Age-Related Changes in Nutrient Utilization by Companion Animals

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Abstract

As companion animals age and pass through various life stages from in utero to the geriatric state, nutrient requirements change along with the manner in which nutrients are utilized by the various organ systems in the body. From the regulatory perspective, recognized life stages include maintenance, growth, and gestation/lactation. Other important life stages include in utero, the neonate, and the senior/geriatric state. Age affects digestive physiological properties, too, and factors such as gut microbiota, digestive hormones, gut morphology, gut immunity, and nutrient digestibility are modified as the animal becomes older. Each of the nutrients is affected in some manner by age, some more than others. Genomic biology offers promise in helping elucidate in greater detail how nutrient utilization is affected by age of the dog and cat.

Contents

INTRODUCTION

Aging is defined as the progressive changes that occur after maturity in various organs, leading to a decrease in their functional ability (3). The aging process is affected by alterations in physiological systems and metabolic processes. Unfortunately, these alterations are not well defined in pet animals (35).

The average life span of companion animals is increasing, mainly because of more effective control of infectious diseases, targeted nutritional intervention programs, and good feeding practices (18). Cats appear to age uniformly, whereas longevity in dogs is correlated negatively with body size. The mean age at death of most common breeds of dogs in the veterinary medical database from 1980–1990 was examined, and it was found that mean age at death differed among dog breeds, with larger dogs dying sooner than smaller dogs (82). Interestingly, the highest median age at death was 9.3 years for the miniature poodle whereas the lowest median age at death was 3.5 years for the Rottweiler. Today, greater than 50% of the dogs in the United States are 6 years of age or older, with a sizable percentage over 10 years of age. Therefore, in feeding companion animals, nutritional goals are to slow or prevent the progression of metabolic changes associated with aging, minimize clinical signs of aging, enhance quality of life of the dog and cat, and, if possible, increase their life expectancy (18). To accomplish these goals, it is important to understand age-related changes in nutrient utilization. This involves consideration of nutrition throughout the various life stages of the dog and cat.

Select designations are needed to describe the life stages that a pet animal may experience. Such designations could include in utero, neonatal, growth, maintenance, gestation/lactation, and finally, senior/geriatric status. The Association of American Feed Control Officials (AAFCO) (4), the agency responsible for writing the laws regulating the production, labeling, distribution, and sale of animal feeds and pet foods, has defined minimum feeding protocols for nutritional adequacy claims for dog and cat foods for the life stages of maintenance, growth, and gestation/lactation. Other life-stage identification systems have been proposed, such as that of Gunn-Moore (29), who identified four life stages for cats based on physical and metabolic changes occurring with age: kitten (birth to 1 year), adult (1–7 years), mature (7–11 years), and geriatric (>11 years).

In this review, three major issues of age-related changes in nutrient utilization are considered. First, digestive physiology outcomes affected by age, including gastrointestinal microbiota effects, effects on digestive hormones, gut morphology characteristics, gut immunity characteristics, and effects on nutrient digestibility, are discussed. Second, evidence regarding each nutrient is presented and evaluated. Finally, a brief review of how the science of genomic biology may enhance our understanding of aging and its effect on nutrient utilization is presented.

DIGESTIVE PHYSIOLOGY OUTCOMES AFFECTED BY AGE

The Gut Microbiota

The microbial population of dogs and cats follows a pattern of colonization similar to that of other animals. At birth, the intestines are sterile but rapidly colonized by environmental bacteria and, by old age, bacterial populations have undergone a number of changes based on diet and microbial species introduction to the gastrointestinal tract (14). Until recently, researchers have been unable to characterize the true nature of intestinal biodiversity owing to the inability to colonize microbiota on an agar plate (95). Advances in molecular techniques such as fluorescent in situ hybridization and 16S ribosomal RNA sequencing and detection have allowed a more detailed view into the intestinal microbiome and, in some instances, an estimate of the quantity of the species that once were characterized only as enteric.

Compared with adult dogs, 1-day-old puppies had higher bacterial counts in stomach contents [~7.5 compared with ~7 log colony forming units (cfu) bacteria/g stomach contents], luminal (~8.75 compared with ~8 log cfu bacteria/g digesta) and mucosal regions of the mid-region of the small intestine (~8.75 compared with ~7 log cfu bacteria/g digesta), and luminal region of the proximal colon (~10 compared with ~9.5 log cfu bacteria/g colonic digesta). The luminal region of the distal colon (~10 log cfu bacteria/g colonic digesta) remained relatively similar between puppies and adult dogs (10). In one study (51), total anaerobic bacteria in senior Beagles (11 years old) increased 41% when compared with 1-year-old Beagles; however, in another study (5), total anaerobic bacteria in senior Beagles (~13 years old; 10.3 log cfu/g colonic contents) remained similar to that of young Beagles (~11 months old; 10.8 log cfu/g colonic contents).

Many genera of bacteria reside in the gastrointestinal tract of companion animals. Typically, *Bacteroides* spp., *Clostridium* spp., *Bifidobacterium* spp., *Lactobacillus* spp., and *Streptococcus* spp. have been reported to reside in canine and feline intestines. Of these, bifidobacteria appear to be difficult to culture, as some studies report a lack of the genus in the feces (10). *Clostridium* spp. were present in the distal colon of 1-day-old puppies at ~6.5 log cfu/g, but this concentration decreased to ~5 log cfu/g at an adult age (10). In senior dogs, *Clostridium* spp. increased 344% compared with young adult dogs (51). *Lactobacillus* spp. were cultured from the distal colon of 1-day-old puppies at ~5 log cfu/g, increasing to ~6 log cfu/g in adult dogs (10). *Lactobacillus* spp. also increased in senior dogs (118% compared with young adult dogs), although not as drastically as *Clostridium* spp. (51). One-day-old puppies also had *Bacteroides* spp. in their distal colon at ~6 log cfu/g, which increased to ~8.5 log cfu/g at day 21 and remained relatively constant through puppyhood to an adult age (10). *Bacteroides* spp. increased 31% in senior dogs as compared with young adult dogs (51); this effect was contradicted in another study in which *Bacteroides* spp. decreased in old (~11 years) dogs (9.88 log cfu/g feces) when compared with younger (2.5 years) dogs (10.23 log cfu/g feces) (101). *Bifidobacteria* spp. decreased with age in Beagles, from 9.5 log cfu/g colonic contents in young dogs (~11 months) to 8.4 log cfu/g colonic contents in senior dogs (~13 years) (5). *Eubacteria* spp. also decreased with age in Beagles, from 10.0 log cfu/g colonic contents in young dogs to 9.4 log cfu/g colonic contents in senior dogs (5). Enteric bacteria were found in the highest concentration in the distal colon of 1-day-old puppies (~9 log cfu/g), decreasing (7 log cfu/g) in adult dogs (10).

