The essential nature of dietary omega-3 fatty acids in dogs

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Determination of dietary essential nutrients often requires use of several methods, such as balance studies, growth studies, tissue saturation, or physiologic responses. Currently, molecular techniques are additionally able to help define the more detailed molecular features for both clinical and cellular nutrition. These methods and techniques comprise important tools for modern nutrition science.

Minimal and optimal nutrition currently encompasses nutrients (eg, phytonutrients, antioxidants, and fatty acids) heretofore not considered by early nutritionists. New standards are being used for evaluation of these nutrients physiologically or at the molecular and cellular levels. In this manner, minimum requirements can be understood both clinically and at the cellular level. The notion of optimal nutrition is also being investigated to better understand how increased amounts of a nutrient beyond a defined minimum can augment health and potentially delay progressive pathological conditions.

A Brief History of Essential Fatty Acids

In 1909, it was discovered that fat-soluble vitamins were a component of dietary fat, which gave dietary fat a functional role beyond providing energy.[1] In 1929, investigators discovered the essential nature of fatty acids (with a focus on the omega-6 fatty acid linoleate) by observing scaly skin lesions in humans after the consumption of fat-free diets.[2] Effects of an absence of dietary fat on dogs was investigated in the late 1940s and yielded similar results.[3,a] However, it was not until 1982 that a recommended change in total parenteral nutrition that included ALA, an omega-3 fatty acid, stimulated interest in the inclusion of this fatty acid type for human nutrition.[4] The patient of that report[4] was a 6-year-old girl who had 300 cm of intestine removed as a result of a gunshot wound. After consuming a preparation rich in LA but low in ALA for 5 months, she had episodes of numbness, paresthesia, weakness, inability to walk, pain in the legs, and blurred vision. When the dietary regimen was changed to an emulsion containing ALA, neurologic symptoms resolved.

The earliest use of dietary fish oil treatment for humans has been traced back to 1783 when it was described as a treatment for rheumatism in the *London Medical Journal*.[5] Information on the dietary habits of Greenland Eskimos and the long-chain marine-based omega-3 fatty acids EPA (20:5[n-3]) and DHA (22:6[n-3]) was published in 1914.[6] After that information was reported, other investigators observed that myocardial infarction and ischemic heart disease rarely occurred in the Eskimo population.[7,8] This finding was believed to be related to an antiatherogenic effect of marine-based oils enriched in the long-chain omega-3 fatty acids consumed by the Eskimo population. The discovery of prostaglandins and other eicosanoids in the 1930s[9] generated additional interest in lipid metabolism during the 1950s and 1960s when these metabolites were found to be biochemically distinct, depending on the type of fatty acid (ie, omega-3 vs omega-6) incorporated into membrane phospholipids.[10,11]

Numerous studies and clinical investigations into fatty acid nutrients have been performed, which makes omega-3 fatty acids one of the most studied nutrients. Long-chain omega-3 fats, most notably EPA and DHA, provide important health benefits in humans and domestic animals, including dogs. There may be similar benefits for cats, although such benefits have not been evaluated extensively in this species. These benefits

ABBREVIATIONS

AA	Arachidonic acid
AAFCO	Association of American Feed Control Officials
ALA	α-Linolenic acid
BW	Body weight
DHA	Docosahexaenoic acid
DM	Dry matter
DPA	Docosapentaenoic acid
EPA	Eicosapentaenoic acid
LA	Linoleic acid
NRC	National Research Council

include cardiovascular health, neurologic development, and mitigation of the inflammatory response.[12] Furthermore, beneficial outcomes have also been observed for controlling hypertension, renal diseases, arthritis, autoimmune disorders, and gastrointestinal tract disturbances[12] and aiding cognitive function[13] and, possibly, cancer therapeutics.[14]

