d). Further studies are needed in male cats to determine their ideal energy intake because evidence suggests that they may need even fewer calories to maintain a moderate body condition. However, a meta-analysis[34] of energy requirements in adult cats provides clear indications that the currently recommended maintenance energy calculations for most typical-sized (4 to 5 kg [8.8 to 11.0 lb]) neutered indoor cats should be reduced from 63 kcal/kg/d (28.6 kcal/lb/d), which was based on 100 $\times$ $(BW^{0.67})$, to 45 to 55 kcal/kg/d (20.5 to 25 kcal/lb/d), with the lower number used for neutered males and the higher number used for neutered females. In addition to this recommended reduction in energy intake, it is highly preferable to condition cats to meal feeding, rather than to allow free-choice access to food. Some active, thin cats are able to effectively self-regulate their food intake; thus, free-choice feeding does not result in obesity; however, this method is still not recommended because owners are less able to observe whether a cat is eating smaller amounts of food or not eating (the best early indicator of ill health in many cats) when there are multiple cats in the household. Finally, it must be remembered that any recommended feeding amount is only a population-based estimate and suitable only as a starting point. Because of the many variables that influence BW, the changing long-term needs of any particular cat can only be determined by feeding it to maintain a moderate body condition score.

Although a simple change in diet may not solve all of the problems of our feline patients, it is reasonable to believe that their lives are influenced by the foods humans feed them in a variety of ways. History has indicated this to be true with respect to the many positive advances through appropriate nutritional management of many diseases. Although all may not agree on the mechanism, few question that nutrition and environment have been associated with the development of obesity and likely play some role in such complex diseases as lower urinary tract disease, inflammatory bowel disease, and type 2 diabetes mellitus in cats.

Good evidence exists that genetic,[121] epigenetic,[122] and early experiences[123] modify animal physiology and affect pets' perceptions of the environment and behavior, which can in turn influence their health and well-being. From this systems perspective, it is easy to understand the difficulty of identifying a single factor that mediates such complex outcomes as health and disease. Despite the number of potential factors, both laboratory and clinical studies[124, 125] in cats with 1 chronic disease syndrome (ie, idiopathic cystitis) have found that environmental improvement was associated with significant improvement in signs of lower urinary tract disease and other concurrent disorders.

The relative importance of diet, in relation to that of other environmental influences, on health and disease for cats has not yet been extensively studied. However, evidence suggests that these environmental factors may be as important or more important than diet. Additionally, in the aforementioned studies[124,125] of cats with idiopathic cystitis, the improvements in health of the cats were independent of diet change. Because of

the complexity of these relationships, numerous additional studies must be conducted before the relative magnitude of these factors can be defined with confidence. However, analysis of the available data suggests that although meeting nutritional needs is necessary for maintenance of the health and well-being of cats, it alone is not sufficient to assure a healthy existence. This perspective requires researchers and clinicians to take a broader view to provide the best solution possible for this carnivore we have moved indoors.

a. Diet search, The Ohio State University College of Veterinary Medicine, Columbus, Ohio. Available at: www.vet.ohio-state.edu/1442.htm. Accessed Jan 10, 2011.
b. Bauer JE, Comparative Animal Nutrition Research Laboratory, Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Tex: Personal communication, 2011.

References

1. Bradshaw JWS. The evolutionary basis for the feeding behavior of domestic dogs (*Canis familiaris*) and cats (*Felis catus*). *J Nutr* 2006;136:1927S–1931S.
2. AVMA. Results of the 2006 AVMA survey of companion animal ownership in US pet-owning households. *J Am Vet Med Assoc* 2008;232:695–696.
3. Pankseep J. Affective consciousness in animals: perspectives on dimensional and primary process emotion approaches. *Proc Biol Sci* 2010;277:2905–2907.
4. Mendl M, Burman OHP, Paul ES. An integrative and functional framework for the study of animal emotion and mood. *Proc Biol Sci* 2010;277:2895–2904.