The early bacterial environment in the kitten was dominated by aerotolerant microbiota (14). Newborn kittens harbored ~9% of total anaerobes as *Bifidobacterium* spp. in their intestinal microbiota, a value that decreased to ~2.5% of total anaerobes as an adult cat and, in some studies, could not be enumerated (14, 113). Newborn kittens also harbored *Clostridium* spp. at ~0.25% of total anaerobes (14), similar to that of adult cats (9.1 log cfu/g feces) (113). *Bacteroides* spp. were found as

~1% of total anaerobes in the newborn kitten, increased to ~12% of total anaerobes at 6 months of age, and finally stabilized at ~6% of total anaerobes as an adult cat (10.4 log cfu/g feces) (14, 113). Adult cats also can harbor *Corynebacteria* spp. (7.5 log cfu/g feces), *Enterobacteria* spp. (8.5 log cfu/g feces), *Lactobacillus* spp. (8.5 log cfu/g feces), *Streptococcus* spp. (8.8 log cfu/g feces), *Clostridium* spp. (9.1 log cfu/g feces), and *Eubacterium* spp. (9.2 log cfu/g feces) (113). Inness et al. (42) observed that healthy cats harbored *Bifidobacterium* spp. (9.34 log cells/g feces) with a slightly lower count of *Bacteroides* spp. (9.07 log cells/g feces), whereas cats with inflammatory bowel disease harbored lower *Bifidobacterium* spp. (7.56 log cells/g feces). Both healthy cats and cats with inflammatory bowel disease in the study of Inness et al. (42) had *Desulfovibrio* spp. in their feces (7.26 and 7.84 log cells/g feces, respectively).

Digestive Hormones

The 2006 National Research Council (NRC) publication (78) lists the digestive hormones relevant to dogs and cats. To our knowledge, no research has been conducted on these hormones with respect to age-related responses in these two species.

Gut Morphology

In comparison with omnivores and herbivores, the dog and cat small intestine was shorter but thicker (9, 70). Cats maintained a greater intestinal length and absorptive surface area during intestinal development when compared with dogs (70). Intestinal absorption of colostral protein resulted in an increase in villus size owing to functional protein insertion in the brush border membrane of dogs, but this change was not observed in cats, as they may have limited protein absorption at the same age (70).

Intestinal weight and length, as well as mucosal weight, increased with age in dogs. The intestinal tract of Beagles grew 7 cm in the first day of life (80.1 cm on day 0 to 87.7 cm on day 1), more than doubled in length by day 42 (199.9 cm), and reached an adult length of 283.1 cm (83). Intestinal weight, in comparison, increased only 3 g in the first day of life (11.0 g on day 0 to 14.1 g on day 1); the intestine weighed 10 times as much on day 42 (110.9 g), and weighed 263.4 g at an adult age (83).

In dogs, villus length decreased at 42 days of life (~874 μm in the jejunum and 737 in the ileum at day 0; ~810 μm in the jejunum and 531 μm in the ileum at day 42) and continued to decrease until an adult (breeding) age was reached (~700 μm in the jejunum and 490 μm in the ileum) (83). Crypt depth was fairly shallow initially (~150 μm in the jejunum and ileum), but increased from day 21 (~350 μm in the jejunum and 292 μm in the ileum) to adulthood (~1100 μm in the jejunum and 611 μm in the ileum) (83).

Kuzmuk et al. (58) observed morphological differences in young (1.2 years) and old (12.1 years) dogs fed either a plant- or animal-product-based diet. Jejunal villus height was significantly increased in young dogs consuming the plant-product-based diet (825 μm) compared with both young dogs consuming an animal-product-based diet (639 μm) and old dogs consuming either a plant- or animal-product-based diet (649 and 626 μm, respectively). Ileal villus height increased in dogs consuming a plant-product-based diet in both young and old dogs (590 and 579 μm, respectively) compared with the animal-product-based diet (457 and 507 μm, respectively). Colonic crypt depth also was greater in old dogs (493 and 459 μm) as compared with young dogs (331 and 310 μm) in that study.

In the cat, intestinal development was slower than in the dog. Intestinal length increased only 4 cm in the first week of life (50 cm on day 1 to 54 cm at week 1) and did not double until 9 weeks of life (116 cm) (9). On day 1 of life, the cat intestine weighed 7.3 g and gained 1.2 g after 1 week; after 9 weeks, the intestine weighed 44.4 g (9). Intestinal thickness increased in the cat from ~1.2 mm at day 1 to 1.7 mm at day 60 (12). Mucosal thickness, however, decreased from ~0.7 mm at day 1 to ~0.6 mm at day 60 in that experiment. At birth, the cat colon

measured ~7 cm and grew to a length of ~15 cm by 60 days of life (12).

Gut Immunity

Neonatal dogs possess a functional humoral immune system (functional B cells and T cells) at birth, but are less responsive to immunization than are adults (45). On the first day after birth, the proportion of T lymphocytes (especially CD8+) was lower and the proportion of B lymphocytes (CD21+) was higher than for adults (115). In that study, conducted from birth to 3 months of age, total T cells, CD8+ T cells, and CD4+ T cells increased and B cells decreased, but did not reach concentrations of young adults (1–2 years old). Felsburg (22) and Somberg et al. (102) reported similar findings in B and T cells among neonatal and adult dogs. These researchers measured lymphocytes until 12 months of age and reported that the CD4:CD8 ratio was elevated at 6 months of age, but reached the adult ratio (1.5–2.0) after 10–12 months of age. Toman et al. (115) also reported that lymphocytes were able to respond to nonspecific mitogen stimulation, demonstrating the functionality of immune cells in newborn pups, which was in agreement with data of Jacoby et al. (45).

In contrast to humans that receive maternal antibodies through placental transfer in utero, newborn puppies and kittens are essentially devoid of maternal antibody at birth (22). Because dogs and cats have endotheliochorial placentas, which allow for a small transfer of maternal immunoglobulin (Ig)G, only 5%–10% of maternal antibody is obtained in utero (22). Colostrum is a major source of immunoregulatory agents for most neonatal animals, passively transferred from mother to neonate to initiate the animal's immune system via localized intestinal protection (31, 65, 98), and is crucial in dogs and cats. It is the primary source of antibodies and must be administered to the neonate within the first 24 hours of birth because the neonate cannot absorb them after this time (98).