Therapeutic Use of Fish Oil Omega-3 Fatty Acids in Dogs

Studies of fish oils have revealed therapeutic effects for several clinical disorders of dogs, including dermatologic, cardiovascular, renal, lipid, and metabolic derangements and disturbances associated with osteoarthritis. Recommended doses of supplemental fish oil containing EPA plus DHA, with metabolic BW adjusted by multiplication factors ranging from 115 to 310, have been published[12] **(Table 1)**. Such therapeutic doses do not necessarily define a minimal requirement for omega-3 fatty acids because they represent a pharmacological use of these dietary nutrients. Furthermore, it is unknown whether incremental amounts of fish oil above a minimum amount would be optimal for health maintenance or could possibly prevent chronic conditions in clinically normal dogs. Nonetheless, the NRC has a recommended allowance of combined EPA plus DHA with a multiplication factor of 30 times the metabolic BW for adult dogs at maintenance.[15] The NRC has also indicated that the EPA-to-DHA ratio should be approximately 1:1.[15] One reason to include both fatty acid types is because EPA and DHA have separate effects in addition to some overlapping benefits. The recommendation infers a minimum requirement for adult dogs at maintenance, although future studies are merited on the necessary amounts of these omega-3 fatty acids. In addition, the 2016 AAFCO nutrient profiles require inclusion of EPA plus DHA as well as ALA.[16]

Table 1—Fish oil doses (in mg) for combined amounts of EPA plus DHA calculated by use of metabolic BW for adult dogs.

Condition	Calculation
Adult maintenance	
NRC recommended allowance	$30 \cdot BW^{0.75}$
NRC safe upper limit	$370 \cdot BW^{0.75}$
Clinical disorder	
Idiopathic hyperlipidemia	$120 \cdot BW^{0.75}$
Kidney disease	$140 \cdot BW^{0.75}$
Cardiovascular disorders	$115 \cdot BW^{0.75}$
Osteoarthritis	$310 \cdot BW^{0.75}$
Inflammatory or immunologic (atopy or inflammatory bowel disease)	$125 \cdot BW^{0.75}$

The BW is measured in kilograms. Doses may be increased (depending on the severity and chronicity of the disorder) up to the NRC safe upper limit. (Adapted from Bauer JE. Therapeutic use of fish oils in companion animals. *J Am Vet Med Assoc* 2011;239:1441–1451. Reprinted with permission.)

Basis for Essential Omega-3 Fatty Acids

Omega-6 fatty acids, namely LA, are widely regarded as an essential nutrient in dogs, and deficiencies of these fatty acids result in skin lesions and retarded growth.[3,a] However, a related issue is whether the analogous omega-3 fatty acid, ALA, is also essential. When addressing this issue, it must be remembered that structural and metabolic differences exist between these 2 fatty acid types. It should be mentioned that the 2 types of fatty acids do not metabolically interconvert. However, dogs readily convert LA into AA and related proinflammatory eicosanoids. By contrast, conversion of ALA to EPA as a precursor of less inflammatory eicosanoids is low, and conversion of ALA to DHA is even lower.[17] Also, the metabolism of LA and ALA is dependent on competitive interactions for the same enzyme systems. Thus, to avoid an overabundance of omega-6 metabolites, inclusion of α-linolenate in the diet to balance inherent dietary linoleate concentrations is recommended.[15] This criterion does not necessarily define α-linolenate as essential per se. However, because some subjects may be able to synthesize enough EPA and possibly DHA from α-linolenate to meet metabolic needs, α-linolenate has generally been considered an essential precursor to the longer-chain omega-3 fatty acids. Nonetheless, in the absence of adequate conversion by all subjects, recognition of the essential nature of longer-chain omega-3 fatty acids is also warranted. In fact, EPA and DHA are included as components of the 2016 AAFCO pet food profiles.[16] Given the aforementioned conditions, 2 questions arise. First, is there a minimal dietary α-linolenate concentration that can provide sufficient DHA synthesis for all life stages? If not, then DHA should be considered an essential fatty acid per se. Second, is metabolic demand for DHA greater during specific life stages such as growth or reproduction? If so, then DHA is conditionally essential.

