



Timely Topics in Nutrition

Metabolic basis for the essential nature of fatty acids and the unique dietary fatty acid requirements of cats

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Cats are unique among mammals with respect to metabolism of fatty acids. Except for some ruminants, all other mammals, including cats, are able to synthesize nonessential saturated and monounsaturated fatty acids de novo from glucose or amino acids via a common precursor, acetyl CoA. The products of this synthesis are 16- and 18-carbon saturated fatty acids that can subsequently be desaturated to monounsaturated fatty acids of the n-7 and n-9 fatty acid families (eg, 16:1n-7 and 18:1n-9). These acids are the result of the introduction of a single double bond between carbons Δ -9 and Δ -10 of the respective saturated acids.¹ Enzymes regulating these reactions are active when high-carbohydrate, low-fat diets are fed but have low activity when high-fat diets are fed. Consequently, animals fed relatively high-fat diets will only synthesize limited amounts of the needed fatty acids. Instead, they directly use the dietary supply of fatty acids.

When low-fat diets that are devoid of essential omega-6 and omega-3 fatty acids are fed, mammals will further elongate and desaturate 18:1n-9, which results in the production of 20:3n-9 (ie, 5,8,11-eicosatrienoic acid). Measurable quantities of the latter fatty acid are a hallmark of EFA deficiency (Figure 1), which leads to classical signs of this disorder, such as poor growth, scaly dermatoses, and scruffy hair as well as numerous



Figure 1—Pathway for synthesis of 20:3n-9 (ie, 5,8,11-eicosatrienoic acid) when low-fat diets devoid of the essential omega-6 and omega-3 fatty acids are fed to cats. There is accumulation of 22:3n-9 via desaturation and chain elongation of 18:1n-9 when suitable amounts of EFAs (ie, linoleic and α -linolenic acids) are lacking in the diet. Elongase = Chain elongase.

ABBREVIATIONS

EFA	Essential fatty acid
LCPUFA	Long-chain polyunsaturated fatty acid
DHA	Docosahexaenoic acid

other metabolic consequences. Of necessity, mammalian diets must include EFAs (both n-6 and n-3 fatty acids) that animals are incapable of synthesizing.

By contrast, plants can manufacture all of the aforementioned fatty acids, including saturated, monounsaturated, and polyunsaturated omega-6 and omega-3 fatty acids. Synthesis of polyunsaturated fatty acids is accomplished via enzymes not found in mammalian tissues that result in the insertion of additional carbon-carbon double bonds in distinct locations into a less unsaturated precursor. This process typically happens at a carbon atom located some distance away from the carboxyl carbon and is a unique characteristic of the enzyme involved. For example, insertion of a double bond between carbon atoms 9 and 10 is performed by stearoyl-Co-A desaturase (a Δ -9 desaturase), whereas insertion between carbon atoms 6 and 7 is performed by a Δ -6 desaturase.

Mammals have both stearoyl-Co-A and Δ -6 desaturases. Plants have additional desaturases, including a Δ -12 desaturase that generates linoleic acid (18:2n-6) from the monounsaturated precursor, oleic acid (18:1n-9), and a Δ -15 desaturase that inserts a double bond into 18:2n-6 to generate α -linolenic acid (18:3n-3).² In this way, terrestrial plants synthesize n-6 and n-3 fatty acids. Furthermore, marine plants are able to insert additional double bonds into 18:3n-3 and subsequently elongate the carbon chain, which accounts for the formation of the omega-3 LCPUFAs and their abundance in marine plants. Terrestrial plants, however, do not analogously insert additional double bonds into 18:2n-6. Thus, arachidonic acid (20:4n-6) is not found in plant tissues.

The inability of animals to synthesize n-6 and n-3 fatty acids via Δ -12 and Δ -15 desaturases is the fundamental basis of the essential nature of these fatty acids and the need for a dietary supply. Once ingested in most mammals, except for felids, these dietary essen-

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tials are actively converted to longer chain derivatives through regulation by Δ -6 desaturases (Figure 2).^{2,4} In cats, these conversions are greatly limited because of low Δ -6 desaturase activity.^{3,6} This latter fact distinguishes the EFA requirements of cats because without Δ -6 desaturase, EFAs are not converted to other physiologically important LCPUFAs, such as arachidonic acid and DHA, to the extent necessary for certain life stages or processes. Thus, the derived omega-6 and omega-3 LCPUFA products may be conditionally essential in felids. For that matter, there is evidence that omega-3 LCPUFAs may also be conditionally essential for dogs and animals of several other species, even though adults of those species have substantial Δ -6 desaturase activity.⁷⁻¹³

Finally, it should be mentioned that mammals are not capable of inserting double bonds into the Δ -12 and Δ -15 positions of precursor fatty acids. Thus, there are no conversions among the n-3, n-6, n-7, and n-9 families.

