# Essential Fatty Acid Deficiency

In n-3 EFA deficiency, neurologic alterations have been observed, including paresthesia, weakness and inability to walk, pain in the legs, and cloudy vision.

From: Tropical Dermatology (Second Edition), 2017

Related terms:

Lipid, Fatty Acid, Lipid Emulsion, Essential Fatty Acid, Fish Oil, Glucose, Linoleic Acid, Liver Disease, Prematurity

View all Topics

# Cystic Fibrosis and Congenital Anomalies of the Exocrine Pancreas

Arthur B. Atlas, Joel R. Rosh, in Pediatric Gastrointestinal and Liver Disease (Fourth Edition), 2011

## Essential Fatty Acids

Essential fatty acid deficiency in CF is well described, and until recently was thought to be due to malabsorption.[116] Studies support the hypothesis that essential fatty acid abnormalities in CF may be due to CFTR dysfunction, because CFTR has a potential role in cellular fatty acid metabolism.[117,118] Chronic inflammation affects fatty acid metabolism, but CFTR-regulated tissue levels may not reflect plasma fatty acid levels.[118] Linoleic acid and docosahexaenoic acid levels are decreased in CF, and eicosatrienoic acid concentration is increased.[116,117] Linoleic and arachidonic acid (a metabolite of eicosatrienoic acid) are n-6 fatty acids, and docosahexaenoic acid is an n-3 fatty acid. The biologic effects of fatty acids depend not only on the absolute levels, but also on the ratio of n-6 to n-3 fatty acids. In CF there is an increased ratio of arachidonic to docosahexaenoic acid. Metabolites of arachidonic acid are proinflammatory agents, and metabolites of docosahexaenoic acid are potent anti-inflammatory agents. The altered ratio may play a role in increased inflammation in CF. Recent studies, however, suggest that linoleic acid concentration is a more clinically relevant biomarker of essential fatty acid status than the

triene:tetraene ratio in children with CF and PI.[119] High doses of docosahexaenoic acid fed to CF-knockout mice not only correct the fatty acid deficiency, but also reverse the histologic inflammatory changes in the pancreas and ileum.[118,120]

> Read full chapter

# Nutritional Diseases

Ana Maria Mosca De Cerqueira, Felipe De Souza Cardoso, in Tropical Dermatology (Second Edition), 2017

## Etiopathogenesis

EFA deficiency is noted in patients with chronic poor absorption, such as in short intestine syndrome, and in those maintained on oral food formulas deficient in EFA and on long-term parenteral nutrition devoid of lipids. The influence of fatty acids on the immune function of the cells and on the immune response has been researched for over 30 years. A deficiency in EFA impairs cellular immunity, which diminishes while the content of fat in the diet grows. The first studies of the effects of fatty acids on the immune system were connected with the family of polyunsaturated fatty acids (PUFA) *n*-6, also known as omega-6 fatty acids; these are found in many vegetable oils. More recently, there has been interest in the effects of omega-3 fatty acids, or PUFA *n*-3, such as EPA and DHA (found in fish oil and walnuts), and the precursor alpha-linolenic acid (found in flaxseed). Gamma-linoleic acid is an *n*-6 essential fatty acid that the body converts into compounds similar to hormones called prostaglandins, which regulate many of the body functions.

> Read full chapter

# ESSENTIAL FATTY ACIDS

R. Shireman, in Encyclopedia of Food Sciences and Nutrition (Second Edition), 2003

## Essential Fatty Acid Deficiency

Human EFAD of dietary origin is not common in Western countries, and most EFAD research has been conducted on rats. It may occur in patients on long-term total parenteral nutrition (TPN) when EFAs are not included in the TPN formulation. In countries where protein malnutrition occurs, EFAD may occur because of either very low dietary EFA or lack of enzyme synthesis. Originally, it was thought that 18:3*n*-3

could substitute for 18:2*n*-6, but this proved not to be so because the products of the metabolism of these PUFA differ in function. Dietary 18:3*n*-3 does not alleviate the dermatitis of EFAD nor promote growth to the same extent as 18:2*n*-6. The estimated minimal 18:3*n*-3 dietary requirement for children is 0.54% of calories, whereas that for 18:2*n*-6 is about 1.1%. The estimated minimal requirement of 18:3*n*-6 for adults is 1–2 energy percent, with an optimum of 3–6% (approximately 1 tablespoon of oil); the optimum for 18:2*n*-3 is about 2%. The estimated ideal intake range of *n*-3/*n*-6 is 1:2 or 1:3. In both children and adults, the ratio of the two should be considered, because an overabundance of either suppresses some of the desaturation/elongation reactions for the other.

