Essential Fatty Acid Metabolism in Cats

KEY POINTS:

FACILITATIVE FATS:

- Add palatability and texture to foods
- Provide a dense source of calories
- Are stored in tissues for energy
- Facilitate the absorption of fat-soluble vitamins from the digestive tract

FUNCTIONAL FATS:

- Contribute to purposeful cellular activities

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DIETARY FATTY ACIDS: FACILITATIVE AND FUNCTIONAL

Two types of dietary fats have been described: facilitative and functional.[1] Fats that are facilitative by nature add palatability and texture to foods, provide a dense source of calories, are stored in tissues for energy, and facilitate the absorption of fat-soluble vitamins from the digestive tract. Many of the facilitative fats for cats include saturated and monounsaturated fatty acid types, which may be present in the food or synthesized by the body when dietary supplies are low. Trans fatty acids, some of which are polyunsaturated, are likely to be facilitative as well, although few studies have been published on the effects of these fats in cats. Studies to date in other species indicate that they and saturated fats are metabolized similarly.

Functional fats contribute to purposeful cellular activities. Most of these fats are also dietary essentials. They are important due to 1) their dietary necessity and 2) their known function with respect to some particular aspect of cell regulation or prevention of metabolic mayhem.

It should be noted that not all functional fats are essential fatty acids. However, all essential fatty acids are functional fats. Two examples of nonessential functional fats are conjugated linoleic acid and medium-chain triglycerides. Examples of functional fats that are essential include the omega-6 fatty acid, linoleic acid (LA), and the omega-3 fatty acid, alpha-linolenic acid (ALA). Longer chain fatty acids that are derived from LA and ALA are also functional fats, including arachidonic acid (AA) from LA and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from ALA. Some of these latter fatty acids may be conditionally essential, especially in cats.

WHAT COMPRISES AN ESSENTIAL FATTY ACID?

First and foremost, a fatty acid is essential because the animal's ability to synthesize it is limited or nonexistent. At the molecular level, however, "essential" is defined by both functional and structural characteristics: Functionally, the fatty acid must contribute in some significant way to health and well-being. Structurally, it must contain at least two double bonds, which must be located in what is known as a methylene interrupted cis, cis-configuration. This precise molecular configuration enables the particular fatty acid to fold upon itself three dimensionally so that it can participate in cell membrane and physiologic

Saturated, Monounsaturated, and Polyunsaturated Fatty Acids

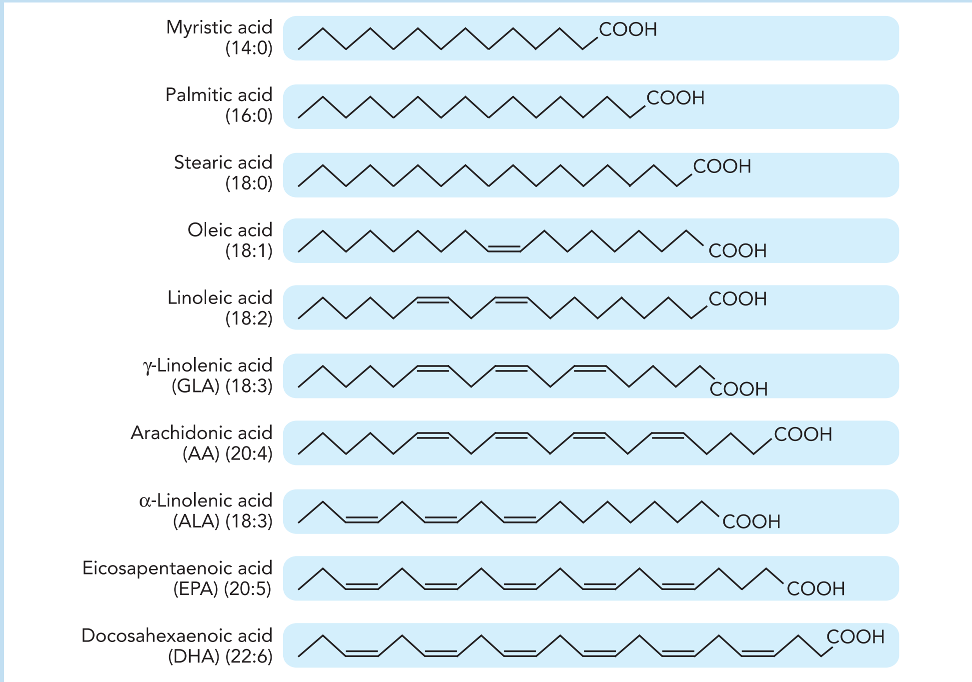

Figure 1. Structural formulas of the saturated, monounsaturated, and polyunsaturated fatty acids also showing the methylene interrupted sequence of the polyunsaturated acids