Fatty Acid Metabolism in Adult Cats During Maintenance

Omega-6 fatty acids—Early studies^{5,14} on EFA metabolism in cats revealed that domestic cats could not convert linoleic acid to arachidonate, which led to speculation that cats do not possess the necessary Δ -6 desaturase to perform this conversion (Figure 2).

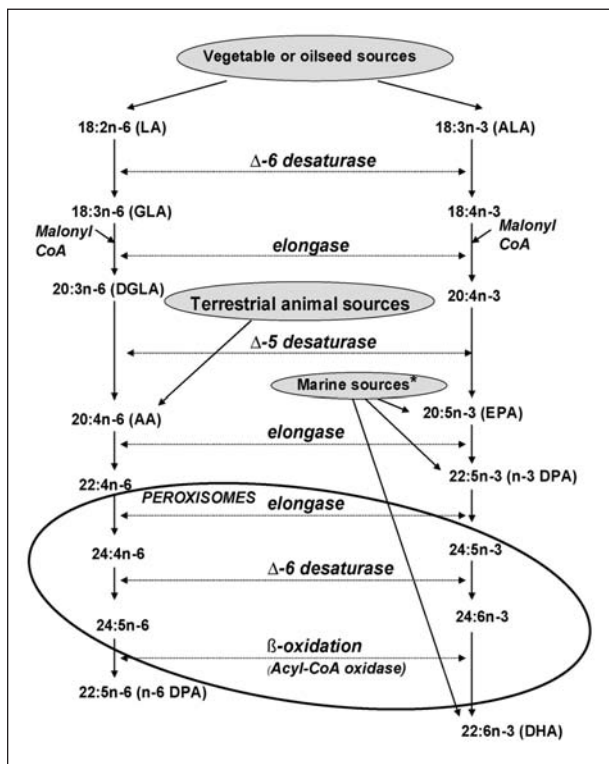


Figure 2—Predominant pathways for metabolism of EFAs in mammals. *Marine sources represent marine plants and animals. LA = Linoleic acid. ALA = α -Linolenic acid. GLA = γ -Linolenic acid. DGLA = Dihomo-GLA. AA = Arachidonic acid. EPA = Eicosapentaenoic acid. DPA = Docosapentaenoic acid. (Adapted from National Academies of Sciences, National Research Council. Fat and fatty acids. *Nutrient requirements of dogs and cats*. Washington, DC: National Academies Press, 2006;81–110. Reprinted with permission.)

Other investigators¹⁵ confirmed and extended those observations and concluded that cats possess both Δ -5 and Δ -8 desaturases, which led to the suggestion that an alternative pathway of arachidonic acid synthesis may exist in cats (Figure 3).^{15,16} Indeed, subsequent studies^{17,18} revealed that when cats were fed diets rich in linoleic acid, plasma and liver concentrations of arachidonic acid were similar to those for cats fed diets containing arachidonate. On the basis of these data, it appeared that cats were able to synthesize arachidonic acid from linoleic acid, although evidence was not provided for an alternate route of synthesis.

Evidence of limited Δ -6 desaturase activity in the liver and brain of cats has been confirmed by use of stable isotope techniques combined with gas chromatography and mass spectrometry.⁶ The limited Δ -6 desaturase activity in these tissues was detected when cats were fed a diet completely devoid of arachidonate. However, neither that study nor any of the aforementioned studies were designed to investigate the existence of an alternate pathway for arachidonate synthesis in tissues of felids.