Evidence of dietary-conditional essential nutrients can be found in feline nutrition. It is widely recognized that cats need arachidonate because they do not convert LA to arachidonate in adequate amounts to meet physiologic needs.[18] However, results from sophisticated stable isotope techniques have revealed that there is conversion, albeit low amounts.[19] Furthermore, investigators of another study[20] speculated that a group of adult female cats apparently did not require dietary arachidonate for maintenance, yet needed it for successful reproduction. The aforementioned observations support the possibility that AA is conditionally essential for reproduction of cats even though it is commonly considered to be a dietary essential for cats of all life stages. Because required amounts of dietary AA are typically low and easily met in feline diets, a universal recommendation for arachidonate has been advocated. It is possible that an analogous situation may exist in dogs regarding the omega-3 fatty acids, given the low conversion rates of ALA to EPA and DHA.[17] Thus, in the event that long-chain omega-3 requirements cannot be met solely by including α-linolenate in the diet, EPA or DHA may also be conditionally essential, especially for growth, development, metabolic balance, and possibly healthy aging. By contrast, adult dogs at maintenance may not require long-chain omega-3 fatty acids because small amounts of EPA or DHA may be present and sufficient. Reasons for this possibility are that DHA is well conserved in tissues, and dietary α-linolenate may meet long-chain omega-3 maintenance in some dogs.[21] Nonetheless, similar to the situation for arachidonate in cats, the NRC[15] and 2016 AAFCO nutrient profiles[16] recommend the inclusion of small amounts of long-chain omega-3 fatty acids in canine diets.

Essential Functions of Long-chain Omega-3 Fatty Acids

Evidence for an essential long-chain omega-3 fatty acid has been based primarily on the role ascribed to DHA for neural membranes, neurologic development, and visual acuity. For these reasons, DHA rather than EPA is more likely to be essential. One reason is because the amount of EPA synthesized from α-linolenate may be sufficient for health maintenance during typical conditions, whereas DHA conversion is more limited. Although EPA can be converted to eicosanoids as well as to resolvins and protectins, many of which have roles in cardiovascular, inflammatory, and other cell processes,[22] no essential role for these EPA metabolites has been reported. Furthermore, concentrations of these metabolites in dogs fed ALA typically are low,[17] and the anti-inflammatory effects of EPA reportedly depend on increased dietary amounts that usually represent only higher pharmacological-type doses of EPA.

By contrast, DHA is present in large amounts in the brain and retinas, which points to an important structural role. In addition, DHA is also needed for development of the nervous system and optimized visual acuity, which suggests a functional role.[23] In the retinas, there is evidence that DHA is highly conserved and recycled into retinal pigment epithelial cells. This phenomenon maintains a reserve of DHA for rod outer segment cells.[21] Moreover, DHA interacts with rhodopsin via phospholipid enrichment and thus plays a key role in the control of visual function.[24,25] In the absence of sufficient amounts of DHA, DPA(n-6), an omega-6 fatty acid, accumulates, which is similar to the response seen in linoleic-deficient mammals and arachidonate-deficient cats. Such a substitution may provide structural integrity, but DPA(n-6) does not appear to compare with DHA, an omega-3 fatty acid, with regard to brain function.[26] Cultured astrocytes, the cell type involved in elongation and desaturation of fatty acid precursors in the brain, primarily produce DHA and AA rather than DPA(n-6), which permits DHA to be available in the CNS.[27] Taken together, these important cellular and physiologic functions as well as the fact that DHA is poorly synthesized from shorter-chain precursor fatty acids support an essential role for preformed dietary DHA, rather than reliance on its limited conversion from ALA.

Accumulation of Unique Fatty Acids During Essential Fatty Acid Deficiencies

Unique fatty acids can accumulate during deficiencies. For example, deficiencies in LA can result in accumulation of Mead acid, an omega-6 trienoic acid (20:3[n-9]). Mead acid is synthesized as a result of oleic acid (18:1[n-9]) being substituted for LA as a substrate for further conversion[28–31] **(Table 2)**. For human blood samples, the Mead acid-to-arachidonate ratio (ie, a triene-to-tetraene ratio) is widely used to characterize fatty acid deficiencies.[29] In cats, diets low in arachidonate but that contain linoleate result in the synthesis of another novel triene fatty acid, cis Δ 7,11,14 eicosatrienoic acid (20:3[n-6]) in plasma, which likely is synthesized from LA.[30] Similarly, in the absence of sufficient amounts of dietary DHA, the omega-6 fatty acid DPA(n-6) (22:5[n-6], also known as cis Δ 4,7,10,13,16 docosapentaenoate) appears in brain tissues as a result of synthesis from arachidonate, its omega-6 precursor.[31] Each of these responses is consistent with the synthesis of alternate fatty acid metabolites from available precursors when a particular essential fatty acid deficiency exists and no functional substitute for the deficient fatty acid is available. Theoretically, a marked increase in DPA(n-6) formed from LA in a pathway parallel to that involved in DHA synthesis might decrease the DHA-to-DPA(n-6) ratio and thus serve as a biomarker of DHA deficiency. However, investigators of a study[32] of preschool children found this was not true. Additional studies are needed to address whether such a biomarker possibly exists in canine species.