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events important for normal health. Once esterified into phospholipids, these essential fatty acids significantly affect many membrane properties, such as fluidity, compressibility, permeability, and fusion. In cats, several of the omega-6 and omega-3 fatty acids meet these criteria.

Figure 1 shows a comparison of selected saturated, monounsaturated, and polyunsaturated fatty acids, all of which have the requisite methylene interrupted sequence. As a matter of contrast, conjugated LA, which contains two double bonds, does not qualify as an essential fatty acid because its double bonds are "conjugated" instead of methylene interrupted. A comparison of the methylene interrupted sequence and the conjugated sequence of double bonds is shown in **Figure 2**.

Both LA and ALA have methylene interrupted double bonds and are essential fatty acids. In addition, each serves as a precursor of unique eicosanoids, which are powerful physiologic mediators of cell function in numerous tissues. These findings have added new complexities to their essential nature because foods generally contain both the 18-carbon precursors and their 20- and 22-carbon long-chain polyunsaturated fatty acid (LCPUFA) derivatives. These derived LCPUFAs are important because under some conditions or life stages there may not be adequate conversion of the precursor 18-carbon acids, making them conditionally essential.

Comparison of Bonding Patterns

C-C=C-C-C=C-C

methylene interrupted double bonds

-C-C=C-C=C-C-

conjugated double bonds

Figure 2. Comparison of methylene interrupted fatty acid sequence (essential) and conjugated sequence (nonessential but potentially functional, eg, conjugated linoleic acid). Note the presence of the carbon atom between the double bonds in the methylene interrupted sequence.

THE UNIQUE FATTY ACID REQUIREMENTS OF CATS

Omega-6 Fatty Acids and Adult Maintenance

In the 1970s, a series of experiments on feline essential fatty acid (EFA) metabolism reported that domestic cats could not convert LA to arachidonate. This finding suggested that cats do not possess the necessary delta-6-desaturase to perform this conversion[2-4] (**Figure 3**). These observations were confirmed and extended by Sinclair et al[5], who concluded that while cats did not have significant delta-6-desaturase activity, they did possess both delta-5- and delta-8-desaturases. These and other authors[6,7] thus proposed an alternative pathway to AA synthesis in cats (**Figure 3**). Subsequent studies found that when cats were fed foods rich in LA, both plasma and liver amounts of AA were similar to when the food also contained tuna oil.[8] Thus, cats appear to be able to synthesize AA from LA at least to some extent and an alternate pathway for its synthesis may exist. More recently, evidence of limited delta-6-desaturase activity in the liver and brain of cats fed a food completely devoid of arachidonate has been confirmed with sophisticated stable isotope techniques combined with gas chromatography and mass spectrometry.[9] However, these data do not rule out the existence of the alternate pathway in cat tissues.

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Omega-6 Fatty Acids, Growth, and Reproduction

A study by Macdonald et al[10] found that male cats fed an LA-deficient food showed tubular degeneration of the testes compared to cats fed a control food. Also, the fatty acid profile of testicular phospholipids had higher arachidonate concentrations when LA was present compared to when it was deficient. In addition, queens were unable to bear live kittens when fed the deficient food. It was concluded that LA appeared to meet the requirement for spermatogenesis but that arachidonate is necessary for reproduction in females.