Colostrum and the milk that follows contain Ig important for gut immunity. For example, canine colostrum samples have been reported to contain IgG, IgA, and IgM in concentrations of 6.7, 3.1, and 2.2 mg/ml (26, 96). Although canine and feline colostrum and milk contain IgG, IgA, and IgM, the proportion of Ig in milk is dependent on species. Whereas canine milk contains much higher IgA concentrations than IgG or IgM, IgG is the predominant Ig in feline milk (114). Passive transfer of Ig is approximately 8–16 weeks in dogs and cats (94).

In newborn puppies that receive colostrum, serum IgG concentrations were similar to those of adults (22). Circulatory IgG concentrations decreased in growing puppies as maternal IgG decreased in milk, but gradually increased owing to their own Ig production. Circulating concentrations of IgM and IgA were much lower in neonates than in adults, but increased with age. Adult concentrations of IgM and IgG were reached by 2–3 months and 6–9 months, respectively. Synthesis of IgA is slower than for other isotypes and does not reach adult levels until ~1 year of age. IgA plays an important role in protecting the animal from viral and bacterial pathogens in the gut to which its mother has been exposed, and is present in milk (65).

Newborn kittens studied by Hanel et al. (31) did not express IgG in their plasma prior to colostrum consumption. Casel et al. (19) and Yamada et al. (122) also reported negligible (<20 mg/ml) circulating IgG concentrations in presuckled kittens. Within two days of receiving colostrum, however, kittens expressed 4092 mg IgG/dl plasma (31). Kittens expressed 0 mg IgG/dl plasma when deprived of colostrum and 1768 mg IgG/dl plasma when deprived of colostrum but supplemented with feline IgG. All three groups of kittens expressed similar concentrations of plasma IgG by day 56 of life.

Cat and dog milk also contains lysozyme, which destroys Gram-positive bacterial cell walls. Lysozyme functions in conjunction with lactoferrin to eliminate Gram-negative bacteria as well. Lactoperoxidase, another milk enzyme, also affects microbial populations in the gastrointestinal tract by using hydrogen peroxide to destroy both Gram-positive and Gram-negative bacteria (65).

At birth, the gut is a sterile environment but is quickly inoculated by the mother and surrounding environment. Puppies and kittens begin harboring microflora in their intestinal tract within the first day of life (10, 14). This challenge to the immune system occurs simultaneously with the intake of colostrum and is important in the development of the gut-associated lymphoid tissues, including Peyer's patches. Peyer's patches are located in the submucosa of the small intestine, over which M-cells are located. M-cells take in antigens and entire microorganisms from the lumen and may trigger a response to previously sampled antigens. Dogs possess functionally mature Peyer's patches at the time of birth and possess intraepithelial lymphocytes with a phenotype similar to that of adult dogs (41).

Although some contradiction is present in the literature, immune function appears to decrease as dogs and cats enter a geriatric life stage. When measuring phagocytically induced respiratory bursts of canine neutrophils, Johnson et al. (47) reported no differences among young adult dogs (mean age 11 months) and old dogs (mean age 11 years). However, old dogs responded more slowly to a dose of bacteriophage than did young Beagles, and older dogs were more variable in their immune response to the phage compared with younger dogs (72). Strasser et al. (105) reported conflicting results, with a lower lymphocyte proliferative response but increased functional activity of the complement system in old (8–13 years) versus young (2–4 years) dogs. Finally, Kearns et al. (52) reported a reduction in several immune indices in geriatric versus young adult dogs, including a decreased ability to respond to sheep red blood cell titers and ability to respond to different mitogens.

Nutrient Digestibility

Puppies and kittens have nutrient transporters present at birth. Nutrient uptakes expressed per milligram of intestinal tissue and uptake capacities normalized to metabolic body weight were maximal at birth (11, 12). Absorptive capacity is complemented by an increased enzyme function, allowing the animal to increase digestibility and utilization of ingested foods. Increased digestion is beneficial during energy-demanding life stages such as growth, gestation, and lactation. However, it also can lead to obesity when the animal is allowed to consume more energy than it expends. In addition, after an animal reaches a senior or geriatric state, nutrient digestibility may decrease, which can lead to loss of lean body mass, and potentially, malnutrition.

Puppies and kittens have lower protein digestibilities than do adult dogs and cats because of lower pepsin secretion in the stomach. Pepsin activity was not detected in 1-day-old puppies, and puppies up to 63 days of age secreted significantly lower pepsin (126 to 475 U/g gastric contents, day 21 and day 63, respectively) than did adult dogs (2208 U/g gastric contents) (13). This phenomenon was attributed to low acid production; however, the gastric pH of puppies at day 1 (3.0) was similar to that of older puppies (pH 3.9 at day 63) or adults (pH 2.5) (13). In puppies, pancreatic trypsin activity was highest at day 21 (~80,000 U/g pancreatic tissue) and lowest at day 63 (~19,500 U/g pancreatic tissue) (13). Adult dogs had a pepsin activity measured at ~40,000 U/g (13). Pancreatic chymotrypsin activity increased from day 1 (~50 U/g pancreatic tissue) to day 21 (~200 U/g pancreatic tissue), stabilized, then increased again (~525 U/g pancreatic tissue) in adult dogs (13). As evidenced by these data, young animals require high-quality, highly digestible protein.

Data reporting apparent digestibility values as related to life stage are limited. Dry matter digestibility increased with breed size (11 weeks: 78.2% for miniature poodles and 84% for Great Danes) and age (60 weeks: 82% for miniature poodles and 85.4% for Great Danes) (120). Crude protein digestibility increased with age in all groups (74.5%–81.5% for miniature poodles; 80.8%–84.8% for Great Danes) (120). Fat digestibility followed the same pattern as dry matter digestibility with respect to size (11 weeks: 89.6% for miniature poodles and 94.2% for Great Danes) and age (60 weeks:

94.4% for miniature poodles and 95.8% for Great Danes). However, medium schnauzers had a lower fat digestibility than did miniature poodles at 11 weeks (88.7%) and a higher fat digestibility than that of Great Danes at 60 weeks (96.2%) (120).