Primary (dietary-related) and secondary etiologies of EFAD in humans are listed in Table 3. There may be other conditions that are secondary to gastrointestinal (GI) pathology or enzyme defects. In cases such as chronic liver disease or hereditary enzyme deficiencies, the EFAD is not due to a lack of 18:2*n*-6 and 18:3*n*-3 in the diet but is due to an inability to metabolize them further to the necessary end products (20:4*n*-6 and 22:6*n*-3). Some experts contend that if 18:2*n*-6 is sufficient in the diet, typical symptoms of EFAD do not occur, but it is accepted by most that *n*-3 FA are needed for normal neuronal development and visual acuity, based on animal studies. The importance of the long-chain 20:4*n*-6 and 22:6*n*-3 in humans is illustrated by the effects of genetic enzyme deficiencies such as Sjogren–Larsson syndrome and acrodermatitis enteropathica; despite normal intakes of 18:2*n*-6, there are severe symptoms of EFAD including mental retardation, ichthyosis, and very abnormal prostaglandin metabolism (Table 4).

Table 3. Etiology and characteristics of primary and secondary EFAD

| *Etiology* | *Result* | *Effect* |
|---|---|---|
| Chronic malnutrition, especially in children | Lack of dietary fat and protein | Very abnormal serum FA patterns |
| Decreased enzyme synthesis | | Low total serum PUFA |
| Long-term fat-free TPN | Lack of dietary EFA | Abnormal serum 20:3*n*-9/20*n*-6 |
| Various fat malabsorption conditions | Secondary to pancreatic insufficiency, bowel cancer, or other serious GI diseases | Low total serum PUFA |
| Sjogren–Larsson syndrome | Genetic enzyme defect in desaturation and elongation | Low serum levels of C20 and 22 PUFA |
| Acrodermatitis enteropathica | Genetic defect in □5 and □6 desaturase activity | Very low levels of 22:6*n*-3 |
| End-stage liver disease | Impairment in desaturase and elongase activities | Very low serum levels of LCPUFA |

Table 4. Characteristics of EFAD in humans

*Known clinical manifestations*

Dermatitis; dry, scaly skin; impetigo; eczema; generalized erythema
Coarse, sparse hair
Increased frequency of stools
Decreased growth rate
Cellular hyperproliferation in skin, alimentary tract, and urinary tract
Possible immune impairment
Slow wound repair

*Suggested manifestations associated primarily with 22:6n-3 deficiency*

Slower early learning behavior (based on animal studies)
Visual perturbations (based on animal studies)
Mental retardation in human genetic defects involving desaturases and elongases

*Known biochemical aberrations*

Serum 20:3*n*-9/20:4*n*-6 greater than 0.4

Increased serum 16:1*n*-7, 18:1*n*-9, and 20:3*n*-9; decreased 18:2*n*-6, 20:3*n*-6, and 20:4*n*-6

In the past, a serum triene/tetraene ratio of 1 was considered a biochemical indication of serious EFAD. An EFA-deficient diet results in insufficient 18:2*n*-6, 20:4*n*-6, and 22:6*n*-3 in tissues, but there is also marked enrichment in eicosatrienoic acid (20:3*n*-9) in blood and liver. Status is now usually measured more accurately as the 20:3*n*-9/20:4*n*-6 ratio in serum phospholipids. A normal value is considered to be about 0.1–0.2. Occasionally, when abnormalities are due to an enzyme deficiency rather than to diet, some other index may be more useful. For example, the normal conversion of 18:2*n*-6 to 20:4*n*-6 results in a ratio of 18:2*n*-6/20:4*n*-6 of about 1.6, but in severe dietary EFAD, it may be 1.2. In achrodermatitis enteropathica, however, very little arachidonic acid is synthesized, and this ratio may be 10 or larger.