Omega-3 fatty acids—In another study,⁶ other investigators evaluated conversion of vegetable-based omega-3 fatty acids to longer chain forms. Similar to the results for linoleic acid, adult cats converted small amounts of α -linolenic acid, which yielded eicosapentaenoic acid (20:5n-3) and docosapentaenoic acid (22:5n-3) in hepatic tissues and plasma. In addition, DHA (22:6n-3) and the omega-6 form of docosapentaenoic acid (22:5n-6) were detected in brain tissues.¹² These findings were of particular interest because the final conversion of DHA was detected only in neural tissues but not hepatic tissues, which lends support to the possibility that omega-3 docosapentaenoic acid that accumulates in plasma phospholipid fractions when cats are fed α -linolenic acid is then transported to the brain and nervous tissues for DHA synthesis.

Fatty Acid Metabolism in Adult Cats During Reproduction

Omega-6 fatty acids—Male cats fed a diet deficient in linoleic acid developed tubular degeneration of the testes.¹⁸ However, when linoleic acid was provided, fatty acid patterns of testicular phospholipids revealed higher arachidonate concentrations, compared with arachidonate concentrations in the deficient, unsupplemented cats. Queens did not bear live kittens when fed a diet deficient in linoleic acid.¹⁸ Thus, it was con-

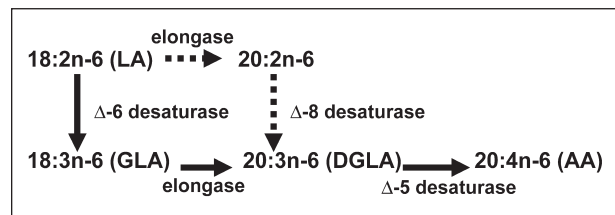


Figure 3—Possible pathways for synthesis of AA from LA. Notice that 1 pathway has a Δ -6 desaturase that is typically active in mammals (arrows with solid lines), whereas an alternative pathway includes conversions that involve Δ -8 desaturase (arrows with dotted lines), which bypasses the need for the Δ -6 desaturation step. See Figures 1 and 2 for remainder of key.

cluded that linoleic acid appears to meet the requirements for spermatogenesis but that arachidonate is necessary for reproduction in females.

The requirement for dietary arachidonate for reproduction in queens was evaluated in 1 study¹⁹ by feeding cats 1 of 3 diets that contained 1% corn oil, 3% corn oil, or 1% corn oil plus 0.02% arachidonate. Queens were fed the assigned diet beginning at the time of mating, and all became pregnant. A high incidence of congenital defects and low viability was found in fetuses of queens fed the diet that contained 1% corn oil. By contrast, the diets that contained 3% corn oil or 1% corn oil plus 0.02% arachidonate supported normal reproduction. Queens did not have effective reproduction when fed the diet low in linoleic acid unless that diet was supplemented with small amounts of arachidonate. However, because the diet that contained 3% corn oil without supplemental arachidonate also supported effective reproduction, it was concluded that other dietary factors may be involved.

Of additional interest is the fact that neonatal kittens from queens fed arachidonate in that study¹⁹ were used in another study.¹² The neonatal kittens were able to synthesize arachidonate from a labeled linoleic acid precursor.¹²

In another study,²⁰ investigators reported the effects of arachidonate-depleted diets on reproduction in male and female cats. Investigators in that study confirmed an earlier finding that males were fertile when fed diets containing linoleic acid but not arachidonate. In that study, 5 male cats fed diets consisting of hydrogenated vegetable oil that was devoid of arachidonate were allowed to mate with queens maintained on commercially available dry-type diets. Twelve of 13 queens conceived, with litter size ranging from 3 to 8 kittens. Sixty-seven kittens were born and were clinically normal, although 4 kittens from 3 litters died after 1 day of age for unspecified reasons. Nonetheless, litter size of those 12 queens exceeded the mean litter size for the colony, which consisted of cats fed commercially available dry-type diets. Therefore, the study confirms that arachidonic acid is not an EFA for growth and reproduction in male cats.

The reproductive outcome of 4 queens fed the hydrogenated vegetable oil diet was also reported.²⁰ All queens came into estrus, were mated, and subsequently had gains in body weight that were consistent with pregnancy. However, most of the kittens born alive were killed by the dams shortly after birth, with the proportion of dam-killed neonatal kittens being much higher for the 4 queens than the historical values for the colony.