Sheffy et al. (99) evaluated 10- to 12-year-old Beagles and 1-year-old Beagles and observed that digestibilities of ash, protein, fat, and energy were higher for the older animals than the younger animals, regardless of diet fed. Buffington et al. (15) evaluated Beagles aged 2–3, 8–10, or 16–17 years and observed that dry matter, nitrogen, and fat digestibilities were statistically similar among age groups. Similarly, Swanson et al. (110) reported no differences in dry matter, organic matter, protein, or fat digestibilities in young adult (1-year-old) compared with geriatric (11- to 12-year-old) Beagles. Interestingly, growing dogs (5 months old) had lower dry matter, organic matter, and fat digestibilities as compared with geriatric dogs in that study.

Harper & Turner (34) observed statistically significant increases in dry matter (82% to 84%), organic matter (84% to 88%), carbohydrate (85% to 88%), protein (83% to 85%), fat (86% to 92%), and energy (83% to 87%) digestibilities in kittens fed both wet and dry diets as they aged from 9 to 32 weeks. As kittens aged to 19–21 weeks, digestibility reached a maximum point for all nutrients except fat, where digestibility peaked at 24–26 weeks. Dry matter (87% compared with 85%), organic matter (85% compared with 82%), and protein (86% compared with 83%) were more digestible in dry diets than in wet diets, respectively, by all age groups of kittens.

Several studies have been conducted in older animals to determine nutrient digestibility. Generally, no change in nutrient digestion by dogs was observed, but in cats, digestion decreased (16). Fat digestion, as discussed in greater detail below, decreased most notably in older cats. Research points to "decreased quantities of pancreatic enzymes or decreased secretion of bile acids" owing to lower intakes and decreased taurine intake (16).

AGE-RELATED CHANGES IN NUTRIENT UTILIZATION

Water

Gregersen (28) was one of the first to study the regulation of water intake in dogs, a topic that has been examined periodically throughout the twentieth century. Numerous factors are known to alter water intake in most species, including exercise, environmental conditions (e.g., heat), food intake, and age. Greater water requirements are likely for dogs during growth and gestation/lactation, but proof is lacking (78).

Age is known to alter the physiological control systems associated with thirst and satiety in humans. Although geriatric humans may consume adequate fluids on a daily basis in controlled environments, decreased thirst sensation and reduced fluid intake often were noted when geriatric humans were challenged by fluid deprivation, a hyperosmotic stimulus, or exercise in a warm environment (reviewed by 53). Similar responses would be expected in dogs and cats.

Energy

Because energy is the primary factor determining food intake, it affects the consumption of all other nutrients in the diet. Thus, nutrient recommendations (4) and diet formulations for dogs and cats must be adjusted for energy density. Because individual food intake may be vastly different according to breed, physiologic life stage, age, etc., nutrient requirements based on energy intake are usually most appropriate.

A significant amount of research has been done in humans and pets over the past few decades to identify relationships between age and maintenance energy requirements (MER). The MER may be defined as the energy required to support energy equilibrium over a long period and includes factors such as resting energy expenditure, the thermic effect of food, and normal activity. Given the wide range of mature body weights (1 to 100 kg) and morphologic differences among the 400 dog breeds in

existence today, deriving a formula from which to calculate an estimated MER suitable for all dogs is very difficult. Include the variance due to neuter status, gender, breed, activity, and age, and accurately estimating caloric needs based solely on calculations becomes nearly impossible. Therefore, energy needs may be calculated, but used only as a starting point. Body condition score must be monitored over time in order to adjust energy needs for each animal. Feline energy requirements also are affected by mature size, which can be quite large in cats (2 to 7 kg), and neuter status, gender, activity, and age. However, the variance among cats is not near as great as is found in dogs.

In today's pets, excess energy consumption that leads to obesity is the greatest issue pertaining to energy metabolism. Recent experiments estimate that approximately 34% of dogs and 35% of cats owned in the United States are considered overweight or obese (67, 68). Obesity in cats and dogs, as in humans, is a major risk factor for several ailments and diseases (e.g., osteoarthritis, diabetes mellitus) and has been demonstrated to shorten life span. Data from a lifetime experiment performed in dogs revealed lower disease incidence, later onset of disease, and increased life span in calorically restricted animals (50). In that study, dogs fed 25% less food than controls lived to an average age of 13.0 years as compared with 11.2 years in controls. Thus, maintaining energy balance and avoiding obesity should be one of the most important goals of pet owners.

Obesity is most prevalent in middle-aged dogs but also may be an issue in aged animals. Similar to humans, most reports suggest that MER of dogs decreases significantly with age. Most reports have estimated a reduction of approximately 20% in old as compared with young adults (23, 57). Changes in body composition, activity level, and metabolic rate often are thought to contribute to this decline. Although contradiction is prevalent in the literature, lower physical activity is likely the major determinant for decreased energy needs. In general, senior dogs have a greater fat mass, lower lean body mass, and lower lean:fat ratio than young adults (33). Because muscle tissue is more metabolically active than adipose, these changes may explain decreased MER in aged animals. However, not all reports agree.

To identify differences in energy metabolism among dogs of different breed/size and age, Speakman et al. (103) measured body composition and resting metabolic rates of three dog breeds (Papillon, mean body weight 3.0 kg; Labrador retriever, mean body weight 29.8 kg; Great Dane, mean body weight 62.8 kg) that varied between 0.6 and 14.3 years of age. In addition to observing great differences among dog breeds, these researchers reported a significant decline in resting metabolism with age in all three breeds. In fact, metabolic rates of the oldest dogs in that study were, on average, only half that of dogs 1–2 years of age. Although decreased lean body mass in old animals is thought to contribute to this phenomena, this was not the case in that study (actually opposite in Papillons), which suggests a more complex causality.

In contrast to dogs, cats do not appear to exhibit a great decline in MER with increasing age. In fact, some reports have shown increased MER in cats >11–12 years old (59). The lack of change with age may have several causes, including a relatively constant physical activity throughout adult life and lack of body composition changes (33). Reduced physical activity is likely the largest factor for decreased MER and lean:fat ratio in elderly dogs. Thus, the lack of change in cats has been hypothesized to be due to the fact that most cats are relatively inactive throughout their adult life; therefore, no obvious changes are observed in advanced age. Because feline MER does not greatly change with age or may actually increase, but digestive efficiency decreases, geriatric cats (>11 years old) are actually more likely to be underweight than obese (3).