Serum FA patterns and symptoms that resemble EFAD occur in a variety of disorders. Marginal or frank EFAD is somewhat common in young cystic fibrosis (CF) patients, but whether this is a consequence of decreased fat absorption or a defect in FA metabolism, or both, is not known. While all serum FA levels are decreased in some CF patients, the fact that fewer desaturation products are present has led to the speculation that there is an enzymatic defect in FA metabolism. Oxidative stress disorders tend to show FA patterns characteristic of EFAD. The reason is unknown. Perhaps reactive oxygen species or products of oxidative damage act to decrease the activity of desaturases. Whereas high amounts of PUFA in the diet are said to increase the requirement for vitamin E, in studies on concomitant EFAD and vitamin E deficiency, measures of autooxidative susceptibilty in rat red blood cells indicated that EFAD actually potentiated the vitamin E deficiency. Patients with malabsorption syndromes or long-term depressed oral intake or TPN may exhaust stores of EFA and exhibit clinical signs of EFAD, especially dermatitis. Also, TPN formulations with very high ratios of *n*-6 to *n*-3 have resulted in symptoms of *n*-3 deficiency, including neuropathy and immune impairment in animals.

Nervous tissues in primates and other animals are rich in *n*-3 PUFAs and their products. There have been numerous reports of learning deficits and other effects on nervous tissue in animals deprived of all *n*-3 PUFAs. If 22:6*n*-3 is not added to the media of retinal photoreceptor cells in culture, they degenerate and die, presumably because of activation of an apoptotic pathway. But reports of effects in humans have been less convincing, largely because long-term controlled dietary experiments cannot be conducted. Episodic numbness, weakness, pain in the legs, and blurring of vision occurred in children on TPN formulas that did not contain *n*-3 PUFA. These effects were reversed after inclusion of *n*-3 FA in the formula. Researchers have noted that some of the physical symptoms of attention-deficit hyperactivity disorder are similar to those of EFAD and that many of the diagnosed children have decreased serum 20:4*n*-6 and 22:6*n*-3 levels. Conversion of 18:2*n*-6 and 18:3*n*-3 requires desaturase and elongase enzymes, which may not be fully active in the preterm infant and neonate. Long-chain PUFAs (LCPUFAs), especially 22:6*n*-3, are particularly important for brain and nerve cell development *in utero*, but the fetus does not synthesize the long-chain EFA to any extent. Thus, maternal intake may be more important than has generally been recognized. Many investigators support the inclusion of *n*-3 PUFA, especially 22:6, in formulas for both premature and term infants. There remains some controversy over whether the inclusion is needed, since several studies have shown no detectable benefits for breast-fed infants whose mothers took supplemental dietary 22:6*n*-3. While there is some evidence of the efficacy of *n*-3 long-chain PUFA in increasing early visual maturation in preterm infants, there is no demonstrated long-term benefit. Six randomized trials with supplementation of infant formulas with LCPUFA were reviewed by Simmer, who concluded that there is little evidence to support the hypothesis that supplementation with 20:5*n*-3 and 22:6*n*-3 conferred any benefit on visual or cognitive development or influenced the growth of term infants.

> Read full chapter

# Fat and fatty acids

Lori K. Warren, Kelly R. Vineyard, in Equine Applied and Clinical Nutrition, 2013

## Essential fatty acids

Linoleic acid (LA; 18:2*n*-6) and □-linolenic acid (ALA; 18:3*n*-3) are essential fatty acids (EFA) that must be supplied by the diet. Mammals lack the Δ12- and Δ15-desaturase enzymes necessary for desaturation of an 18-carbon fatty acid at the omega-3 (or Δ15) or omega-6 (or Δ12) positions. Therefore, LA and ALA cannot be synthesized in the body and are deemed “essential.” By comparison, plants and algae contain

ample amounts of the Δ12- and Δ15-desaturase enzymes and, as a result, LA and ALA are two of the most prevalent fatty acids found in plant tissues and oils.