The need for dietary arachidonate for successful reproduction in queens was recently revisited by feeding one of three foods containing either 1% corn oil, 3% corn oil, or 1% corn oil plus 0.02% arachidonate before mating and throughout pregnancy.[11] All animals became pregnant but a high incidence of congenital defects and low viability was found in the 1% corn oil group. By contrast, the food containing 3% corn oil without arachidonate supported reproduction. This study showed that queens are incapable of effective reproduction when maintained on a food low in polyunsaturates, including LA, but that the addition of small amounts of arachidonate restored this function. However, because the food containing 3% corn oil without arachidonate also supported reproduction, it was concluded that other

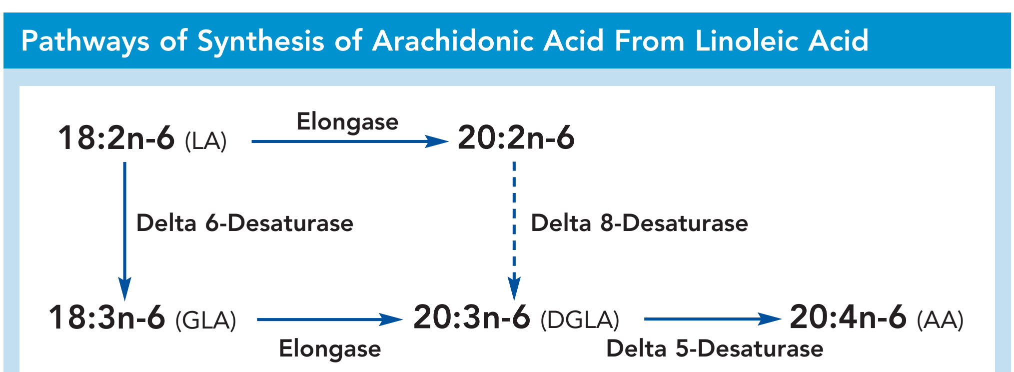

Figure 3. Pathways of synthesis of arachidonic acid from linoleic acid, showing an alternate scheme involving delta 8- and delta 5-desaturation and bypassing the delta 6-desaturation step.

dietary factors may be involved. Of additional interest is that neonatal kittens from queens fed arachidonate in this study were found to also synthesize it from labeled LA precursor.[12]

More recently, Morris and colleagues reported the effect of arachidonate-depleted foods on both male and female feline reproduction.[13] They confirmed their earlier finding that male cats fed foods containing LA but not arachidonate are fertile. In their study, 5 male cats provided foods containing hydrogenated vegetable oil without arachidonate mated with queens either individually or in small groups. The queens had been given commercial dry-type food. Of the 13 queens that mated, 12 conceived and had litters of 3 to 8 kittens. All kittens were observed to be clinically normal, although of the 67 live births, 4 kittens from 3 litters died after one day for unspecified reasons. Nonetheless, the litter size exceeded the colony average of the other animals in the laboratory that were given commercial food. Results of this study dietary essentially confirm that AA is not a dietary essential fatty acid for male cats for reproduction.

The picture with respect to reproduction in queens fed this same hydrogenated vegetable oil food devoid of arachidonate was somewhat different, however. In this instance, 4 queens were given this food and all entered estrus, mated, and had subsequent body weight gains consistent with pregnancy.[13] However, most of the live kittens born in these litters were eaten after birth, with the proportion much higher than the historical normal for this colony. Following this initial study, 2 of the queens were supplemented with 0.5 ml of AA and 2 were given 1.0 ml of AA once weekly for 10 weeks using a fungi-derived oil containing 40.7% AA. The queens were bred again, but none conceived after this supplement. It was concluded that some other fatty acid(s), whether alone or in combination with arachidonate, may be necessary for successful reproduction. Which fatty acid this may be is presently unknown.

Linoleic acid appears to meet the requirement for spermatogenesis in male cats but arachidonate is necessary for reproduction in females.

Omega-3 Fatty Acids in Cats

The effects of vegetable-based alpha-linolenic acid on reproduction of queens fed one of two levels of linseed oil (50 or 150 g/kg food) were compared to those of a safflower oil (50 g/kg food) control food[14] (3 queens per group). In the 50 g/kg linseed group, the 3 queens gave birth to litters of 3 to 4 kittens. One queen had a second litter of 2 kittens that both died. The other 2 queens did not have any more litters. In the 150 g/kg linseed oil group, only 1 queen gave birth to 1 kitten, which also died. Cats fed the linseed oil foods ultimately lost body weight. Their tissues were found to contain low concentrations of long-chain omega-6 acids and they developed signs of essential fatty acid (EFA) deficiency. Because feline delta-6-desaturase competes for both ALA and LA, high dietary ALA may preclude the already limited conversion of LA to arachidonate. Thus, excessive amounts of omega-3 acids relative to omega-6 fatty acids may be contraindicated in cats.