Given the widespread prevalence of obesity and its association with metabolic diseases, initiatives aimed at identifying effective weight loss or maintenance strategies are usually given high priority. Many of the problems facing geriatric pets, however, pertain to a decreased ability to consume and/or utilize adequate energy

sources, leading to weight loss and lean tissue wasting. A reduction in energy utilization, an indirect outcome of reduced carbohydrate, protein, or lipid digestibility, has been observed in some aged dogs and cats. Peachey et al. (86) reported significantly lower fat and energy digestibilities and a trend for decreased protein digestibility in senior (11.6 years old) as compared with young adult (3.0 years old) cats. These same cats were used in another study to test whether changes in feeding behavior (number and size of meals per day) contributed to the decreased digestibility noted in senior cats (87). However, daily feeding patterns were similar among senior and young adult cats in that study, suggesting changes in absorptive or metabolic efficiency.

Dysregulation of pathways or systems associated with meal response or energy metabolism also may occur with increasing age. In addition to a diminished ability to smell and taste foods, geriatric animals may have a reduced responsiveness to exogenous or endogenous stimuli, including those associated with food intake or metabolism. In humans, aging has been shown to affect glucose tolerance following a meal (49). Similar responses have been noted in aged dogs. Larson et al. (60) measured glucose tolerance and insulin sensitivity in restricted-fed and control-fed dogs as part of the lifetime experiment cited above. In that study, intravenous glucose tolerance tests were performed annually from 9 to 12 years of age. As expected, restricted-fed dogs had significantly lower peak insulin concentrations and greater insulin sensitivity than control-fed dogs. Although blood glucose peak and change from baseline did not change with age, basal insulin concentrations, insulin peak, and insulin change from baseline all increased significantly with age in that study. In fact, by 12 years of age, insulin sensitivity was not different between restricted-fed and control-fed dogs (60).

The recent discovery of leptin and ghrelin has created a new avenue of research pertaining to appetite and energy metabolism. However, very little focus has been placed on identifying the changes that occur with aging. Hormonal response to ghrelin, an orexigenic peptide produced by the gastric mucosa, was reduced in old (7–12 years old) as compared with young adult (13–17 months old) dogs (6). Although food intake was not an outcome of this experiment, these results suggest a diminished responsiveness to ghrelin, possibly contributing to decreased appetite in many aged pets. Ishioka et al. (44) reported a weak, but significant, correlation between plasma leptin concentration and age ($r = 0.37$). However, these researchers failed to identify a relationship in a follow-up study. Ishioka et al. (43) studied 166 dogs of varying body condition score, age, gender, and breed in veterinary clinics in Japan and noted higher plasma leptin concentrations in obese versus lean dogs, but no differences owing to age, gender, or breed.

Although there is some evidence of reduced nutrient digestibility with age, identifying the factors affecting energy requirements, appetite, and the utilization of energy-yielding nutrients following absorption seems to be the major issue to focus on in future research ventures. Furthermore, if the primary goal of life-stage nutritional management is the progression of the pet to a long and healthy old age, the current literature indicates that energy intake throughout life is perhaps the one factor that above all else is key and may need to be redefined in requirement terms for the modern pet. As a consequence, the ratio of nutrients to energy may need to be recalculated such that marginal undernutrition of energy is achieved without malnutrition of other nutrients (66).

Carbohydrates

There appears to be no change in ability to absorb monosaccharides and sugar alcohols as companion animals age; however, with age, glucose tolerance decreases due to a decreased insulin response (75, 104). Hayek et al. (36) observed that older dogs (9.6 years) consuming either a corn/sorghum diet or a corn/sorghum/rice diet initially absorbed glucose more slowly (peak: 60 min) than young dogs (0.7 years; peak: 30 min) and that glucose

values for older dogs did not return to baseline after 240 min of diet ingestion, whereas young dogs took 180 min postprandial to return to baseline glucose concentrations. The glucose response was greater in older dogs consuming the corn/sorghum/rice diet (115% change from baseline versus 110%) because additional rice in the diet increased the amount of available glucose in the bloodstream. Also, older dogs consuming the corn/sorghum/rice diet had significantly elevated insulin concentrations (850% increase), perhaps indicating that these dogs were not as sensitive to insulin as were dogs fed the corn/sorghum diet (450% increase). These data indicate that low-glycemic ingredients may be most beneficial in diets of senior dogs.

Puppies and kittens maintain high lactase concentrations while nursing, but concentrations decrease as the animal ages (78). In cats, lactase has been shown to decrease from 96 U/g protein as a kitten to 7 U/g protein as an adult (56). Maltose is generally found in dog and cat foods as a result of starch degradation. Maltase activity appears not to change over time in dogs or cats (78). Sucrose can be added to dog and cat diets as a palatant and can be found naturally occurring in ingredients added to the diet. Sucrase activity is similar to that of maltase and does not change with age in either the dog or the cat unless the animal is fed a diet with added soy, lactose, or sucrose, in which case sucrase activity increases (38, 59, and 66 U/g protein, respectively) (54).

Starch is the major carbohydrate found in companion animal diets. Both dogs and cats utilize alpha-amylase to digest starch; dogs have higher alpha-amylase activity than cats (78). Puppies have very low pancreatic amylase activity (7.1 U/g) at 4 weeks of age, but this activity increases dramatically (251.5 U/g) at 8 weeks and continues to increase as the dog reaches its adult amylase concentrations (4665.0 U/g at 2 years) (54). Adult cats have an average pancreatic amylase activity of 74.6 U/g when fed starch-containing diets (55).

Low fermentable dietary fibers are not recommended for inclusion in young animal diets because they dilute energy and result in water retention in the large intestine and stool bulking (78). They are useful in formulating weight-loss diets for adult dogs because they decrease fat absorption and can decrease absorption of other macronutrients as well (17, 76).

Lipids

The amount of fat required by cats does not change with age (78). In contrast, puppies and bitches in lactation/gestation require more fat (21.3 g/1000 kcal metabolizable energy) than do adult dogs at maintenance (10 g/1000 kcal metabolizable energy) (78). Puppies consume approximately 12% to 30% fat (dry matter basis) in bitch milk (61). In cats, long-chain fatty acids predominate in the milk provided to the kittens by the queen, and the fat content of the milk provided ranges from 25% to 40% (dry matter basis) over the course of the suckling period (61). Requirements for total fat and n-3 fatty acids for dogs and cats have been increased in an attempt to prevent deficiencies, provide adequate supplies for metabolic activities, and give the animal a more thrifty appearance in general, as these nutrients have been observed to improve skin and coat appearance (78).

