Today's Dietitian
The Magazine for Nutrition Professionals
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TODAY'S DIETITIAN

Achieving a Healthful Omega Balance

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Suggested CDR Learning Codes: 2020, 3100, 4040, 5160; Level 2
Suggested CDR Performance Indicators: 8.1.4, 8.3.6, 10.4.4

The impact of dietary fat intake on health is an evolving topic, with new research frequently emerging to shift opinions and justify changing recommendations to prevent and treat specific disease conditions and promote overall health.

One area of growing interest is the importance of essential fatty acid (EFA) balance. Omega-3 and omega-6 fatty acids, also referred to as n-3 and n-6 fatty acids, are polyunsaturated fatty acids (PUFAs) that must be consumed in the diet because they cannot be synthesized by the human body. While PUFAs have long been touted as the most healthful fats, there is increasing attention paid to understanding the differing health impact of the two classes of dietary PUFAs in order to develop more effective dietary recommendations.

A key concern is the balance of the two PUFA subtypes, according to Harris and Klurfeld: "Although the health benefits of omega-3 fatty acids are widely appreciated, those of the omega-6 fatty acids have become somewhat controversial in recent years, with some viewing them as harmful at current intakes and others … supporting the status quo."[1]

Consumption data demonstrate that the average American has a relatively high intake of omega-6 and consumes too little omega-3. There's increasing evidence that this imbalance contributes to increased risk of chronic diseases, particularly those in which inflammation plays a role. Improving the balance of PUFA types, rather than just increasing intake of PUFAs overall, is now considered a worthwhile approach to promoting optimal health.

This continuing education course reviews the physiologic functions of omega-3 and omega-6 fatty acids and their role in promoting optimal health and preventing or improving the symptoms of certain diseases, including cardiovascular disease (CVD) and chronic inflammatory conditions. It also discusses the optimal ratio of omega-3 to omega-6 intake, how American diets measure up, and the role of supplementation in helping individuals achieve a balanced intake.

Types of Omega-3 and Omega-6 Fats and Their Essentiality

Omega-3 and omega-6 fatty acids have multiple double or "unsaturated" bonds in their carbon chains, making them PUFAs. Following the naming convention, the first double bond in the omega-3 family occurs between the third and fourth carbons, while that of the omega-6 family occurs between the sixth and seventh carbons. Although humans can synthesize certain other fatty acids from raw materials in the body, we lack the enzymes needed to place a double

bond at one of these positions in the carbon chain. Because of that, omega-3 and omega-6 fats must be consumed in the diet.

The parent fatty acid in the omega-3 family is alpha-linolenic acid (ALA), which is converted into a number of longer chain fatty acids. Two of these, DHA and EPA, have physiologically important roles.

The conversion rate of omega-3 ALA to DHA and EPA is small. In young women, approximately 21% of ALA consumed in the diet is converted to EPA and 9% is converted to DHA; in young men, only 8% of dietary ALA is converted to EPA, and 0% to 4% is converted to DHA.[2] Therefore, it's beneficial to consume some EPA and DHA directly from foods. Unfortunately, EPA and DHA are found in relatively few foods, mainly oily fish, algae, and organ meats, which puts adequate access to these important nutrients out of reach for many.[2,3] ALA itself is present in green leafy vegetables and certain nut and seed oils including flax, chia, and walnut.

Linoleic acid (LA), the parent fat of the n-6 family, is converted to the n-6 arachidonic acid (AA). In contrast with omega-3 fatty acids, LA is found in a wide variety of oils common in the daily diets of Americans. This contributes to the imbalanced intake of omega-3 and omega-6 fatty acids. Blood concentrations are directly affected by intake, and because one set of enzymes metabolizes both types of fats, the relative effects of the omega-3 and omega-6 families is dependent upon their relative amounts in the bloodstream. Thus, achieving a balanced dietary intake of EFAs is a worthwhile goal.[4]

The typical American diet provides at least 10 times more omega-6 than omega-3 fatty acids, and some estimates place the ratio of omega-6 to omega-3 as high as 25:1.[3,5] According to Simopoulos in a 2008 article in ***Society for Experimental Biology and Medicine***, there's evidence that historical intakes of EFAs were more balanced, possibly as close as 1:1. For reasons discussed below, there's broad agreement that increasing consumption of omega-3s to reduce the omega-6:omega-3 ratio will promote better health.[3]

Physiologic Function

Omega-3 and omega-6 PUFAs perform a number of important functions in the body. They're embedded in cell membranes, affecting the permeability and fluidity of these structures. They are also part of the brain and central nervous system, protecting nerves and supporting connectivity between synapses. These fatty acids are needed for cell division, growth, and repair, including that which takes place in hair, skin, and bone development. They affect enzyme activity and regulate the expression of certain genes, particularly those involved in inflammation and in the synthesis and metabolism of fatty acids.[2,3]

DHA, the major fatty acid in the brain, is important in brain development and function, including in signal transduction between neurons. AA is also found in high concentrations in the brain, and together DHA and AA make up 20% of the fatty acids in the brain.[6] DHA is incorporated into the membranes of the retina of the eye and plays an important role in development of the retina and proper vision.

AA and EPA are converted into hormonelike compounds called eicosanoids, including prostaglandins, thromboxanes, and leukotrienes, which help regulate a wide variety of physiologic functions, in particular immune and inflammatory processes. The eicosanoids formed from the omega-6 AA are released in response to injury and stress, generally with proinflammatory effects, while those derived from the omega-3 EPA have opposite effects, partly due to their ability to inhibit the production of the omega-6-derived eicosanoids.[7] Because of their anti-inflammatory effects, omega-3s may protect against diseases with persistent inflammatory components, including CVD, rheumatoid arthritis, asthma, inflammatory bowel disease, cancer, neurodegenerative illnesses, and other conditions.[3]