5. Darwin C. *The expression of emotions in man and animals*. London: John Murray, 1872.
6. Hemsworth PH. Human-animal interactions in livestock production. *Appl Anim Behav Sci* 2003;81:185–191.
7. Kraft W. Geriatrics in canine and feline internal medicine. *Eur J Med Res* 1998;3:31–41.
8. Buffington CAT. External and internal influences on disease risk in cats. *J Am Vet Med Assoc* 2002;220:994–1002.
9. Myrcha A, Pinowski J. Weights, body composition and caloric value of post-juvenile molting European tree sparrows. *Condor* 1970;72:175–178.
10. Austad S, Kristan D. Does caloric restriction of laboratory mice mimic natural food intake of wild mice? *Gerontology* 2002;42:8–18.
11. Mutze GJ, Green B, Newgrain K. Water flux and energy use in wild house mice and the impact of seasonal aridity on breeding and population levels. *Oecologia* 1991;88:529–538.
12. Angilletta MJ. Estimating body composition of lizards from total body electrical conductivity and total body water. *Copeia* 1999;3:587–595.
13. Hall JM, Hung F, Zurich MW. The influence of diet on the body condition of the house cricket and consequences for their use in zoo animal nutrition. *Zool Garten* 2003;73:238–244.
14. Morris JG. Idiosyncratic nutrient requirements of cats appear to be diet-induced evolutionary adaptations. *Nutr Res Rev* 2002;15:153–168.
15. MacDonald ML, Rogers QR, Morris JG. Nutrition of the domestic cat, a mammalian carnivore. *Ann Rev Nutr* 1984;4:521–562.
16. Zoran DL. The carnivore connection to nutrition in cats. *J Am Vet Med Assoc* 2002;221:1559–1567.
17. National Research Council. Protein and amino acids. In: *Nutrient requirements of dogs and cats*. Washington, DC: National Academies Press, 2006;111–145.
18. Rogers QR, Morris JG. Up regulation of nitrogen catabolic enzymes is not required to readily oxidize excess protein in the cat. *J Nutr* 2002;132:2819–2820.
19. Rogers QR, Morris JG, Freedland RA. Lack of hepatic enzyme adaptation to low and high levels of dietary protein in the adult cats. *Enyzme* 1977;22:348–356.
20. 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* 1999;67:205–206.
21. Tanaka A, Inoue A, Takeguchi A, et al. Comparison of expression of glucokinase gene and activities of enzymes related to glucose metabolism in livers between dogs and cats. *Res Vet Comm* 2005;29:477–485.
22. Hiskett EK, Suwitheechon O, Lindbloom-Hawley S, et al. Lack of glucokinase regulatory protein expression may contribute to low glucokinase activity in feline liver. *Res Vet Comm* 2009;33:227–240.
23. Green AS, Ramsey JJ, Villaverde C, et al. Cats are able to adapt protein oxidation to protein intake provided their requirement for dietary protein is met. *J Nutr* 2008;138:1053–1060.
24. Evans W. Functional and metabolic consequences of sarcopenia. *J Nutr* 1997;127:998S–1003S.
25. Dardevet D, Sornet C, Bayle G, et al. Postprandial stimulation of muscle protein synthesis in old rats can be restored by a leucine supplemented meal. *J Nutr* 2002;132:95–100.
26. Ramsey JJ, Hagopian K. Energy expenditure and restriction of energy intake: could energy restriction alter energy expenditure in companion animals. *J Nutr* 2006;136:1958S–1966S.
27. Fujita S, Dreyer HC, Drummond MJ, et al. Nutrient signaling in the regulation of human muscle protein synthesis. *J Physiol* 2007;582:813–823.
28. Vasconcellos RS, Borges NC, Goncalves NC, et al. Protein intake during weight loss influences the energy required for weight loss and maintenance in cats. *J Nutr* 2009;139:855–860.
29. Kimball SR, Farrell PA, Jefferson LS. Exercise effects on muscle insulin signaling and action: invited review. Role of insulin in translational control of protein synthesis in skeletal muscle by amino acids or exercise. *J Appl Physiol* 2002;93:1168–1180.
30. Hienze CR, Larsen JA, Kass PH, et al. Plasma amino acid and whole blood taurine concentrations in cats eating commercially prepared diets. *Am J Vet Res* 2009;70:1374–1382.
31. Belsito KR, Vester BM, Keel T, et al. Impact of ovariohysterectomy and food intake on body composition, physical activity and adipose gene expression in cats. *J Anim Sci* 2009;87:594–602.