An EFA deficiency has not been described for the horse, even in those consuming diets almost devoid of fat. Sallmann et al (1991) observed no clinical abnormalities in ponies fed very low fat diets containing 0.03% and 0.14% linoleic acid for 7 months. The absence of signs of deficiency in these ponies may have resulted from mobilization of body fat stores that could have met EFA needs during the prolonged period of low intake. In other species EFA deficiency is characterized by dry or scaly skin, dry coat, hair loss and decreased reproductive efficiency. The NRC (2007) has recommended a LA intake of 0.5% DM for horses although justification for this recommendation was not described. For a 500 kg horse with a DM intake of 2% BW, the NRC recommendation would amount to a daily intake of 50 g of LA. Across a variety of other mammalian species, a minimum of 1% of total dietary energy intake as LA has been given as a general recommendation to prevent EFA deficiency (Gurr et al 2002). Extrapolating this to a 500-kg horse consuming 20 Mcal DE/day, and assuming a conservative estimate of 50% availability, the LA requirement is 45 g/day. Thus, the NRC (2007) recommendation for LA in horses appears to approximate the minimum intake guideline for other mammalian species. This requirement is likely to be met in horses consuming adequate quantities of good quality forage and is easily met by diets supplemented with fat, as most high-fat feedstuffs and oils are rich in LA (Table 7-1). Currently there are no guidelines for minimum daily ALA intake, although a horse consuming adequate amounts of fresh forage and/or good quality hay will likely receive ample amounts of ALA in the diet (Table 7-1). Supplementation with both LA and ALA should be considered in horses receiving poor quality or limited amounts of forage for prolonged periods of time. Because an ALA requirement has not been established for horses or other herbivores, provision of ALA in amounts resulting in a 5□:□1 to 10□:□1 ratio of LA□:□ALA might be considered adequate, as this has been recommended for other species (NRC 2005).

## Key Points

•Linoleic acid (omega-6) and □-linolenic acid (omega-3) cannot be made by the horse and must be supplied by the diet.•**E**ssential fatty acid requirements have not been established for horses.•Most equine diets will likely meet essential fatty acid needs unless poor quality rations are consumed for prolonged periods.

> Read full chapter

# Breast pain and nodularity

Hughes, Mansel & Webster's Benign Disorders and Diseases of the Breast (Third Edition), 2009

## Evening primrose oil

The fatty acid deficiency hypothesis has led to the testing of treatment by supplementing the diet with an EFA. One preparation which has proved valuable is evening primrose oil (EPO) which is unique in containing 7% linolenic acid and 72% linoleic acid and represents the richest natural source of EFAs known (Fig. 8.14).

Early trials showed EPO to be useful for treating mild cases of cyclical mastalgia.[104] This agent is potentially useful in mild to moderate cases as it has virtually no side effects. Patient acceptance is high as it is viewed as a 'natural substance' rather than a hormone or drug. Interestingly, the trials of EPO also suggested that noncyclical pain is unresponsive to this therapy, as had been found in the bromocriptine trial, although this conclusion has been modified with further analysis of the noncyclical group, as discussed later. The positive balance of moderate effectiveness and minimal side effects leads us to use it as the first-line treatment in patients with mastalgia of moderate severity. In our own clinic experience, of 85 patients treated with EPO as first-line therapy, 58% had a clinically useful response (CBS I or II). In our overall experience of 241 patients treated only 9 (4%) complained of a significant adverse effect.

However, more recent studies have suggested that the efficacy of EPO may be limited. Blommers et al. carried out a study of evening primrose oil and fish oil in chronic severe mastalgia, and were not able to demonstrate a significant improvement on EPO.[105] Furthermore, a recent large multicentre UK study of EPO with and without antioxidants and multivitamins in the primary and secondary care settings showed a high placebo response, and EPO was not shown to be better than placebo.[106] As a result of these data and other equivocal results, EPO has been removed from prescription lists in the UK, but it remains available over the counter in a variety of chemists and health food stores. We still suggest that patients with mild/moderate mastalgia try this medication as the first-line therapy, as most women do have some response and side effects are minimal.