Omega-6 and omega-3 fatty acids are also involved in the regulation of certain genes that govern inflammation. Omega-3 PUFAs interact with the transcription factors nuclear factor κB and peroxisome proliferator-activated receptors to reduce the production of inflammatory proteins. EPA and DHA inhibit the production of interleukin 6 and interleukin 8, immune proteins that cause inflammation in response to trauma and which are implicated in a variety of chronic illnesses, as well as tumor necrosis factor alpha (TNF-α), a type of cytokine, or cell signaling protein, that triggers systemic inflammation in response to acute injury or illness and leads to cell death.[7]

Inflammation

Inflammatory processes are influenced by the proportion of fatty acid types in cell membranes, which are in turn influenced by fatty acid intake.[7]

Because omega-3 PUFAs, especially those from fish and fish oils, have strong anti-inflammatory power, there's great interest in determining the potential benefit of supplementation with these oils for a host of inflammatory conditions associated with diet-related disease, including rheumatoid arthritis, Crohn's disease, ulcerative colitis, asthma, allergies, type 1 diabetes, atherosclerosis, and obesity.[7]

There's evidence that omega-3 fatty acids can reduce the chronic, low-grade inflammation associated with obesity that occurs primarily in adipose tissue.[8] Adipose or fat cells secrete TNF-α, interleukins, and other proteins that trigger an inflammatory response. This abnormality is believed to contribute to the metabolic complications associated with obesity. Omega-3 PUFAs also improve glucose metabolism and alleviate insulin resistance induced by a high-fat diet, with an effect as great as that of insulin-sensitizing drugs.[8]

Because omega-3 and omega-6 fats balance some of each other's effects in the body, especially when it comes to inflammation, according to Wang and Huang, "The ratio of dietary n-6 to n-3 PUFA, rather than the absolute amount of n-3 PUFA, is important in determining the development of inflammatory response."[8]

CVD

The benefits of omega-3s on CVD risk were first suspected in the 1970s, when observations were made that the Inuit people, whose diet consists of large amounts of marine omega-3 fatty acids, have extremely low rates of inflammatory and immune diseases, including CVD.[9] Since then, a significant body of research has confirmed the reduction in CVD risk with increasing

consumption of omega-3s. The protective effect results from a variety of mechanisms, including improved blood lipid profiles, decreased blood pressure, normalization of heart rhythm, and decreased inflammation.

Omega-3s decrease levels of triglycerides, which are a major risk factor for heart disease. Fish oil supplements exert the strongest effect, reducing triglycerides by as much as 30%. Both omega-3 and omega-6 PUFAs improve cholesterol profiles, increasing levels of the protective HDL particle and reducing LDL cholesterol. High doses of fish oil (eg, 3 g per day) may also be effective in reducing blood pressure in people with hypertension.[5] EPA reduces the inflammation in blood vessels that can trigger heart attacks and strokes. DHA increases blood flow and reduces inflammation primarily in the brain.[3]

A 2009 review of 11 randomized controlled trials evaluating the cardioprotective effects of omega-3 supplementation found a decrease in cardiac deaths, all-cause mortality, and other cardiovascular events with supplementation.[10] The benefits were greatest for those at high risk.[10] The average dose of EPA/DHA was 1.8 +/- 1.2 g/day, and supplements were taken for at least one year.[10] The authors concluded that omega-3 supplementation should be used in the secondary prevention of cardiovascular events, and that a dose of at least 1 g per day is needed for a treatment effect.[10]

There is conflicting evidence about the effect of omega-6 fatty acids on CVD. Numerous observational studies have found an association between omega-6 PUFAs and reduction of CVD risk factors such as blood pressure and LDL cholesterol, as well as lowered risk of death from heart disease.[11] However, experimental trials designed to evaluate this cause-and-effect relationship are scarce. A 2015 review found only four randomized controlled trials evaluating the impact on CVD risk with an increase or decrease of omega-6 intake, and ultimately determined that there is insufficient evidence of any effect on CVD risk factors with omega-6 intake.[12]

A potential explanation for the conflicting evidence of the impact of omega-6 PUFAs on CVD risk is that they may have a protective effect when they replace other dietary components that are known to increase risk of heart disease, rather than having a direct benefit themselves. Indeed, replacing saturated fatty acids or refined carbohydrates with omega-6 PUFAs in the diet improves the cholesterol profile and decreases the risk of CVD. According to Harris et al, “The replacement of 10% of calories from saturated fatty acid with omega-6 PUFA is associated with an 18-mg/dL decrease in LDL cholesterol, greater than that observed with similar replacement with carbohydrate.”[13] A 2009 review of the association between omega-6 fatty acids and CVD calculated a 16% reduction of CVD risk when 10% of saturated fat calories were replaced with omega-6 PUFAs in subjects’ diets.[11]

Another line of thinking suggests that because omega-6s promote inflammation, and because inflammation is an important contributor to CVD, reduction in these fatty acids would have a protective effect.[13] Specifically, according to Al-Khudairy et al, “There is concern that high levels of dietary of omega-6 will have a proinflammatory effect by increasing the production of 2-series prostaglandins and 4-series leukotrienes” and, thus, increase CVD risk.[12]

A second mechanism proposed for the potential negative effect of omega-6 PUFAs on CVD risk is the fact that, when incorporated into LDL particles, omega-6 PUFAs are highly susceptible to oxidation. An LDL particle thus damaged can promote vascular inflammation and contribute to CVD etiology.[13]

To add to the uncertainty, a 2009 science advisory from the American Heart Association synthesized a body of research on the impact of omega-6 PUFAs on CVD risk factors and found that both higher consumption and higher plasma levels of omega-6 PUFAs were associated with lower levels of inflammatory markers.[13]

Although the jury is out on whether omega-6 fatty acids increase or decrease CVD risk, there is ample evidence that increased omega-3 status benefits heart health. However, it's important to note that not every study points to a beneficial role for omega-3s. For instance, a meta-analysis of 11 randomized controlled trials found that supplementation with DHA from algal oil may have both positive and negative effects on heart disease risk factors.[14] Most of the studies lasted six weeks and provided a median dose of 1.68 g per day of DHA. The researchers observed a 15% decrease in triglycerides and a 5% increase in HDL cholesterol, changes that should help reduce CVD risk. However, there was also an 8% increase in LDL cholesterol in participants supplemented with algal oil;[14] an increase in LDL cholesterol is believed to elevate risk of CVD.