32. Hoenig M, Ferguson D. Effects of neutering on hormonal concentrations and energy requirements in male and female cats. *Am J Vet Res* 2002;63:634–639.
33. Kienzle E, Edtstadtler-Pietsch G, Rudnick R. Retrospective study of the energy requirements of adult colony cats. *J Nutr* 2006;136:1973S–1975S.
34. Bermingham EN, Thomas DG, Morris PJ, et al. Energy requirements of adult cats. *Br J Nutr* 2010;103:1083–1093.
35. Newsholme P. Why is L-glutamine metabolism important to cells of the immune system in health, postinjury, surgery, or infection? *J Nutr* 2001;131:2515S–2522S.
36. David RT. Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia. *Clin Nutr* 2007;26:389–399.
37. Metayer S, Seiliez I, Collin A, et al. Mechanisms through which sulfur amino acids control protein metabolism and oxidative status. *J Nutr Biochem* 2008;19:207–215.
38. Jobgen WS, Fried SK, Fu WJ, et al. Regulatory role for the arginine-nitric oxide pathway in metabolism of energy substrates. *J Nutr Biochem* 2006;17:571–588.
39. 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.
40. Pion PD, Kittleson MD, Rogers QR, et al. Myocardial failure in cats associated with low plasma taurine: a reversible cardiomyopathy. *Science* 1987;237:764–767.
41. Hoenig M, Thomaseth K, Waldron M, et al. Insulin sensitivity, fat distribution, and adipocytokine response to different diets in lean and obese cats before and after weight loss. *Am J Physiol Regul Integr Comp Physiol* 2007;292:R227–R234.
42. Nguyen P, Damon H, Martin L, et al. Weight loss does not influence energy expenditure or leucine metabolism in obese cats. *J Nutr* 2002;132:1649S–1651S.
43. Laflamme DP, Hannah SS. Increased dietary protein promotes fat loss and reduces loss of lean body mass during weight loss in cats. *Int J Appl Res Vet Med* 2005;3:62–68.
44. German AJ, Holden S, Bissot T, et al. Changes in body composi-

tion during weight loss in obese client owned cats: loss of lean tissue mass correlates with overall percentage of weight lost. *J Feline Med Surg* 2008;10:452–458.
45. Fujita S, Volpi E. Amino acids and muscle loss with aging. *J Nutr* 2006;136:277S–280S.
46. Muscaritoli M, Anker SD, Argiles J, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia, in a document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics." *Clin Nutr* 2010;29:154–159.
47. Fahey GC, Barry KA, Swanson KS. Age-related changes in nutrient utilization by companion animals. *Ann Rev Nutr* 2008;28: 425–445.
48. Harper EJ. Changing perspective on aging and energy requirements: aging and digestive function in humans, dogs and cats. *J Nutr* 1998;128:2632S–2635S.
49. Taylor EJ, Adams C, Neville R. Some nutritional aspects of aging in cats and dogs. *Proc Nutr Soc* 1995;54:645–656.
50. Hoenig M, Thomaseth K, Waldron M, et al. Fatty acid turnover, substrate oxidation, and heat production in lean and obese cats during the euglycemic hyperinsulinemic clamp. *Domest Anim Endocrinol* 2007;32:329–338.
51. German AJ. The growing problem of obesity in dogs and cats. *J Nutr* 2006;136:1940S–1946S.
52. Huang TT, Drewnosksi A, Kumanyrka S, et al. A systems oriented multilevel framework for addressing obesity in the 21st century. *Prev Chronic Dis* 2009;6:1–10.
53. Gluckman PD, Hanson MA. Developmental and epigenetic pathways to obesity: an evolutionary-developmental perspective. *Int J Obes* 2008;32:S62–S71.
54. Nguyen PG, Dumon HJ, Siliart BS, et al. Effects of dietary fat and energy on body weight and composition after gonadectomy in cats. *Am J Vet Res* 2004;65:1708–1713.
55. Backus RC, Cave NJ, Keisler DH. Gonadectomy and high dietary fat but not high dietary carbohydrate induce gains in body weight and fat of domestic cats. *Br J Nutr* 2007;98:641–650.