The addition of long-chain n-6 and n-3 fatty acids to diets of the bitch prior to breeding and extending through the weaning stage of the life of the puppy, as well as for senior dogs, has been shown to have beneficial effects, particularly because these fatty acids are conditionally essential during these life stages. Puppies whose mothers had been fed a diet with 12.1 g/kg n-6 and 13.6 g/kg n-3 fatty acids had eight times higher plasma docosahexaenoic acid concentrations in the preweaning period and responded faster to electroretinograph testing than did puppies whose mothers had been fed 17.7 and 2.0 g n-6 and n-3 fatty acids/kg, respectively (40). Geriatric Beagles fed a diet with a 1.4:1 ratio of n-6:n-3 fatty acids had higher n-3 fatty acids (12.9 g/100 g fatty acids) in blood plasma after 36 weeks when compared with geriatric Beagles fed a diet with a 40:1 ratio of n-6:n-3 fatty acids (1.4 g/100 g fatty acids) (30). In

a comparison of differing concentrations of a 1:1 n-6:n-3 fatty acid mixture, eicosapentaenoic acid and docosahexaenoic acid were found to be in the highest concentrations in plasma of dogs consuming diets with 6.3 and 9.8 g fatty acids/kg food, and the highest sum (15.1 g and 18.0 g/100 g fatty acids) of plasma n-3 fatty acids and lowest ratio (2.0 and 1.8) of plasma n-6:n-3 fatty acids (30) were observed.

As dogs enter the geriatric state (age >7 years), their energy expenditure decreases and their lean-to-fat ratio—the lean muscle mass of an animal compared to its fat mass—tends to decrease as well (33). Adding to these problems as regards canine health, fat digestibility may increase as dogs age (32), making them more susceptible to obesity and other health problems. In the literature, however, conflicting information is present about fat digestibility in dogs because some research demonstrated an increased fat digestibility in older dogs (63, 99), whereas other research reported no change (15, 64, 112).

It is well documented that cats require both arachidonic and linoleic acids for growth and reproduction. Female cats require more arachidonic acid during gestation and lactation to prevent the formation of defects in the kittens because cats have limited delta-6 desaturase activity and therefore cannot synthesize enough arachidonate from linoleate to meet requirements, even in a maintenance state (78, 85). Reproducing tomcats also can benefit from linoleic acid in the diet. Diets containing linoleic acid increased testes arachidonic and docosapentaenoic acid concentrations, prevented degeneration of the testes, and increased sperm count when compared with diets without linoleic acid (69, 74).

Although resting energy rates do not decrease in geriatric cats (88), many senior cats begin their senior years obese but lose fat mass as they age (89). This phenomenon may be caused by decreased fat digestibility observed in senior cats (86, 89). Fat digestibility decreases due to both physiological and metabolic changes occurring as part of the natural aging process. Whereas fat content of commercial senior feline diets is decreased due to this change, it should potentially be increased to assist the cat in maintaining a normal body weight.

Proteins

Puppies and kittens require high amounts of protein for optimal growth. Kittens receive 30% to 40% protein (dry matter basis) in queen milk, whereas puppies receive 21.5% to 30% protein (dry matter basis) in bitch milk (61). Protein requirements for kittens after weaning and puppies aged 4 to 14 weeks ranged from a minimum intake of 180 g/kg (dry matter basis) to a recommended intake of 225 g/kg (dry matter basis) (78). As puppies aged to 14 weeks, their protein requirements decreased to a minimum intake of 140 g/kg and continued to decrease to 85 g/kg after weaning (78).

Adequate intakes of dietary protein for dogs at maintenance vary widely. The NRC (78) recommends intake of crude protein for an adult dog at maintenance at 100 g/kg diet. Based on the size of the breed as well as the activity level of the dog, the protein intake required to maintain body function and healthy lean mass may change. Gestating and lactating dogs require double the amount of protein (200 g/kg) as adult dogs at maintenance, only slightly less than that of young puppies (78).

The true dietary protein requirement for the cat has been difficult to establish. Purified diets are rarely used for this purpose because they are not well accepted. The NRC (78) value for recommended allowance of dietary protein intake for an adult cat at maintenance is 200 g crude protein/kg diet. An adult maintenance diet for cats with a crude protein concentration less than 265 g/kg is not available commercially. Cats require 50% more protein during lactation (300 g/kg) and there is a slight increase in protein requirements during gestation (213 g/kg) (78).

Beyond the amino acid requirements of most species, cats require taurine as an essential component of their diet. Taurine deficiencies in the cat result in many problems, the most important of which are feline central

retinal degeneration, which leads to blindness, and dilated cardiomyopathy, which leads to heart failure (37, 38, 90–92). Studies also have shown that queens with low taurine reproduce poorly, but that the observed problems in reproduction occur after ovulation (20, 106–108).

Senior cats often lose significant body weight after 10 years of age, partially due to lower digestibility of nutrients, including protein (89). Twenty percent of senior (age >14 years) cats digest only 77% or less dietary protein (normal range 85%–90%). Both dogs and cats experience muscle wasting in the senior state and, thus, should consume more dietary protein to counterbalance this effect. It has been postulated that the amount of increased dietary protein intake would need to be equal to a biological value of that presented in the original diets formulated by Wannemacher & McCoy (119) and upon whose casein-based diets all recommendations have been established (16). Laflamme (59) suggested that 25% of the calories in the diet should come from protein to allow the senior dog to support protein turnover because senior dogs require 50% more protein than younger dogs to maintain nitrogen balance, and three times more protein than this to maintain protein turnover (119). As adult cats require more than 5 g protein/kg body weight (~34% of calories) to maintain proper protein turnover, the senior cat would likely require more than this to maintain its body protein stores and proper protein turnover (59).

Minerals

AAFCO (4) and NRC (78) have recommended requirements for 12 minerals. The body of literature in this area has focused primarily on identifying adequate mineral intakes and/or means by which to minimize mineral imbalances occurring in disease states. Thus, very few studies have focused on age-related differences in mineral absorption and/or metabolism.

The study performed by Sheffy et al. (99) is one of the few that focused on testing the effects of age on mineral absorption. In young adult (1-year-old) and geriatric (10- to 12-year-old) Beagles, it was reported that Ca, P, Mg, Zn, Cu, Fe, K, and Na apparent digestibilities were not different owing to age, but were highly variable among dogs.