Still, researchers suggest that studies showing a negative or neutral effect of omega-3 fats on CVD risk have anomalous results because they do not use a therapeutic dose in their intervention. In a 2014 meta-analysis on the impact of omega-3 PUFA supplementation on the incidence of cardiovascular events in people with peripheral arterial disease, only two of five trials used therapeutic doses greater than 1 g per day.[15]

A majority of research overwhelmingly points to a benefit of omega-3 fats on cardiovascular risk. And, according to the National Institutes of Health (NIH) Office of Dietary Supplements, consumption of fish oil reduces the risk of heart disease by reducing triglyceride levels and lowering blood pressure, among other effects. Fish oil intake also reduces the risk of heart attack and death from heart disease.[3]

Population studies support this recommendation. In the Health Professionals Follow Up Study, 45,722 men were followed for 14 years. The data reflected that those who had higher intakes of omega-3 PUFAs from either plant or marine sources had lower risk of coronary heart disease regardless of consumption levels of omega-6 PUFAs.[16]

Finally, there is growing evidence that the ratio of omega-3 to omega-6 intake has an impact on CVD. EFA intake directly influences tissue fatty acid content. A higher intake of the omega-6 LA inhibits incorporation of omega-3 fats into cell membranes. The omega-3 index is the sum of EPA and DHA as a percentage of total fatty acids in erythrocyte or red blood cell membranes[1] and has been proposed as a biomarker for cardiovascular health, with lower omega-3 index associated with an increased risk of CVD.[17]

Brain Development and Neurological Function
The omega-3 DHA is important for brain development and neurological function, especially in the developing fetal brain.

Resolvins are a class of compounds produced from EPA and DHA that help reduce inflammation in the brain. The DHA-derived resolvin reduces inflammation that occurs in the brain during ischemic events that block or slow blood flow. EPA works in the brain in a manner similar to the way it functions elsewhere in the body, by downregulating the production of proinflammatory eicosanoids.[3,18]

Omega-3 PUFAs play a role in cognitive decline. Concentrations of EPA, DHA, and total omega-3s are significantly reduced in the blood of patients with dementia.[19]

In older adults, fish intake and plasma concentrations of DHA are inversely associated with cognitive decline.[20] Although EPA and DHA supplementation in healthy adults appears to have no benefit, supplementation in adults with mild cognitive impairment has a positive effect.[20,21] The OmegAD Study, in which participants received either 1.7 g per day of DHA or placebo for six months, and then all received supplementation with DHA for six months, found that DHA supplementation slowed the rate of cognitive decline only in the subgroup of participants with mild cognitive impairment and had no effect on the population overall.[20] In these types of studies, DHA doses vary widely, leading to difficulty assessing the body of research through meta-analysis. Additionally, the ideal dose of DHA and/or fish/fish oil needed to maintain good memory and cognitive function during aging is a subject of continuing research.[20]

Mood Disorders and Depression
Both low omega-3 fatty acid consumption and low circulating levels of omega-3 fatty acids have been associated with depression.[22] However, randomized controlled trials have had differing outcomes, with some showing no effect of omega-3 fatty acid supplementation on depressed mood. A randomized controlled trial providing 1.5 g of omega-3s (630 mg EPA, 850 mg DHA) per day for three months did not affect the moods of 218 individuals with mild to moderate depression.[23]

Other studies investigating this relationship have also not found a benefit of omega-3 fatty acids on symptoms of depression.[23,24] Although fish intake has been associated with protection against depressive symptoms, this effect seems to be confounded by more healthful lifestyles of fish eaters.[24]

Nevertheless, a 10-year longitudinal study published in ***The American Journal of Clinical Nutrition*** in 2011 found a decreased risk of clinical depression with increasing ALA:LA ratio in a cohort of women, and an increased risk associated with higher intake of LA.[25] The same study did not find a protective effect from fish.

Other research suggests that the ratio of EPA to DHA is an important factor, and some researchers support the notion that EPA, and not DHA, is responsible for the benefit.

A 2011 meta-analysis of clinical trials in depression found that supplements containing ≥60% EPA, in dosages between 200 mg and 2,200 mg of EPA in excess of DHA, had a positive effect on depression.[26] A meta-analysis of 28 studies evaluating the impact of omega-3 supplementation on depressive symptoms found that symptoms were significantly reduced in 13 studies using supplements containing greater than 50% EPA and in eight studies using EPA alone, whereas symptoms were not significantly reduced in studies containing only DHA, or in those in which supplementation with >50% DHA was used.[27]

Impact of Omega-3 Fats on Other Conditions

Omega-3 fats are purported to improve symptoms related to type 2 diabetes, metabolic syndrome, inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and osteoporosis.[3]

Several studies suggest that people with rheumatoid arthritis who take fish oil may have less joint swelling and pain and may reduce their need for NSAIDs.[5] A 2014 prospective cohort study of more than 32,000 women of middle and older age found an inverse relationship between intake of EPA and DHA and incidence of rheumatoid arthritis.[28] Intake consistently higher than 0.21 g/day (equivalent to at least one serving per week of fatty fish or four servings per week of lean fish) cut the risk of developing rheumatoid arthritis by one-half, and consumption of fish once or more per week during the 10-year study period reduced risk by almost one-third.[28]

The theory that omega-3 fats may benefit these inflammatory conditions is reasonable, given the important role of these nutrients in controlling inflammation in the body. Yet current evidence is conflicting and/or insufficient to establish recommendations. More research is needed to determine the precise role and optimal intake of omega-3 fats for these conditions.

Food Sources of Omega-3 and Omega-6 Fats

The type of fatty acids consumed in the diet directly affects levels of specific fatty acids in the body. This is also true for food animals. While both LA and ALA are found in plant foods, LA is present in much higher amounts; AA produced from the metabolism of LA is thus found in good amounts in the meat of land animals such as beef cattle that live on grasses and other land-based plant foods. Because sea plants like algae and phytoplankton contain good amounts of DHA and EPA, fish that eat algae from the sea have a high concentration of these fatty acids in their flesh. Food products from land animals that eat omega-3-rich plants or are fed omega-3 supplements in their diets may also have significant amounts of EPA and DHA in their flesh. Grass-fed beef and omega-3-enriched eggs are examples of the latter.

