Article Published in Journal of Food Lipids; 1996:Vol 3, 4, 233-249

# Long Chain Fatty Acids in Health and Nutrition

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**Abstract:**

The typical western diet high in long chain omega-3 fatty acids and low in long chain omega-6 fatty may not supply the appropriate balance for optimal metabolism. The imbalance is believed to cause many varied disease symptoms ranging from cardiovascular disease, hypertension, inflammatory and auto-immune disorders, depression and disrupted neurological functions. In the area of cardiovascular disease new research in areas of arrhythmias is exciting and shows that application of omega-3 fatty acids can produce rapid results. In addition omega-3 fatty acids are showing benefits in preventing restenosis following angioplasty in approximately half of the reported studies.

Significant research in infant nutrition indicates that long chain polyunsaturated fatty acids are "conditionally essential' for growth and development. Adequate intake of DHA and AA is critical during pregnancy, lactation and infancy for proper development of the fetus and infant. Premature babies are particularly at risk for inadequacies.

Recommendations by many academic and governmental bodies propose that daily intakes on long chain omega-3 fatty acids be increased as a step in reducing certain chronic diseases. Many specialist groups are recommending that infant formulas include long chain fatty acids at levels matching breast milk.

## Introduction

The 1980s were a period of rapid expansion in scientific knowledge about polyunsaturated fatty acids (PUFA) in general, and omega-3 PUFA in particular. Both omega-3 and omega-6 PUFA are precursors of hormone-like compounds known as eicosanoids, which are involved in many important biological processes in the human body(64). Recently it has been suggested that the typical "western" diet, which is relatively high in omega-6 PUFA and low in omega-3 PUFA, may not supply the appropriate balance of PUFA for proper biological function(64,58). This imbalance is believed to cause many varied disease symptoms ranging from cardiovascular disease, hypertension, inflammatory and auto-immune disorders, depression and certain disrupted neurological functions. Long chain PUFA are now considered "conditionally essential" for infant growth and development

## Evolution Of The Human Diet

Prehistoric humans evolved on a diet that consisted primarily of fresh fruits, leafy vegetables and animals. These foods provided a relatively equal balance of omega-6 and omega-3 PUFA upon which physiological and metabolic processes were established. The omega-6 to omega-3 ratio of approximately 1:1 remained virtually unchanged for millions of years (64,44,34). Over the past 150 years, significant changes in the composition of the food supply of western societies resulted in an increase in consumption of omega-6 PUFA and a corresponding decrease in intake of omega-3 PUFA.

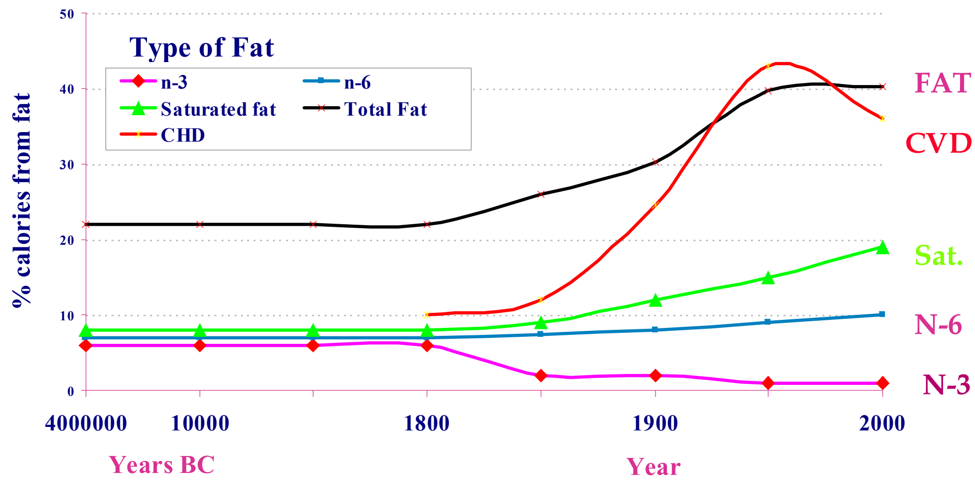
Today, the ratio of omega-6 to omega-3 in North America is estimated to be in the range of 10:1 to 25:1 (64,44,34,55). This alteration in the food supply and subsequent shift in the ratio of omega-6 to omega-3 PUFA is attributed to a number of factors. Modern food production methods decreased the omega-3 fatty acid content of many foods, including animal meats, eggs and fish(34). Wild animals, once free to roam and feed upon wild vegetation, were leaner and had significantly more omega-3 fatty acids in their tissues than today's farm raised commercial livestock. The use of grain feeds, which are rich in omega-6 but poor in omega-3 PUFA, has altered the fatty acid composition of domestic livestock and thus meats and eggs in the modern food supply(64,34). Today, domestic beef contains little to no detectable amounts of omega-3 PUFA(64). Similarly, modern aquaculture produces fish that contain less omega-3 PUFA than those that grow naturally and feed on plankton in the oceans, rivers, and lakes.

In addition to evolutionary changes cultural trends have also influenced fat intakes as well. The industrial revolution introduced vegetable oil technology and popularized the use of cooking oils from sunflower, peanut, and corn, all good sources of omega-6 PUFA. (64) Critically for infants these trends have produced a reliance upon infant formula has increased in the latter half of this century. In contrast to human milk, North American formula is devoid of the essential omega-3 PUFA docosahexaenoic acid (DHA) (34).

Figure 1.