56. Zimmer P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001;414:782–787.
57. Levin BE. Synergy of nature and nurture in the development of childhood obesity. *Int J Obes* 2009;33:S53–S56.
58. Haemer MA, Huang TT, Daniels SR. The effect of neurohormonal factors, epigenetic factors, and gut microbiota on risk of obesity. *Prev Chronic Dis* 2009;6:11–19.
59. Johnson SR, Patterson-Kane EG, Niel I. Foraging enrichment for laboratory rats. *Anim Welfare* 2004;13:305–312.
60. Nithianantharajah J, Hannan AJ. Enriched environments, experience dependent plasticity and disorders of the nervous system. *Nat Rev Neurosci* 2006;7:697–709.
61. Rochlitz I. A review of the housing requirements of domestic cats (*Felis silvestris catus)* kept in the home. *Appli Anim Behav Sci* 2005;93:97–109.
62. Griffin B. Prolific cats: the impact of their fertility on the welfare of the species. *Compend Contin Educ Pract Vet* 2001;23:1058–1069.
63. Martin LJ, Siliart B, Lutz TA, et al. Postprandial response of plasma insulin, amylin, and acylated ghrelin to various test meals in lean and obese cats. *Br J Nutr* 2010;103:1610–1619.
64. Bissot T, Servet F, Vidal S, et al. Novel dietary strategies can improve the outcome of weight loss programmes in obese client owned cats. *J Feline Med Surg* 2010;12:104–112.
65. Buffington CA. Management of obesity—the clinical nutritionist's experience. *Int J Obes Relat Metab* 1994;18(suppl 1):S29–S35.
66. Adolph EF. Tolerance to heat and dehydration in several species of mammals. *Am J Physiol* 1947;151:564–575.
67. Johnson WE, Eizirik E, Pecon-Slattery J, et al. The late Miocene radiation of modern felidae: a genetic assessment. *Science* 2006;311:73–77.
68. Driscoll CA, Macdonald DW, O'Brien SJ. From wild animals to domestic pets, an evolutionary view of domestication. *Proc Natl Acad Sci U S A* 2009;106(suppl 1):9971–9978.
69. Driscoll CA, Clutton-Brock J, Kitchener AC, et al. The taming of the cat. Genetic and archaeological findings hint that wildcats became housecats earlier—and in a different place—than previously thought. *Sci Am* 2009;300:68–75.
70. O'Brien SJ, Johnson WE. The evolution of cats. Genomic paw prints in the DNA of the world's wild cats have clarified the cat family tree and uncovered several remarkable migrations in their past. *Sci Am* 2007;297:68–75.
71. Driscoll CA, Menotti-Raymond M, Roca AL, et al. The near Eastern origin of cat domestication. *Science* 2007;317:519–523.
72. Anderson RS. Water balance in the dog and cat. *J Small Anim Pract* 1982;23:588–598.
73. Beuchat CA. Structure and concentrating ability of the mammalian kidney: correlations with habitat. *Am J Physiol* 1996;271:R157–R179.
74. Seefeldt SL, Chapman TE. Body water content and turnover in cats fed dry and canned rations. *Am J Vet Res* 1979;40:183–185.
75. Kohn CW, DiBartola SP. Composition and distribution of body fluids in dogs and cats. In: DiBartola SP, ed. *Fluid therapy in small animal practice*. Philadelphia: WB Saunders Co, 1992;1–34.
76. O'Connor WJ, Potts DJ. The external water exchanges of normal laboratory dogs. *Q J Exp Physiol Cogn Med Sci* 1969;54:244–265.
77. Ziegler EE, Fomon SJ. Potential renal soluted load of infant formulas. *J Nutr* 1989;119:1785–1788.
78. Funaba M, Hashimoto M, Yamanaka C, et al. Effects of a high-protein diet on mineral metabolism and struvite activity product in clinically normal cats. *Am J Vet Res* 1996;57:1726–1732.
79. Hawthorne AJ, Markwell PJ. Dietary sodium promotes increased water intake and urine volume in cats. *J Nutr* 2004;134:2128S–2129S.
80. Funaba M, Yamate T, Hashida Y, et al. Effects of a high-protein diet versus dietary supplementation with ammonium chloride on struvite crystal formation in urine of clinically normal cats. *Am J Vet Res* 2003;64:1059–1064.
81. 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.