The major sources of omega-6 fatty acids are vegetable oils, nuts, seeds, and some vegetables; most of this is in the form of LA, while meats, poultry, and eggs provide some AA.

The most common sources of ALA are soybean, canola, and flaxseed oils. Soybean and canola oils are by far more ubiquitous in the food supply, finding their way into American diets through processed and prepared foods; unfortunately, these oils contain substantially more omega-6 PUFA than omega-3 PUFA and thus their intake maintains the omega-6 to omega-3 ratio at higher than optimal levels. Flaxseed oil, which is readily available in grocery stores but

is not often used in prepared or processed foods, has a much higher omega-3 than omega-6 content and is therefore a better choice when available. In addition, chia seeds and hemp seeds are plant foods with high levels of the omega-3 ALA. Marine sources, in particular fatty fish, contribute the bulk of EPA and DHA to the diet. Varieties of fish have differing fatty acid content. Certain fatty fish, especially mackerel, albacore tuna, sardines, salmon, halibut, and herring, are good sources of EPA and DHA. Organ meats such as brains and liver are an additional source of EPA and DHA.

Table 1 shows the omega-3 content of selected foods.

TABLE 1

Food Sources of Alpha-Linolenic Acid

FOOD	ALPHA-LINOLENIC ACID CONTENT PER 100 g OF FOOD	LINOLEIC ACID CONTENT PER 100 g OF FOOD
Oil, flaxseed, cold pressed	53.4 g	14.2 g
Seeds, chia seeds, dried	17.8 g	5.8 g
Oil, canola	9.1 g	18.6 g
Seeds, hemp seed, hulled	8.7 g	27.4 g
Oil, soybean, salad or cooking	6.8 g	50.4 g
Nuts, walnuts, black, dried	2.7 g	33.8 g

— SOURCE: USDA

Seed oils contribute a good portion of the ALA to the average diet. ALA also is found in smaller amounts in a variety of plant foods. Purslane, which has the highest ALA content of any green vegetable, contains 0.4 g of ALA per 100 g of food. Other sources are soybeans, lima beans, lentils, and other legumes; the bran or germ of grains such as wheat, corn, and rice; spirulina (seaweed); and, to a lesser degree, green leafy vegetables such as spinach and kale and fruits including avocado, strawberries, and raspberries.[29] The attention on increasing omega-3 intake has also given rise to foods that are manufactured to provide added omega-3s. Omega-3-enriched eggs, peanut butter, and certain margarines are widely available as alternative dietary sources.

Imbalances in the Western Diet

The ubiquity of omega-6s in the food supply is a major reason for the imbalance in EFA intake in the United States.

The seed oils such as safflower, sunflower, corn, and soy that are used widely in processed foods and consumed in large amounts in the American diet are very rich in LA, and intake data show that Americans can consume up to 25 times more omega-6 than omega-3 fatty acids.

Evidence indicates that the ratio of essential fatty acid intake in the Paleolithic era was close to 1:1. This balance resulted in part from a diet rich in the leaves of wild plants containing the omega-3 ALA, and animals that fed on them, whose fat contained 4% EPA; in contrast, domestically raised animals have undetectable levels of EPA in their fat tissue.[29] Paleolithic diets consisted of other whole foods, including fish, nuts and seeds; this, together with the absence of processed foods, resulted in a more balanced essential fatty acid ratio.[29]

Consumption data demonstrate that American intake of omega-6 fats increased significantly in the last century, due in part to the introduction of soybean oil into the food supply. According to Blasbalg et al, "The estimated per capita consumption of soybean oil increased >1,000-fold throughout the 20th century,"[17] and the ratio of omega-6 to omega-3 rose with it. In 1909, the ratio of LA to ALA was 6.4:1; at the end of the century it was 10:1.[17] This shift likely had the secondary effect of decreasing the EPA and DHA content of human tissues over the 20th century.[17] LA and ALA compete for the same enzymes to be metabolized into their downstream products. Therefore, when dietary intake of LA is much higher than that of ALA, the balance of the omega-6 AA to that of the omega-3 EPA and DHA may be suboptimal. This has an impact on overall health, inflammation, and other conditions as described above. Furthermore, if LA consumption is too high to allow conversion of ALA to EPA and DHA in amounts adequate to meet physiologic needs, then the latter fatty acids become conditionally essential, meaning they must be consumed in the diet to avoid deficiency.

Today, PUFAs contribute approximately 7% of the total energy intake for adults the United States.[29] Close to 90% of that comes from the omega-6 LA.[29] Average omega-3 fatty acid intake is approximately 1.6 g per day, or about 0.7% of energy intake. The majority of this is ALA (about 1.4 g), with the remaining 0.1 g to 0.2 g coming from EPA and DHA directly.[29]

Dietary Recommendations and Supplementation

The Dietary Guidelines for Americans 2015–2020 provides specific fat intake recommendations only for saturated fat and does not make target intake recommendations for either omega-3 or omega-6 fatty acids as a proportion of total caloric intake. Americans are instructed to limit saturated fat intake to less than 10% of calories, replacing them with monounsaturated fatty acids and/or PUFAs to lower cholesterol levels and thus reduce risk of CVD. The only explicit recommendation linked to omega-3 or omega-6 fatty acids is to to consume 8 oz of seafood per week to reach a goal of 1,750 mg of EPA+DHA, because, according to the Guidelines, "Consumption of about 8 oz per week of a variety of seafood, which provide an average consumption of 250 mg per day of EPA and DHA, is associated with reduced cardiac deaths among individuals with and without preexisting CVD."[30]

Table 2 lists seafood varieties that are high in EPA+DHA content.