Regarding the conversion of vegetable-based omega-3 fatty acids to longer chain forms, adult cats were found to produce eicosapentaenoic acid (20:5 omega-3) and docosapentaenoic acid (22:5 omega-3) in liver and plasma and docosahexaenoic acid (22:6 omega-3 and 22:5 omega-6) in the brain.[11,12] Of particular interest from these findings is that the final step of desaturation to form DHA appears to occur only in cats' nervous tissue and not liver.

The important clinical question is whether the synthetic capacities of cats for the long-chain omega-3 fatty acids are adequate under various life stages. Following their earlier study, Pawlosky et al[12] used foods with various amounts of corn oil and hydrogenated coconut oil prior to mating, and during pregnancy and subsequent lactation. Two reference foods containing AA and DHA also were evaluated. The corn oil foods were capable of maintaining AA concentrations in the developing retina and brain, but only those foods containing DHA could support the high concentrations of DHA generally found in these tissues. Low concentrations of docosapentaenoic acid (22:5 omega-6) were also found, suggesting that kittens

Table 1: Summary of the Essential and Conditionally Essential Fatty Acids for Life Stages in Cats

Nutrient	*Growth*	*Adult*	*Gestation/Lactation*
Omega-6			
LA	X[a]	X	X
AA	C[a]	—	C
Omega-3			
ALA	Rec[b]	—	Rec
EPA[c]	—	—	—
DHA[c]	C	Rec	C

a. X, Essential fatty acid; C, Conditionally essential for the respective life stage
b. Rec, Recommended but no requirement established
c. Many omega-3 LCPUFA sources contain both EPA and DHA; EPA should not exceed 60% of EPA + DHA total

Male cats are able to synthesize enough arachidonate for reproduction, but females require an exogenous source for successful pregnancies and normal litters. For conception to occur, arachidonate may not be needed.

have a low capacity to produce this omega-6 fatty acid as well as DHA. Differences in electroretinograms were observed in the LCPUFA-deficient groups compared to control animals as an index of neural development.

The LCPUFA-deficient foods of Pawlosky et al did not provide kittens with an adequate supply of omega-3 fatty acids for proper accumulation of neural and retinal DHA during development and thus were inadequate for support of optimal visual function.[12] Conversion of either the omega-6 or omega-3 18-carbon precursors may simply not occur to the extent needed in developing or immature cats. Finally, where practical foods were concerned, the presence of small amounts of dietary AA, EPA, and DHA (ie, 0.14%, 0.02%, and 0.03%, as-is basis) in combination with high LA (ie, 4.2%, as is) resulted in insignificant conversion of ALA to LCPUFA when supplied as 0.88% (as is) in the foods of 19- to 20-month-old cats.[15]

SUMMARY AND CONCLUSION

Similar to the situation in other mammals, cats do not synthesize LA and require a dietary supply. Cats also have a limited capacity to synthesize AA and an alternative pathway for it may exist in addition to that defined by limited delta-6-desaturase activity. For maintenance needs, male, female, and neutered cats may be able to meet their requirements at very low levels of dietary inclusion of AA. A summary of the essential and conditionally essential fatty acids of cats is presented in **Table 1**. Specific recommended allowances for each life stage have been made as part of the 2006 National Research Council Nutrient Requirements for Dogs and Cats.[16]

With respect to reproduction, male cats are able to synthesize enough arachidonate for this purpose, but females require an exogenous source for successful pregnancies and normal litters. For conception *per se* to occur, however, arachidonate may not be needed.

For the omega-3 fatty acids, high dietary amounts of alpha-linolenic acid relative to LA may be contraindicated, leading to EFA deficiency signs. As with the omega-6 acids, adult cats can synthesize small amounts of long-chain omega-3 acids from precursors. Nonetheless, in order to support the high retinal and nervous tissue concentrations of DHA needed for development, kittens may require this fatty acid, as conversion of precursors may be insufficient to meet this need.

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Cats do not synthesize linoleic acid and they require a dietary supply.

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