82. Gaskell CJ. Nutrition and diseases of the urinary tract in dogs and cats. *Vet Annu* 1985;25:383–390.
83. Cottam YH, Caley P, Wamberg S, et al. Feline reference values for urine composition. *J Nutr* 2002;132:1754S–1756S.
84. Buffington CA, Chew DJ. Intermittent alkaline urine in a cat fed an acidifying diet. *J Am Vet Med Assoc* 1996;209:103–104.
85. Kienzle E, Wilms-Eilers S. Struvite diet in cats: effect of ammonium chloride and carbonates on acid base balance of cats. *J Nutr* 1994;124:2652S–2659S.
86. Ching SV, Fettman MJ, Hafner DW, et al. The effect of chronic dietary acidification using ammonium chloride on acid base and mineral metabolism in the adult cat. *J Nutr* 1989;119:902–915.
87. Laflamme DP, Long G. Evaluation of two diets in the nutritional management of cats with naturally occurring chronic diarrhea. *Vet Ther* 2004;5:43–51.
88. Guilford WG, Jones BR, Markwell PJ, et al. Food sensitivity in cats with chronic idiopathic gastrointestinal problems. *J Vet Intern Med* 2001;15:7–13.
89. Lubbs DC, Vester BM, et al. Dietary protein concentration affects intestinal microbiota of adult cats: a study using DGGE and qPCR to evaluate differences in microbial populations in the feline gastrointestinal tract. *J Anim Phys Anim Nutr* 2009;93:113–121.
90. Janeczko S, Atwater D, Bogel E, et al. The relationship of mucosal bacteria to duodenal histopathology, cytokine mRNA, and clinical disease activity in cats with inflammatory bowel disease. *Vet Microbiol* 2008;128:178–193.
91. Inness VL, McCartney AL, Khoo C, et al. Molecular charcterisation of the gut microflora of healthy and inflammatory bowel disease cats using fluorescence in situ hybridization with special reference to *Desulfovibrio* spp. *J Anim Phys Anim Nutr* 2007;91:48–53.
92. Ugarte C, Guilford WG, Markwell P, et al. Carbohydrate malabsorption is a feature of feline inflammatory bowel disease but does not increase clinical gastrointestinal signs. *J Nutr* 2004;134:2068S–2071S.
93. Backus RC, Puryear LM, Crouse BA, et al. Breath hydrogen concentrations of cats given commercial canned and extruded diets indicate gastrointestinal microbial activity vary with diet type. *J Nutr* 2002;132:1763S–1766S.
94. Cave NJ, Marks SL. Evaluation of the immunogenicity of dietary proteins in cats and the influence of the canning process. *Am J Vet Res* 2004;65:1427–1433.

95. Laflamme DP, Xu H, Long GM, et al. Effect of diets differing in fat content on chronic diarrhea in cats. *J Vet Intern Med* 2011;25:230–235.
96. Buffington CAT, Westropp JL, Chew DJ, et al. A case-control study of indoor-housed cats with lower urinary tract signs. *J Am Vet Med Assoc* 2006;228:722–725.
97. Stella JL, Lord LK, Buffington CAT. Sickness behaviors in response to unusual external events in healthy cats and cats with feline interstitial cystitis. *J Am Vet Med Assoc* 2011;238:67–73.
98. Buffington CAT, Westropp JL, Chew DJ, et al. Clinical evaluation of multimodal environmental modification in the management of cats with lower urinary tract signs. *J Feline Med Surg* 2006;8:261–268.
99. Bradesi S, McRoberts JA, Anton PA, et al. Inflammatory bowel disease and irritable bowel syndrome: separate or unified? *Curr Opin Gastroent* 2003;19:336–342.
100. Grover M, Herfarth H, Drossman DA. The functional-organic dichotomy: postinfectious irritable bowel syndrome and inflammatory bowel disease-irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2009;7:48–53.
101. Rajendran N, Kumar D. Role of diet in the management of inflammatory bowel disease. *World J Gastroenterol* 2010;16:1442–1448.
102. Graff LA, Walker JR, Clara I, et al. Stress coping, distress, and health perceptions in inflammatory bowel disease and community controls. *Am J Gastroenterol* 2009;104:2959–2969.