TABLE 2

Seafood High in EPA+DHA

SEAFOOD	EPA+DHA mg/4 oz
Atlantic, Chinook, and Coho salmon	1,200 to 2,400
Anchovies and herring	2,300 to 2,400
Atlantic and Pacific mackerel	1,350 to 2,100
Bluefin and Albacore tuna	1,700
Atlantic and Pacific sardines	1,100 to 1,600
Pacific oysters	1,550
Freshwater trout	1,000 to 1,100
White (Albacore) canned tuna	1,000

— SOURCE: *DIETARY GUIDELINES FOR AMERICANS, 2010.* HTTP://HEALTH.GOV/DIETARYGUIDELINES/DGA2010/DIETARYGUIDELINES2010.PDF

The Institute of Medicine, which sets standards for essential nutrient intake, has established Adequate Intakes (AIs) for the parent fatty acids in both the omega-3 and omega-6 families. Given the fact that omega-3 and omega-6 PUFAs are essential in the diet because they cannot be synthesized in the body, the AI is the amount believed to prevent nutrient deficiency and provide for the physiologic needs of most people. The AI for the omega-6 LA is 12 g per day for women and 17 g per day for men; the AI for the omega-3 ALA is 1.1 g per day for women and 1.6 g per day for men.[31] There is no AI established for EPA or DHA.

The Academy of Nutrition and Dietetics recommends consuming 0.6% to 1.2% of energy intake as ALA and 500 mg EPA+DHA per day, with 3% to 10% of energy from omega-6 PUFAs.[32] The World Health Organization recommends 0.5% to 2% of intake from omega-3s with a minimum of 0.5% from ALA and a target of 250 mg EPA+DHA per day, and 2% to 3% of energy from LA.[32] The American Heart Association recommends eating fatty fish two or more times per week and consuming 5% to 10% of energy as LA.[32]

According to the NIH Office of Dietary Supplements, “There is now general scientific agreement that individuals should consume more omega-3 and fewer omega-6 fatty acids for good health.”[3] The question remains as to whether an ideal ratio exists. Although current recommendations range from 1:1 to 4:1, an optimal ratio of omega-6 to omega-3 fatty acids has not been established, and there is uneven support in the research community for a focus on ratio. A 2008 review of the effect of decreasing omega-6:omega-3 ratios for a variety of disease conditions found a beneficial effect of a 4:1 ratio on CVD death, a 2.5:1 ratio on colorectal cancer, a 2:1 to 3:1 ratio for rheumatoid arthritis, and a 5:1 ratio for asthma.[33] The same study found that a higher omega-6:omega-3 ratio of 4:1 did not benefit colorectal cancer,

even when the amount of omega-3 was the same.[33] Interestingly, a 10:1 ratio had adverse effects on asthma. The author concluded that the ideal therapeutic ratio of omega-6:omega-3 fatty acids for any given disease depends on the particular condition and its severity, and that at minimum, a lower omega-6:omega-3 ratio will benefit a variety of chronic diseases in Western society.[33]

Ample evidence demonstrates the positive health effects of increasing omega-3 intake, both in levels achievable by following dietary recommendations (eg, two to three fish meals per week) as well as through supplementation. It is generally agreed that increasing consumption of ALA, EPA, and DHA will improve overall, and especially cardiovascular, health, even in the context of a diet rich in LA, such as that for the average American. This is perhaps an indirect way of endorsing a lower omega-6 to omega-3 ratio; in other words, any substantial increase in omega-3 intake will reduce the ratio. While there is arguably good benefit from reducing consumption of omega-6-rich seed oils from processed foods as a means to improve overall diet quality (eg, by increasing the proportion of whole, fresh foods), a wide variety of foods common in the American diet provide good amounts of LA, and it may be challenging to make meaningful reductions in omega-6 intake in the short term. Fortunately, individuals may still achieve better omega balance fairly quickly and easily by adding omega-3 rich foods and/or supplements to their diet.

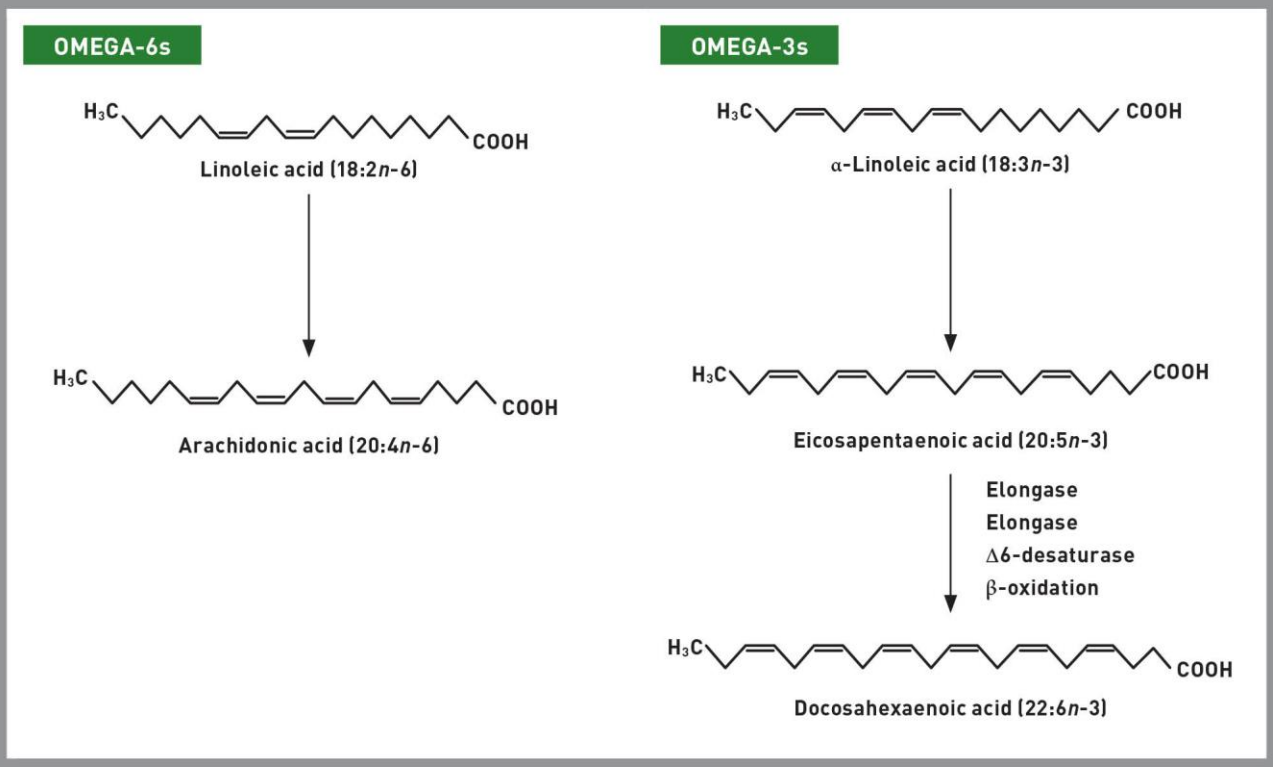
Most omega-3s are consumed in the form of ALA, which has a poor conversion rate to EPA and DHA, and especially so in the context of a diet rich in LA. According to the Third National Health and Nutrition Examination Survey (spanning from 1988 to 1994), only 25% of the population directly consumes EPA or DHA in their daily diet.[3] In 1999, a working group convened at the NIH to determine recommendations for omega-6 and omega-3 fatty acid intake.[34] The group proposed AIs based on a 2,000-calorie diet of 4.44 g of LA, 2.22 g of ALA, and 0.65 g of EPA+DHA per day.[34]