Of the minerals, Ca is found in the greatest quantity in the body and has been studied in the greatest detail. There appears to be some evidence that Ca absorption is affected in growing puppies as compared with adults. Calcium is absorbed via passive and active mechanisms in all ages of dog, but passive absorption is more important in young puppies. In growing puppies (6–27 weeks of age), Tryfonidou et al. (116) reported a linear increase in Ca absorption with increasing dietary Ca. Consequently, growing puppies may absorb Ca in greater quantities than do adults when fed diets containing high Ca concentrations (39).

After Ca, P is the second most prevalent mineral present in the body. Age-related changes in P metabolism have not been studied.

Very little data pertaining to age-related changes in Mg utilization are available in dogs, but two such studies have been performed in cats. There appears to be a negative correlation between age and apparent Mg absorption in growing kittens. In one study evaluating kittens 15 to 39 weeks of age, apparent Mg absorption was reported to decrease with increasing age (80). In a follow-up study, Mg absorption decreased from 81% to 12% in 11- and 39-week-old kittens, respectively (81). Data for other macrominerals and trace minerals are lacking in dogs and cats as pertains to age and requires further study.

Vitamins

To our knowledge, vitamin nutrition as related to age or life stage has not been studied in these species.

USE OF GENOMIC BIOLOGY TO EVALUATE NUTRIENT UTILIZATION AS AFFECTED BY AGE

Despite the remarkable progress made in the field of companion animal nutrition in the

twentieth century, many gaps in our knowledge still exist. Age-related physiologic differences among dogs and cats of various life stages and the outcomes of modifying the diet at these times are still largely untested. Even now, the recommendations for many nutrients, especially micronutrients, are educated guesses based on small datasets from a single life stage. Further evaluation of nutrient utilization and requirements throughout the life cycle is needed. In contrast to livestock species used primarily for food production, companion animal health must be managed over their entire natural life span (up to 15–20 years of age). Thus, identifying relationships between nutrition and chronic disease incidence, quality of life, and longevity are key issues in canine and feline research.

Genotype, environmental factors (e.g., nutrition, exercise), and breed size are known to contribute to the aging process in dogs. Most of these factors also contribute to aging processes in cats. Given the wide range of genetic and environmental backgrounds of pet dogs, chronological age is often quite different from physiological age. Breed size is one of the most notable factors affecting diseases associated with aging. For example, small (<9 kg), medium (10–22 kg), large (23–40 kg), and giant (>40 kg) breeds are considered to be geriatric after approximately 11.5, 10.9, 8.9, and 7.5 years of age, respectively (25). Although mechanisms contributing to the disparity observed among canine breeds are not well understood, many theories of aging have been proposed and may contribute.

Postulated mechanisms of aging include cumulative DNA damage (leading to genomic instability), epigenetic alterations (leading to altered gene expression patterns), telomere shortening in replicating cells, oxidative damage by reactive oxygen species, and nonenzymatic glycation of long-lived proteins (46, 48). One of the main factors contributing to or greatly affected by the aging process is how nutrients are utilized by the body. Therefore, identifying strategies to study nutrient-gene interactions and how they may be affected by aging or contribute to an advanced rate of aging are of importance in this discussion.

Federally funded genome sequencing and mapping initiatives have supplied researchers with highly robust canine and feline genome sequence data from which to work. These genome sequence data, coupled with continued advancements in biotechnology, have supplied researchers with a powerful arsenal of tools with great accuracy and precision, potential for high throughput, and automation. Such efforts have enhanced the ability to measure DNA, gene transcripts (mRNA), proteins, and metabolites, and to identify nutrient-gene interactions and genes associated with aging and disease. Although this section covers some opportunities to study nutrient utilization changes with age using genomic biology, readers may refer to Swanson (109) for a more complete discussion.

Although an animal's genotype may affect how the body absorbs, metabolizes, transports, or excretes nutrients, nutrition, in turn, affects epigenetic, genomic, and proteomic events in the host. Thus, it is likely that key nutrient-gene interactions that either hasten or slow the aging process, some of which may involve a reduced ability to utilize nutrients, exist. The term "nutrigenetics" may be used to describe the effect of genotype on nutrient absorption, metabolism, and transport. To date, the presence of polymorphisms has been tested only in a few canine genes involved with nutrition or metabolism. Because the canine genome sequence data required to perform these analyses are now available in public databases, this should change in the future. Although many polymorphisms (variations in DNA) have no impact on gene function, a considerable number have mild effects on protein functionality. Genome sequencing has allowed the mapping of single-nucleotide polymorphisms, and in the case of the dog, the availability of a commercial "single-nucleotide polymorphism chip." Genome screening techniques may not only become an important means by which to recommend diets and/or prescribe drugs in the future, but also to identify groups within a

population that are susceptible to age-related functional decline.

Despite the vast genetic diversity within the canine and feline species, factors other than DNA sequence, such as temporal and spatial gene expression patterns, alternative splicing, post-translational modification, and protein-protein interactions, also are important determinants of phenotype and are likely more relevant in the current discussion. Applying genomic technology to epigenetic and functional genomic research endeavors may be highly rewarding. Epigenetic inheritance is due to heritable changes in gene expression and regulation that are independent of changes in DNA sequence. Methylation patterns of DNA and histone modification are the primary mechanisms known to affect gene expression. Epigenetic changes made early in life may affect life-long metabolic status and have been termed "metabolic programming." This area of research continues to gain interest owing to its link to chronic diseases such as obesity, diabetes, heart disease, and behavioral disorders. Although proper nutrient status of gestating and lactating bitches and queens has been appreciated for quite some time, the effect of modifying diet in utero or early in life on the long-term metabolic response of the offspring has not been tested.

It is now believed that epigenetic alterations are not only important during development, but also occur throughout life, affecting gene expression and numerous biological processes. In a study of global and locus-specific differences in DNA methylation and histone acetylation of a large cohort of monozygotic twins, Fraga et al. (24) concluded that widespread epigenetic drift is associated with human aging. Such differences would be expected to occur in dogs and cats and may explain differences among individuals as they age. The DNA sequence and tools for measuring DNA methylation and histone modifications and their relation with age-related differences in gene expression and biological function are now available and require attention. In general, the aging process is associated with a progressive reduction in an animal's ability to cope with physiological challenges, many of which appear to be the result of aberrant gene expression (71). Nutrition is believed to be an important modulator of the aging trajectory, but with the exception of caloric restriction, there is little proof that any dietary factor influences longevity (71). However, evidence of nutritional effects on gene expression suggests a strong role of diet on the biology of aging. Gene expression may be regulated by nutrients via epigenetic means as described above or by a labile process controlled by transcriptional activators and repressors whose nuclear concentrations, covalent modifications, and subunit associations fluctuate extensively. High-throughput techniques for measuring mRNA, protein, and metabolite profiles are now available and may shed light on age-related differences pertaining to nutrient uptake, transport, and metabolism.