103. Rand JS, Fleeman LM, Farrow LM, et al. Canine and feline diabetes mellitus: nature or nurture? *J Nutr* 2004;134:2072S–2080S.
104. Hall TD, Mahony O, Rozanski E, et al. Effect of diet on glucose control in cats with diabetes mellitus treated with twice daily insulin glargine. *J Feline Med Surg* 2009;11:125–130.
105. Kirk CA. Feline diabetes mellitus: low carbohydrates versus high fiber. *Vet Clin North Am Small Anim Pract* 2006;36:1297–1306.
106. Mazzaferro EM, Greco DS, Tuner AS, et al. Treatment of feline diabetes mellitus using an alpha-glucosidase inhibitor and a low-carbohydrate diet. *J Feline Med Surg* 2003;5:183–189.
107. Bennett N, Greco DS, Peterson ME, et al. Comparison of a low carbohydrate, low fiber diet and a moderate carbohydrate, high fiber diet in the management of feline diabetes mellitus. *J Feline Med Surg* 2006;8:73–84.
108. Boari A, Aste G, Rocconi F, et al. Glargine insulin and high protein, low carbohydrate diet in cats with diabetes mellitus. *Vet Res Commun* 2008;32(suppl 1):S243–S245.
109. Marshall RD, Rand JS, Morton JS. Treatment of newly diagnosed diabetic cats with glargine insulin improves glycaemic control and results in higher probability of remission than protamine zinc and lente insulins. *J Feline Med Surg* 2009;11:683–691.
110. Mori A, Sako T, Lee P, et al. Comparison of three commercially available prescription diet regimens on short-term post-prandial serum glucose and insulin concentrations in healthy cats. *Vet Res Commun* 2009;33:669–680.
111. Verbrugghe A, Hesta M, Van Weyenberg S, et al. The glucose and insulin response to isoenergetic reduction of dietary energy sources in a true carnivore: the domestic cat (*Felis catus*). *Br J Nutr* 2010;103:1–8.
112. Buffington CAT. Dry foods and risk of disease in cats. *Can Vet J* 2008;49:561–563.
113. Cannon WB. *Bodily changes in pain, hunger, fear, and rage*. New York: Appleton-Century, 1929.
114. Forlani G, Lorusso C, Moscatiello S, et al. Are behavioural approaches feasible and effective in the treatment of type 2 diabetes? A propensity score analysis vs. prescriptive diet. *Nutr Metab Cardiovasc Dis* 2009;19:313–320.
115. Kane E. Feeding behavior of the cat. In: Burger IH, Rivers JPW, eds. *Waltham symposium: nutrition of the dog and cat*. 7th ed. Cambridge, England: Cambridge University Press, 1989;147–158.
116. Bradshaw JW, Goodwin D, Legrand-Defretin V, et al. Food selection by the domestic cat, an obligate carnivore. *Comp Biochem Physiol A Physiol* 1996;114:205–209.
117. Horowitz DF, Mills DS, Heath S. *BSAVA manual of canine and feline behavioral medicine*. Quedgeley, Gloucester, England: British Small Animal Veterinary Association, 2002.
118. Wyrwicka W, Long AM. Observations on the initiation of eating of new food by weanling kittens. *J Biol Sci* 1980;15:115–120.
119. Yeates JW, Main DCJ. Assessment of positive welfare: a review. *Vet J* 2008;175:293–300.
120. Lund EM, Armstrong PJ, Kirk CA, et al. Prevalence and risk factors for obesity in adult cats from private US veterinary practices. *Int J Appl Res Vet Med* 2005;3:88–96.
121. Gluckman PD, Hanson MA. Living with the past: evolution, development, and patterns of disease. *Science* 2004;305:1733–1734.
122. Feinberg AP. Epigenetics at the epicenter of modern medicine. *J Am Med Assoc* 2008;299:1345–1351.
123. Gluckman PD, Hanson MA, Cooper C, et al. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med* 2008;359:61–68.
124. Westropp JL, Kass PH, Buffington CAT. Evaluation of the effects of stress in cats with idiopathic cystitis. *Am J Vet Res* 2006;67:731–735.
125. Buffington CAT, Westropp JL, Chew DJ, et al. Clinical evaluation of multimodal environmental modification in the management of cats with lower urinary tract signs. *J Feline Med Surg* 2006;8:261–269.