> Read full chapter

# Essential Fatty Acid Deficiency in Cystic Fibrosis

S. Van Biervliet, B. Strandvik, in Diet and Exercise in Cystic Fibrosis, 2015

## 40.3.2 Etiology of Fatty Acid Disturbances

Initially the EFA deficiencies were exclusively considered to be attributed to the malnutrition, pancreatic insufficiency and low energy intake in severely ill patients [21–25]. The lack of a correlation between nutritional status, pancreatic function and EFA deficiency as well as the persistence of the EFA deficiency despite increased fat intake pleads against this theory [24,25,27,37,42,48]. Further on, the fatty acid abnormalities were commonly present in the first weeks of life [49]. There is furthermore a significant association between EFA deficiency and the genotype severity, suggesting a mutation related problem [37,38]. Also without specific supplementation, some studies were able to demonstrate an association between fatty acid intake and serum fatty acids [50], suggesting that in the context of a high fat intake, EFA's were not used for energy [51].

As described above, eicosanoids are important derivatives of LCPUFA. In CF, in contrast to other EFA deficient patients, the increased systemic eicosanoid production is maintained despite of the LA deficiency [13]. Carlstedt-Duke et al. demonstrated a defective $PLA_2$ regulation in CF leading to an increased AA turnover [52], which was confirmed by other research groups [53,54]. The increased inflammatory state has been demonstrated in multiple studies not only demonstrating pulmonary inflammation even in absence of bacterial infection [55,56] but also intestinal inflammation [11]. The prostaglandin overproduction was associated to genotype rather than disease severity [57]. The increased expression and activity of fatty acid desaturases further supported this rapid transformation to LCPUFA [58–61]. A rapid turn-over of phospholipids might also be related to changes in thiol and phospholipid metabolism suggested by others [14,62].

Recent studies support the indications for defective $PLA_2$ inhibition [52]. Bensalem et al. described a low annexin 1 in both patients with CF and CF knockout mice [63]. Annexin 1 is a potent $PLA_2$ and Cox 2 inhibitor [64]. Although the study results in CF concerning ceramides, important for phagocytosis [65], are not unequivocal, the associations to the plasma fatty acid pattern as well as to the CFTR mutations are interesting [66,67], especially since CF patients are known to display defective pseudomonas internalization [68]. The importance of these pathways in CF have further been demonstrated by Radzioch et al. showing a normalization of LCPUFA and ceramide levels in CF mice by giving fenrenitide, a IL-1 □ inhibiting retinoid, which interferes with the ceramide transformations [66,69].

Finally, as PUFAs are very susceptible for peroxidation, this could also play a role in the PUFA deficiency. CF is characterized by an increased oxidative stress, and antioxidative supplementation has been shown to improve lung function [70,71]. Furthermore, a relationship between DHA and vitamin E has been demonstrated

[37], which might account for decreased DHA concentrations in CF, since DHA is very susceptible for peroxidation [72].

> Read full chapter

# Fat Requirements

Linda P. Case MS, ... Melody Foess Raasch DVM, in Canine and Feline Nutrition (Third Edition), 2011

## DEFICIENCIES AND EXCESSES

Low amounts of fat in the diet can lead to deficiencies in both total energy and EFAs. In addition, the palatability of dog and cat diets is strongly affected by fat content. To a limit, increasing fat results in enhanced palatability. Similarly, decreasing fat below a certain level causes decreased acceptability of the diet. This effect is believed to be the result of both the texture and the flavor that fat contributes to a pet food. Because low-fat diets may not be readily accepted by pets, their potential for causing an energy or EFA deficiency is exacerbated by their causing a decrease in food intake.

Because linoleic acid is important for the maintenance of the epidermal water barrier, and because skin cells have a high rate of turnover, the skin is particularly vulnerable to EFA deficiencies. In dogs, linoleic acid deficiency results in a dry, dull coat; hair loss; skin lesions; and poor wound healing. Over time, the skin becomes pruritic, greasy, and susceptible to infection. A change in the surface lipids in the skin alters the normal bacterial flora and can predispose the animal to secondary bacterial infections.[30] Epidermal peeling, interdigital exudation, and otitis externa have also been reported in EFA-deficient dogs.[31] Linoleic acid deficiency in cats results in similar dermatological signs. In addition, kittens will fail to grow normally, and may develop fatty degeneration of the liver and fat deposition in the kidneys.[32,33]

Although not reported in dogs and cats, deficiency signs of n-3 fatty acids in other species include nervous system abnormalities, decreased visual acuity, retinal abnormalities, and reductions in learning and memory.[34,35] These signs reflect the high concentrations of n-3 LCPUFAs found in the brain and retinal rod cells of most species and the importance of these fatty acids during early development. Although signs of n-3 EFA deficiency have not been reported in dogs and cats, the high concentrations of DHA in nervous and retinal tissues and high demands during reproduction and early development suggest that deficiencies in dogs and cats would produce similar signs.