Table 2—Accumulation of unique fatty acids during essential fatty acid deficiencies.

Fatty acid deficiency	Substituted substrate	Fatty acid accumulated	Enzyme cascade sequence	Reference
LA (18:2 [n-6])	Oleic acid (18:1 [n-9])	Δ 5,8,11 eicosatrienoic acid (20:3 [n-9])*	Δ-6 desaturase, chain elongase, and Δ-5 desaturase	29
AA (20:4 [n-6])†	LA (18:2 [n-6])	Δ 7,11,14 eicosatrienoic acid (20:3 [n-6])	Δ-5 desaturase and chain elongase	30
DHA (22:6 [n-6])	AA (20:4 [n-6])	Δ 4,7,10,13,16 DPA(n-6) (22:5 [n-6])	Chain elongase, chain elongase, Δ-6 desaturase, and β partial oxidation	31

*Also known as Mead acid. †In cats.

Role of Dietary DHA in Dogs

Studies on the role of omega-3 fatty acids have revealed that DHA is involved in several life stages of dogs.

Cognition and healthy aging

Critical gaps exist in our knowledge about this area. In humans, DHA may support healthy aging, and low amounts of DHA have been correlated with cognitive impairment.[33,34] Although there are published reports on the benefits of omega-3 fatty acids for aging and cognition, data for dogs are lacking. Antioxidant-enriched diets containing a small amount of DHA have been found to be potentially beneficial in dogs, so the data are not currently definitive on this topic.[35] In 2 studies, one that involved the use of research colony dogs[35] and the other that involved the use of client-owned dogs,[36] investigators found that diets enriched with several antioxidants and mitochondrial cofactors helped mitigate age-related cognitive dysfunction. The DHA content of these diets was reported to be only 0.01%, which provides support for the contention that antioxidants were a major factor. Therefore, defining a minimum amount of DHA to ensure healthy aging is currently not possible. Studies on cognition of older dogs are being conducted. In addition, a few existing reports have found associations between DHA and seizure treatment of dogs[37] and possibly aggression of dogs.[38]

Development of puppies

Feeding studies in which investigators evaluated the effect of fish oil omega-3 fatty acids on development of puppies have provided insights into minimal and optimal nutrition for omega-3 fatty acids. In 1 study[39] of puppies and adult dogs, researchers investigated canine retinal phospholipids by use of commercially prepared diet mixtures with low and high amounts of long-chain omega-3 fatty acids containing α-linolenate. Retinas from the high omega-3 group had significantly higher amounts of both DPA(n-3) and DHA but not EPA or α-linolenate, and plasma was enriched in DPA(n-3).[39] In other studies,[40,41] a group of pregnant dogs were fed a diet containing > 12 times as much α-linolenate as DHA from the time of breeding through gestation, parturition, and lactation. Two other groups were fed diets containing moderate and high amounts of fish oil along with α-linolenate. Milk from dams fed the high α-linolenate diet was markedly enriched in α-linolenate,[40] and puppies suckling the milk of those dams had substantial accumulation of DHA in plasma phospholipids.[41] However, the puppies appeared to lose their ability to convert α-linolenate to DHA after weaning, even though they were weaned onto the same diet that had been fed to their dams.[41] This lack of conversion of DHA from α-linolenate in those puppies is similar to that reported for adult dogs.[17] Thus, neonatal dogs appear to synthesize DHA when suckling α-linolenate–enriched milk at a time of life when demand for DHA is especially high, but they do not synthesize it thereafter. It should be mentioned that because the α-linolenate content of the diet in those studies[40,41] was markedly increased, a dose response for dietary α-linolenate was not determined. The minimum amount of α-linolenate in milk that might be required to provide sufficient conversion to DHA is unknown. Finally, electroretinography of 12-week-old puppies from the aforementioned study[41] revealed a significant improvement in visual function for animals in the high fish oil group, compared with results for the other groups.