Americans would have to quadruple their fish consumption to achieve the recommended intake of 0.65 g per day of EPA and DHA combined.[29] For this reason, fish oil supplements are an important component of the approach to improve the EFA ratio. National health data indicate that fish oil supplements are the most commonly consumed nonvitamin/nonmineral natural product in the United States. In 2012, almost 8% of American adults, or 18.8 million people, took fish oil supplements.[35]

Including fish oil in the diet increases the proportion of omega-3 PUFAs in the phospholipids of cell membranes. AA makes up about 10% to 20% of the fatty acids in the blood cell membranes of individuals following a typical Western diet, while EPA and DHA concentrations are typically low, about 0.5% to 1% and 2% to 4%, respectively.[7] Consumption of omega-3 fatty acids from marine sources can shift this ratio quickly, in a matter of weeks with sufficient dose.[7] There is a 10-fold increase in the proportion of EPA in cell phospholipids after just four weeks of supplementation with fish oil capsules containing 2.1 g EPA plus 1.1 g DHA per day, and a 20% reduction in AA after 12 weeks.[36]

FIGURE 1

Chemical Structures of Omega-3 and Omega-6 Fatty Acids



Recommended therapeutic intakes for fish oil range from less than 1 g per day to 4 g per day or more, depending on the health status of the individual, what they're using the fish oil for, and whether they are taking any other medications or supplements.[2] According to a recent review of the effects of omega-3 fatty acids on CVD, "Approximately 1 g/day of eicosapentaenoic acid plus docosahexaenoic acid is recommended for cardioprotection. Higher dosages of omega-3 fatty acids are required to reduce elevated triglyceride levels (2 to 4 g/day)."[37]

Safety

It's important to be aware of potential safety risks when recommending any dietary supplement. Omega-3 supplements typically do not cause negative side effects.[35] According to the NIH Office of Dietary Supplements, a review of 148 studies in which 10,000 subjects took omega-3 supplements in dosages from 0.3 to 8 g/day for at least one week to more than seven years showed minimal to no adverse effects. When side effects did occur, they were minimal, largely gastrointestinal in nature (eg, diarrhea), and occurred in less than 7% of subjects.[3]

Although evidence overwhelmingly suggests that omega-3 fatty acid supplements typically do not have negative side effects, there are a handful of safety aspects worth considering. According to the National Institutes of Health National Center for Complementary and Integrative Health, it's unclear whether people with fish or shellfish allergies can safely consume fish oils, which are the most common form of omega-3 supplementation in the United

States.[35] Individuals with fish allergies should consume omega-3 supplements derived from plant sources such as flaxseed oils.

Omega-3 supplements theoretically may interact with drugs that affect blood clotting.[35] The Natural Medicines Comprehensive Database, which catalogues safety and efficacy information on dietary and herbal supplements and their interactions with pharmaceutical therapies, reports no known interactions between omega-6 fatty acids or omega-3 ALA and medications.[38,39] There are potential drug-supplement interactions for EPA and DHA, which can have pharmacologic effects including thinning blood and lowering blood pressure.[40,41] People on anticoagulant and antihypertensive drugs should inform their health care providers that they are taking EPA and/or DHA supplements so potential interactions can be monitored.

Conclusion

Clear data demonstrate that increasing consumption of omega-3 fatty acids can have a health-promoting effect. Mixed evidence exists for reducing consumption of omega-6 fatty acids. Historical intakes of EFAs (eg, from the Paleolithic era) were more balanced than those of the current day. Only in the last hundred years has the ubiquity of seed oils in the food supply sharply increased dietary intake of omega-6 PUFAs. In this context, a vast body of evidence has emerged to support the recommendation to increase omega-3 fatty acid consumption and reduce omega-6 consumption.

Yet while there are physiologically relevant reasons for a focus on EFA balance, there is controversy over the value of including an optimal ratio of omega-6 to omega-3 in dietary recommendations.