Today, overt EFA deficiencies are not common in dogs and cats. When they do occur, deficiencies are usually associated with the consumption of diets that are either poorly formulated or have been stored improperly. Most well-formulated diets contain sufficient amounts of EFAs. However, exposure to high environmental temperatures and humidity for long periods can promote oxidation of the unsaturated fatty acids in the food. This process is commonly referred to as *rancidity*. If insufficient antioxidants are present, EFA activity is destroyed. As the unsaturated fats are destroyed by oxidation, not only is EFA activity lost, but so are the vitamins D, E, and biotin. EFA deficiency in dogs and cats can also occur as a complication of other diseases, such as pancreatitis, biliary disease, hepatic disease, and malabsorption.

Although uncommon, essential fatty acid (EFA) deficiency results in a dry, dull coat; hair loss; skin lesions; and poor wound healing. Over time, the skin becomes pruritic, greasy, and susceptible to infection. A change in the surface lipids in the skin alters the normal bacterial flora and can predispose the animal to secondary bacterial infections. EFA deficiency can result from feeding poorly formulated or rancid foods, but it can occur secondary to pancreatitis, biliary disease, hepatic disease, or malabsorption.

Although commercially prepared foods will not normally cause fat or EFA deficiency, many pet owners believe that supplementing their pet's diet with corn oil or some other type of fat will improve coat quality. This will only be effective if the pet is truly suffering from an EFA or fat deficiency. If that is the case, completely changing the diet to a well-formulated pet food that supplies all of the essential nutrients in their correct proportions, including fat and EFAs, is recommended. Simply adding a source of fat or EFAs to a deficient diet without assessing levels of both n-3 and n-6 fatty acids in the diet may or may not solve the EFA deficit and has the potential to further imbalance a food that is already inadequate. Conversely, fatty acid supplementation or altering the fatty acid levels or ratios in the diet can be effective in treating certain inflammatory and hyperproliferative skin diseases in companion animals. Recent research indicates that modifying the fatty acid profile of the diet can promote the formation of fewer inflammatory agents, resulting in a reduction in clinical signs (see Section 5, pp. 386-395 for a complete discussion).

Excess fat intake can also be detrimental to a pet's health. As stated previously, dogs and cats are able to digest and assimilate diets containing high levels of fat. However, providing more fat than the gastrointestinal tract can effectively digest and absorb results in fatty stools (steatorrhea) and diarrhea. This problem is most commonly observed when pet owners provide their dog or cat with table scraps composed predominantly of fatty foods. The long-term consumption of diets that are very high in fat may lead to weight gain and obesity because of the high palatability and energy density of the diet. Feeding diets that are very high in fat and do not have all

other nutrients balanced relative to energy density may result in the development of deficiencies in other essential nutrients.

Lastly, excessive levels of LCPUFAs in the diet cause an increase in an animal's vitamin E requirement. Vitamin E functions as an antioxidant in the body, protecting cellular membrane lipids from peroxidation. The vitamin is preferentially oxidized before the unsaturated fatty acids, thus protecting the fatty acids from rancidity; however, vitamin E is destroyed in this process. Therefore as the level of unsaturated fatty acids in an animal's diet increases, so does the animal's requirement for vitamin E. If a pet food contains very high levels of LCPUFAs or if an owner is supplementing a balanced diet with high amounts of corn or vegetable oil, vitamin E in the diet must concomitantly be increased. For example, when hunting dogs were fed high amounts of high fat food scraps as their primary diet, they developed clinical signs of vitamin E deficiency.[36] Similarly, a condition called *pansteatitis*, or "yellow fat disease," occurs in cats when their diets are high in unsaturated fatty acids and marginal or low in vitamin E (see Section 4, p. 279).

> Read full chapter