Electroretinographic responses and cognitive assessments of puppies fed DHA-enriched diets have been evaluated.[42] In that study, DHA-enriched diets were fed to puppies beginning at weaning, rather than to the dams throughout gestation, parturition, and lactation. On the basis of results of earlier studies, this period is one in which puppies have lost the ability to convert α-linolenate to DHA. There was a strong correlation between DHA content of the diets fed (both moderate and high DHA groups) and improved visual function (as assessed by use of electroretinography). Cognitive function tests conducted when puppies were between 8 and 13 weeks of age revealed that puppies fed the moderate or high DHA diets had fewer errors for reversal tasks as well as other significant differences for cognitive function tests, compared with results for puppies fed a low DHA diet. Comparing dietary composition data from the 2 latter studies,[41,42] an initial interpretation of the role of omega-3 fatty acids and optimized dietary amounts can be proposed.

Although far from establishing omega-3 as an essential fatty acid, concentrations of control diets used in the aforementioned studies support the use of low yet reasonable concentrations of omega-3 fatty acids, similar to the concentration of arachidonate, in cats for reproduction and puppies for development. Thus, on the basis of the aforementioned studies, recommended amounts for growth and development of puppies beginning at 6 to 8 weeks of age (assuming a 4,000 kcal/kg of DM diet) are as follows: 0.016% to 0.022% DHA (DM basis), equivalent to 0.04 to 0.055 g/1,000 kcal; 0.08% to 0.14% ALA (DM basis), equivalent to 0.2 to 0.35 g/1,000 kcal; and 1.1% to 2.2% LA (DM basis), equivalent to 2.75 to 5.5 g/1,000 kcal. However, with regard to optimal neurologic development of puppies, studies[41,42] have found that 0.2% DHA (DM basis), equivalent to 0.5 g/1,000 kcal in a 4,000 kcal/kg of DM diet, provides substantial retinal and cognitive improvements, compared with results for puppies fed a control diet. Although these studies included diets with small and similar amounts of α-linolenate, it should be mentioned that conversion of α-linolenate to DHA in puppies after weaning (approx 6 weeks of age) is minimal. However, the aforementioned dietary recommendations should be used with caution and serve only as a point of embarkation for future validation studies.

Clinical Summary

Evidence exists to support a conditionally essential role for DHA in dogs, as determined on the basis of puppy feeding studies, mainly because of its roles in brain and visual function. This conclusion is especially notable in view of low DHA conversion from omega-3 precursors in puppies after weaning. Increased dietary amounts of fish oil containing DHA provide benefits to development of puppies, compared with development of control puppies. Although assessments of visual function and cognition were improved for puppies eating diets with a higher dietary omega-3 content, control diets with only small amounts of omega-3 fatty acids did not result in clinical impairments under the conditions of the studies. Thus, it is difficult to conclude that diets lower in omega-3 content are deficient. However, optimizing development is a worthwhile outcome. Although more precise studies are needed, analyses of existing fatty acid composition data from published studies have indicated preliminary quantitative amounts of omega-3 fatty acids necessary to meet essential cellular functions.

Provision of dietary DHA may also be important for any subset of adult dogs that cannot synthesize sufficient amounts of DHA from precursors. The problem is that it currently is not known which dogs belong to this subset. Hence, a recommendation for DHA may be preferred for all life stages, even though some adult dogs may synthesize enough DHA to meet their needs. Although α-linolenate may play a supportive role, it is unknown whether it can feasibly be provided in sufficient amounts to support cellular DHA metabolism. Thus, preformed DHA is needed. Furthermore, although α-linolenate can be used to provide measureable, yet modest, EPA synthesis, there is no evidence that omega-3–based eicosanoids synthesized from EPA are essential metabolites, even though they may be beneficial (under some conditions) via displacement of arachidonate in cell membranes.

Finally, suckling puppies apparently can accumulate DHA from dietary α-linolenate. However, this conclusion is based on the result of only 1 study[41] in which high amounts of α-linolenate were fed. This finding should ideally be replicated for diets with lower amounts of α-linolenate. Because marine oils typically contain both EPA and DHA, α-linolenate may not be needed unless balancing dietary linoleate is desirable and additional essential roles for α-linolenate are discovered. Should a separate dietary source of DHA (algal sources rich in DHA) be used, it may be prudent to also provide α-linolenate. Feral dogs would be expected to obtain both α-linolenate and DHA from liver and nervous tissues of small rodents or birds that more readily convert dietary omega-3 precursors in plants to longer-chain derivatives.

Footnotes

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