Most published studies measuring mRNA, protein, or metabolite profiles in dogs or cats have concentrated their efforts on microarray analysis of tissues collected from diseased versus healthy populations. Although identifying differences in the diseased state may be important in devising prevention or treatment strategies, measuring natural changes that occur with age may highlight genes or biological systems contributing to reduced nutrient utilization or abnormal metabolism. For example, our laboratory is currently testing the effects of diet and age on mRNA profiles of geriatric versus young adult dogs. The initial focus has been on tissues that are important metabolically and/or are greatly affected during the aging process (liver, colonic epithelia, skeletal muscle, adipose, and cerebral cortex). These datasets (e.g., 111) are providing a wealth of information about the metabolic state of the tissues in aged dogs and a platform on which to base future nutrigenomic studies. Similar age-related changes to protein profiles have been measured in canine (79) and feline tissues (117). Finally, nuclear magnetic resonance was recently used to generate and compare age-related metabolite profiles of canine urine samples (118).

A significant hindrance to studying intestinal microbiota has been the inability to effectively identify and quantify microbial species. Researchers have been reliant upon microbial culturing methods, which are not only laborious, time-consuming, and often inaccurate (27), but also greatly limited in scope. For those that survive in culture, identification among species or genera is difficult, if not impossible. Because 60%–80% of intestinal microbes have not yet been cultivated (2, 8, 62), DNA-based, culture-independent methods that have recently emerged have great utility. The sequencing of several bacterial genomes, including *Bacteroides* (121), *Lactobacillus* (1, 93), *Bifidobacterium* (97), *Clostridium* (100), *Enterococcus* (84), and *E. coli* (7) species have been completed. These efforts provide crucial data that may be used for identification and/or functional studies.

An average bacterial 16S rRNA gene has a length of ~1500 nucleotides and contains regions with different degrees of variability, enabling researchers to distinguish organisms at different phylogenetic levels (species to domain) (2, 77). Several molecular tools based on microbial 16S rDNA sequence, such as fluorescent in-situ hybridization, denaturing gradient gel electrophoresis, quantitative dot blot hybridization, restriction fragment length polymorphism, and large-scale 16S rDNA sequencing, can be used to overcome some of the limitations of culture-based techniques. Further identification and characterization of canine and feline microbiota will be useful in evaluating the effects of age on intestinal health.

SUMMARY AND CONCLUSIONS

Companion animals are living longer, healthier lives today as a result of advances in both veterinary medicine and nutrition. The life-stage approach appears to be the most efficacious in understanding the complexities of companion animal metabolism beginning in utero and extending through the geriatric state. One life stage affects another, but the nature of the scientific progress in this area has resulted in the various life stages being studied in relative isolation, with little attempt made to correlate how a previous life stage might influence a subsequent one. The key challenge is to match the nutrients being supplied by the diet to the specific needs of the companion animal at a specific life stage. In the case of the dog, excess nutrients often will be supplied for nutritional management purposes, i.e., providing a highly digestible (>85%) diet for purposes of controlling waste elimination behavior of animals housed indoors.

As explained by McNamara (73), the best food of the neonate is mother's milk. If this is not available, a good quality milk replacer must be substituted. Good eating habits should be established for young growing animals, where a properly balanced diet is fed without allowing excess energy consumption. Animals nearing mature body weight need food with proper concentrations of nutrients to allow optimal growth of organs and bone. Companion animals at maintenance need a proper mix of nutrients, but in lower concentrations to allow for tissue repair, not growth. Reproducing females in the last trimester of gestation should be fed a diet high in nutrients, but the animal should not be allowed to gain or lose significant weight other than fetal tissue. In lactation, dogs and cats may consume two to three times as much food as normal while at the same time losing body fat. Senior and geriatric companion animals should be fed a highly digestible diet containing highly bioavailable nutrients to ensure sufficient nutrient intake, especially if total food intake decreases.

Genomic biology undoubtedly will play a role in the future in helping to understand interrelationships among life stages. It is recognized today that optimal nutrient requirements may differ from minimal nutrient requirements, and that select nutrients may be conditionally essential while select ingredients may play a functional role in certain life stages but not in others. Recognition of these facts and the availability of new technologies to monitor changes in companion animal metabolism with age will no doubt provide major insights into these issues in the years to come.

SUMMARY POINTS

1. In companion animals, as is the case for humans, nutritional interventions related to age must address life stages beginning in utero and extending to the senior/geriatric state.
2. Major changes exist in the digestive physiology of dogs and cats at different life stages that affect nutritional and health status.
3. Maintaining energy balance and avoiding obesity should be the most important goals of pet owners.
4. Low-glycemic ingredients appear to be beneficial in diets of senior dogs.
5. Certain fatty acids are conditionally essential for the weanling puppy as well as the senior dog.
6. Amino acid requirements differ for the puppy aged 4–14 weeks as compared with animals greater than 14 weeks of age.
7. Nutritional effects on gene expression suggest a major role of diet in the biology of aging.

FUTURE ISSUES

1. Alterations in physiological systems and metabolic processes that are affected by aging must be defined in much greater detail.
2. Establish why large breed dogs age more rapidly than small breed dogs, thus dying at an earlier age.
3. Quantify how the large bowel microbiota affect health outcomes of companion animals, and establish the significance of those responses as regards aging.
4. Define the significance of the interactions among gut microbiota, gut immunity, and the aging process.
5. Define the precise energy requirement of dogs and cats at all life stages.
6. More research in the area of mineral and vitamin requirements is needed, especially those micronutrients that affect factors related to the aging process.
7. Use the latest technologies in the genomic biology area to study the many facets of the companion animal aging process as affected by nutrition.
8. Establish dietary formulas that are optimal for pets at the various life stages.

DISCLOSURE STATEMENT

The authors are not aware of any biases that might be perceived as affecting the objectivity of this review.

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Errata

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