After completion of that study,²⁰ 2 of the queens were administered 0.5 mL of arachidonic acid, whereas the other 2 queens were administered 1.0 mL of arachidonic acid once weekly for 10 weeks by use of a fungal-derived oil that contained 40.7% arachidonic acid. All 4 queens were again mated; however, none of the queens conceived after this treatment. Again, it was concluded that some other fatty acid or fatty acids, alone or in combination with arachidonate, may be necessary for successful reproduction in cats. However, the fatty acid or fatty acids necessary are currently unknown.

Omega-3 fatty acids—A study^a was conducted to evaluate the effects of vegetable-based α -linolenic acid on reproduction of queens fed 1 of 2 amounts of linseed oil (50 or 150 g/kg of diet, respectively), safflower oil (50 g/kg of diet), or a control diet. There were 3 queens/dietary group. The 3 queens fed the diet that contained 50 g of linseed/kg of diet gave birth to litters of 3 or 4 kittens. One queen subsequently had a second litter of 2 kittens, both of which died shortly after birth, whereas the other 2 queens did not have any additional litters. Only 1 queen fed the diet that contained 150 g of linseed oil/kg of diet gave birth; there was only 1 kitten in the litter, and it died shortly after birth. Queens fed the diets that contained linseed oil ultimately lost body weight, and their tissues contained low concentrations of long-chain omega-6 fatty acids. They also developed signs of EFA deficiency. Because α -linolenic acid and linoleic acid compete for the limited amounts of Δ -6 desaturase in cats, high dietary amounts of α -linolenic acid may preclude the conversion of linoleic acid to arachidonate. Hence, excessive amounts of omega-3 fatty acids relative to omega-6 fatty acids may be contraindicated in felids.

Independent of the site of tissue synthesis, the important clinical concern is whether the synthetic capacities for long-chain omega-3 fatty acids in cats are adequate for reproduction. In another study,¹² investigators fed diets that contained various amounts of corn oil and hydrogenated coconut oil to cats before mating, during pregnancy, and throughout the subsequent lactation. Two reference diets that contained arachidonic acid and DHA were also evaluated. Diets that contained corn oil were capable of maintaining arachidonic acid concentrations in the developing retinas and brain of kittens, but only those diets that contained DHA could support the high concentrations of DHA generally found in these tissues. Low concentrations of an omega-6 fatty acid, 22:5n-6, were also detected, which suggested that kittens have a low capacity to generate either 22:5n-6 or DHA.

Differences in electroretinograms, an index of neural development, were observed in the kittens whose queens were fed diets deficient in LCPUFAs, compared with electroretinograms for control kittens. It was concluded that the LCPUFA-deficient diets in that study¹² did not provide kittens with an adequate supply of n-3 fatty acids for proper accumulation of neural and retinal DHA during development and thus were inadequate for support of optimal visual function. There may have been insufficient conversion of the n-6 or n-3 18-carbon precursors needed for developing or immature kittens.

Clinical Summary

Similar to the case in other mammals, cats do not synthesize linoleic acid and require a dietary supply. Also, cats have a limited capacity to synthesize arachidonic acid, but it is unknown whether some alternative pathway, other than that defined by limited Δ -6 desaturase activities, may exist for synthesis of arachidonic acid. Regardless, the limited amount of arachidonate synthesized from linoleic acid may be sufficient for maintenance needs of adult cats, especially when linoleic acid is in abundant supply, which it is in many current commercial diets formulated for cats.

With regard to reproduction, male cats are able to synthesize sufficient amounts of arachidonate from linoleate to enable spermatogenesis. However, queens require an exogenous source of arachidonate for successful outcomes for pregnancies and normal litters, although queens can conceive when linoleic acid is provided in the diet without arachidonate.

Finally, for omega-3 fatty acids, high dietary amounts of α -linolenic acid, relative to the dietary amount of linoleic acid, may be contraindicated and lead to signs of EFA deficiency. The reason for this phenomenon may be the known competition of linoleic and α -linolenic acids for limited Δ -6 desaturases. Similar to the synthesis of omega-6 fatty acids, adult cats can synthesize small amounts of long-chain omega-3 fatty acids from precursors. Nonetheless, to support the high concentrations of DHA in the retinal and neural tissues needed for development, kittens may require an exogenous source of DHA (such as a diet supplemented with DHA) because conversion of precursors may be insufficient to meet this need.

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