According to Simopoulos, “The presence of ALA in the diet can inhibit the conversion of the large amounts of LA in the diets of Western industrialized countries, which contain too much dietary plant oils rich in omega-6 PUFAs (eg, corn, safflower, soybean oils). The increase of ALA, together with EPA and DHA, and reduction of vegetable oils with high LA content, are necessary to achieve a healthier diet in these countries.”[34]

Furthermore, according to Harris et al, “Higher omega-6 PUFA intakes can inhibit the conversion of ALA to eicosapentaenoic acid, but such conversion is already quite low, and whether additional small changes would have net effects on [coronary heart disease] risk after the other benefits of LA consumption are taken into account is not clear.”[13]

What, ultimately, can RDs recommend to their clients for improving omega balance? On the one hand, conflicting evidence as to the benefits and drawbacks of omega-3 and omage-6 PUFAs makes it difficult to determine clear intake recommendations. However, some recommendations can be made to help clients achieve a better omega balance. First and foremost, RDs should encourage their clients to increase intake of omega-3 fatty acids, in particular from marine sources (except in the case of those with fish/shellfish allergy or dietary restrictions against seafood). The broad goal of 1,750 mg of EPA+DHA can be met with just 8 oz of seafood consumption per week. Second, RDs should make clients and patients aware that excess consumption of omega-6 PUFAs from widely used and inexpensive vegetable oils may have adverse inflammatory effects, especially if omega-3 consumption is low. Oils used

for cold preparation, such as salad dressing, can be replaced with omega-3-rich flaxseed oil, for example. Increasing intake of nuts and seeds, especially hemp and chia seeds, which are high in omega-3s, is another good strategy. Third, omega-3 supplements may have some health benefit, especially for individuals at risk of CVD. Supplements may include fish oils or nonmarine sources of omega-3s, and dosages can range from 0.5 g for disease prevention to up to 2 to 4 g to achieve a therapeutic dose for individuals with cardiovascular risk factors.

Overall, a shift toward greater omega-3 fatty acid consumption, likely with the reduction of omega-6 consumption, appears to be warranted.

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References

1. Harris WS, Klurfeld,DM. Twentieth-century trends in essential fatty acid intakes and the predicted omega-3 index: evidence versus estimates. ***Am J Clin Nutr***. 2011;93(5):907-908.

2. Micronutrient information center: essential fatty acids. Oregon State University Linus Pauling Institute website. http://lpi.oregonstate.edu/mic/other-nutrients/essential-fatty-acids

3. Omega-3 fatty acids and health: fact sheet for health professionals. National Institutes of Health Office of Dietary Supplements website. https://ods.od.nih.gov/factsheets/Omega3FattyAcidsandHealth-HealthProfessional/. Updated October 28, 2005.

4. Davidson MH. Omega-3 fatty acids: new insights into the pharmacology and biology of docosahexaenoic acid, docosapentaenoic acid, and eicosapentaenoic acid. ***Curr Opin Lipidol***. 2013;24(6):467-474.

5. Complementary and alternative medicine guide: supplement: omega-6 fatty acids. University of Maryland Medical Center website. https://umm.edu/health/medical/altmed/supplement/omega6-fatty-acids. Updated August 5, 2015.

6. Rapoport SI. Arachidonic acid and the brain. ***J Nutr***. 2008;138(12):2515-2520.

7. Calder PC. Omega-3 fatty acids and inflammatory processes. ***Nutrients***. 2010;2(3):355-374.

8. Wang Y, Huang F. N-3 polyunsaturated fatty acids and inflammation in obesity: local effect and systemic benefit. ***Biomed Res Int***. 2015;2015:581469.

9. De Caterina R. n-3 fatty acids in cardiovascular disease. ***N Engl J Med***. 2011;364(25):2439-2450.

10. Marik PE, Varon J. Omega-3 dietary supplements and the risk of cardiovascular events: a systematic review. ***Clin Cardiol***. 2009;32(7):365-372.

11. Katan MB. Omega-6 polyunsaturated fatty acids and coronary heart disease. ***Am J Clin Nutr***. 2009;89(5):1283-1284.

12. Al-Khudairy L, Hartley L, Clar C, Flowers N, Hooper L, Rees K. Omega-6 fatty acids for the primary prevention of cardiovascular disease. ***Cochrane Database Syst Rev***. 2015;11:CD011094.

13. Harris WS, Mozaffarian D, Rimm E, et al. Omega 6 fatty acids and risk for cardiovascular disease: a science advisory from the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. ***Circulation***. 2009;119(6):902-907.

14. Bernstein AM, Ding EL, Willett WC, Rimme EB. A meta-analysis shows that docosahexaenoic acid from algal oil reduces serum triglycerides and increases HDL-cholesterol and LDL-cholesterol in persons without coronary heart disease. ***J Nutr***. 2012;142(1):99-104.

15. Enns JE, Yeganeh A, Zarychanski R, et al. The impact of omega-3 polyunsaturated fatty acid supplementation on the incidence of cardiovascular events and complications in peripheral arterial disease: a systematic review and meta-analysis. ***BMC Cardiovasc Disord***. 2014;14:70.

16. Mozaffarian D, Ascherio A, Hu FB, et al. Interplay between different polyunsaturated fatty acids and risk of coronary heart disease in men. ***Circulation***. 2005;111(2):157-164.

17. Blasbalg TL, Hibbeln JR, Ramsden CE, Majchrzak SF, Rawlings RR. Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century. ***Am J Clin Nutr***. 2011;93(5):950-962.

18. Calder PC. Fatty acids and inflammation: the cutting edge between food and pharma. ***Eur J Pharmacol***. 2011;668(Suppl 1):S50-S58.

19. Dyall SC. Long-chain omega-3 fatty acids and the brain: a review of the independent and shared effects of EPA, DPA and DHA. ***Front Aging Neurosci***. 2015;7:52.

20. Cederholm T, Salem N Jr, Palmblad J. n-3 fatty acids in the prevention of cognitive decline in humans. ***Adv Nutr***. 2013;4(6):672-676.

21. Salem N Jr, Vandal M, Calon F. The benefit of docosahexaenoic acid for the adult brain in aging and dementia. ***Prostaglandins Leukot Essent Fatty Acids***. 2015;92:15-22.

22. Baghai TC, Varallo-Bedarida G, Born C, et al. Major depressive disorder is associated with cardiovascular risk factors and low Omega-3 Index. ***J Clin Psychiatry***. 2011;72(9):1242-1247.

23. Rogers PJ, Appleton KM, Kessler D, et al. No effect of n-3 long-chain polyunsaturated fatty acid (EPA and DHA) supplementation on depressed mood and cognitive function: a randomised controlled trial. ***Br J Nutr***. 2008;99(2):421-431.

24. Suominen-Taipale AL, Partonen T, Turunen AW, Männistö S, Jula A, Verkasalo PK. Fish consumption and omega-3 polyunsaturated fatty acids in relation to depressive episodes: a cross-sectional analysis. ***PLoS One***. 2010;5(5):e10530.

25. Lucas M, Mirzaei F, O'Reilly EJ, et al. Dietary intake of n-3 and n-6 fatty acids and the risk of clinical depression in women: a 10-y prospective follow-up study. ***Am J Clin Nutr***. 2011;93(6):1337-1343.

26. Sublette ME, Ellis SP, Geant AL, Mann JJ. Meta-analysis of the effects of eicosapentaenoic acid (EPA) in clinical trials in depression. ***J Clin Psychiatry***. 2011;72(12):1577-1584.

27. Martins JG. EPA but not DHA appears to be responsible for the efficacy of omega-3 long chain polyunsaturated fatty acid supplementation in depression: evidence from a meta-analysis of randomized controlled trials. ***J Am Coll Nutr***. 2009;28(5):525-542.

28. Di Giuseppe D, Wallin A, Bottai M, Askling J, Wolk A. Long-term intake of dietary long-chain n-3 polyunsaturated fatty acids and risk of rheumatoid arthritis: a prospective cohort study of women. ***Ann Rheum Dis***. 2014;73(11):1949-1953.

29. Kris-Etherton PM, Taylor DS, Yu-Poth S, et al. Polyunsaturated fatty acids in the food chain in the United States. ***Am J Clin Nutr***. 2000;71(1 Suppl):179S-188S.

30. US Department of Agriculture, US Department of Health and Human Services. ***Dietary Guidelines for Americans, 2015–2020***. http://health.gov/dietaryguidelines/2015/guidelines/

31. Food and Nutrition Board of the Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. https://fnic.nal.usda.gov/sites/fnic.nal.usda.gov/files/uploads/energy_full_report.pdf

32. Vannice G, Rasmussen H. Position of the Academy of Nutrition and Dietetics: dietary fatty acids for healthy adults. ***J Acad Nutr Diet***. 2014;114(1):136-153.

33. Simopoulos AP. The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. ***Exp Biol Med (Maywood)***. 2008;233(6):674-688.

34. Simopoulos AP. Omega-6/omega-3 essential fatty acid ratio and chronic diseases. ***Food Rev Int***. 2004;20(1):77-90.

35. Omega-3 supplements: in depth. National Center for Complementary and Integrative Health website. https://nccih.nih.gov/health/omega3/introduction.htm. Updated March 23, 2016.

36. Yaqoob P, Pala HS, Cortina-Borja M, Newsholme EA, Calder PC. Encapsulated fish oil enriched in alpha-tocopherol alters plasma phospholipid and mononuclear cell fatty acid compositions but not mononuclear cell functions. ***Eur J Clin Invest***. 2000;30(3):260-274.

37. Jain AP, Aggarwal KK, Zhang PY. Omega-3 fatty acids and cardiovascular disease. ***Eur Rev Med Pharmacol Sci***. 2015;19(3):441-445.

38. Omega-6 fatty acids. Natural Medicines Comprehensive Database website. http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?pt=100&id=496. Updated March 30, 2016.

39. Alpha-linoleic acid. Natural Medicines Comprehensive Database website. http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?pt=100&id=1035&ds=alsoknowns. Updated March 30, 2016.

40. EPA (eicosapentaenoic acid). Natural Medicines Comprehensive Database website. http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=994&ds=&name=Eicosapentaenoic+Acid+(EPA+(EICOSAPENTAENOIC+ACID))&searchid=55976104. Updated March 30, 2016.

41. DHA (docosahexaenoic acid). Natural Medicines Comprehensive Database website. http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=&s=ND&pt=100&id=864&ds=&name=Docosahexaenoic+Acid+(DHA+(DOCOSAHEXAENOIC+ACID))&searchid=55976104. Updated March 30, 2016.

Quiz

1. Which of the following foods is a good source of omega-3 fatty acids?
A. Sesame seeds
B. Pumpkin seeds
C. Chia seeds
D. Sunflower seeds

2. How many ounces of fish and seafood provide the recommended weekly intake of EPA+DHA?
A. 4 oz
B. 6 oz
C. 8 oz
D. 10 oz

3. Which of the following foods is likely high in omega-6 fats?
A. Packaged, shelf-stable muffins containing soybean oil
B. Mashed potatoes made with butter and milk
C. Homemade cake made with butter and coconut oil
D. Salad dressing made with flaxseed oil

4. Which is the major fatty acid in the brain?
A. Linolenic acid
B. Alpha-linoleic acid
C. EPA
D. DHA

5. Data suggest that the ratio of omega-6 to omega-3 polyunsaturated fatty acids in the typical American diet could be as high as which of the following?
A. 1:1
B. 3:1
C. 25.1
D. 10.1

6. Which of the following oils is high in omega-3 fatty acids?
A. Olive oil
B. Flaxseed oil
C. Coconut oil
D. Corn oil

7. Eicosanoids, the class of hormonelike compounds produced from essential fatty acids, are integral to what type of physiologic response?
A. Cell growth
B. Hunger and satiety
C. Inflammation
D. Detoxification

8. What is the recommended weekly intake of EPA+DHA, according to the Dietary Guidelines for Americans?
A. 1,200 mg
B. 1,750 mg
C. 2,000 mg
D. 3,000 mg

9. Evidence suggests that the minimum therapeutic dose of omega-3 fatty acid supplementation needed to protect against cardiovascular disease is which of the following?
A. 0.2 g per day
B. 1 g per day
C. 2 g per day
D. 4 g per day

10. A diet that is very high in omega-6 fatty acids and very low in omega-3 fatty acids is likely to exacerbate which of the following negative physiologic responses?
A. Systemic inflammation
B. High cholesterol
C. Mitochondrial dysfunction
D. Obesity