Relative Percentages of Fat and Fatty Acid Families in the Evolution of Human Nutrition

# Fat Intake and Incidence of Coronary Heart Disease (CHD)




Leaf and Weber, (41)

## <u>Functions of Fats</u>

Fats are found in a wide range of both animal and vegetable foods and serve many functions within the human body. Fat is stored by the body until it is needed for energy and is a component of cell membranes. This helps cells maintain their shape, flexibility and control the passage of substances into and out of the cell. Dietary fat is crucial for the proper physiological functioning of every body tissue. It helps maintain the health of the skin and hair and protects the body organs from temperature extremes and mechanical shock. It is involved in the metabolism and transport of lipids, in regulating blood pressure and in the production of eicosanoids the family of hormone-like chemicals that regulate certain bodily functions.

Finally fats act as carriers of fat soluble vitamins A, D, E and K and help in their absorption and as well provide foods with flavor and texture(33).

## Chemical Structure and Nomenclature of Fatty Acids

Fatty acids form the basic chemical structure of fats. Structurally, all fatty acids have a chain like structure varying in length from 2 to 20 or more carbons. The most common fatty acids in foods have an even number of carbon atoms ranging from 12 to 22 carbons.

The names of fatty acids are often abbreviated according to their chemical structure; for example, eicosapentaenoic acid (EPA) is also referred to as 20:5 n-3, signifying twenty carbons and five double bonds.

## Saturated and Unsaturated Fatty Acids

Fatty acids are classified as saturated, monounsaturated or polyunsaturated depending on the number of double bonds.(33). The most common saturated fatty acids in foods are lauric (12:0), myristic (14:0), palmitic (16:0), and stearic (18:0) (33,52).

Saturated fatty acids are predominantly found in animal foods: meats and dairy products such as cheese, milk, butter and eggs and fats from beef and pork(44,3). They are also abundant in the tropical oils, coconut, palm and palm kernel and vegetable shortening.

The term “unsaturated” means the hydrocarbon chain contains at least one double bond. Unsaturated fatty acids fall into two categories, monounsaturated (MUFA) and polyunsaturated (PUFA). Monounsaturated fatty acids contain only one double bond and are synthesized within the human body(64). Oleic acid (18:1 n-9) is the most common dietary monounsaturated fatty acid and found in most animal fats including poultry, beef and lamb as well as nuts, seeds and corn (44,52).

Polyunsaturated fatty acids contain two or more double bonds. There are two classes of PUFA: omega-6 and omega-3. The distinction between omega-6 and omega-3 PUFA is based on the location of the first double bond, counting from the methyl end of the fatty acid chain . Linoleic acid, an omega-6 fatty acid with 18 carbons and two double bonds, is the most predominant PUFA in the western diet and commonly found in the seeds and oils of most plants (with the exception of coconut, cocoa, and palm, which have relatively low levels of omega-6 fatty acids) Table 1 (44,3,24).

Alpha-linolenic acid, an omega-3 fatty acid with 18 carbons and three double bonds, is found in appreciable amounts in green leafy vegetables, soybeans, linseed, rapeseed and canola oils, as well as phytoplankton, algae and fish Table 1 (44,24).

Linoleic acid and alpha-linolenic acid are precursors or "parent" compounds of omega-6 and omega-3 long chain PUFA. Linoleic acid and alpha-linolenic acid can be metabolized within the human body into longer-chain fatty acids of 20 to 22 carbon atoms or more through a process of chain elongation and desaturation. Linoleic acid can be metabolized into gamma-linolenic acid (GLA), dihomo-gamma linolenic acid (DGLA) and arachidonic acid (AA).

Alpha-linolenic acid can be metabolized into eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA can also be obtained directly from the diet from fish oils of both marine and freshwater sources. Table 1 (44,3).

**Essential Fatty Acids**

Linoleic acid and alpha-linolenic acid are considered to be essential fatty acids (EFA) for human health because humans cannot synthesize them and must obtain them from dietary sources(7,8). If there is a shortage of linoleic acid in the diet, its longer chain metabolite, arachidonic acid (AA), is also considered essential. Similarly, DHA and AA may be considered conditionally essential fatty acids under certain circumstances, particularly during infancy when the body's capacity to convert alpha-linolenic acid and linoleic acid is limited (8,15,37,54).

Table 1. Dietary sources of various fatty acids

| ***Polyunsaturated fatty acid*** | |
|---|---|
| omega-6 | omega-3 |
| **Linoleic acid (18:2 n-6)** | **Alpha-linolenic acid (18:3 n-3)** |
| Safflower seed (55-81%) | Freshwater fish (1-6%) |
| Evening primrose (70-75%) | Marine fish (*1%) |
| Sunflower seed (20-75%) | Linseed (45-60%) |
| Grape seed (58-78%) | Green leaves (56%) |
| Soybean (44-62%) | Rapeseed (10-11%) |
| Sesame seed (35-50%) | |
| Corn (34-62%) | |
| Cotton seed (33-59%) | |
| Groundnut (13-45%) | |
| Black walnut (*62%) | |
| English walnut (*55%) | |
| Pine nut (*44%) | |
| Black currant (44%) | |
| Borage (38%) | |
| Peanut (29%) | |
| Olive (11%) | |
| Egg yolk (11%) | |

| Gamma-linolenic acid(18:3 n-6) | Eicosapentaenoic acid(20:5 n-3) |
|---|---|
| Borage (*20%) | Freshwater fish (5-13%) |
| Black currant (*20%) | Pacific anchovy (18%) |
| Evening primrose(*10%) | Capelin (codfish) (9%) |
| | Mackerel (8%) |
| | Herring (3-5%) |
| | Sardine (3%) |
| | |
| | **Docosahexaenoic acid(22:6 n-3)** |
| | Sardine (9-13%) |
| | Pacific anchovy (11%) |
| | Mackerel (8%) |
| | Capelin (codfish) (3%) |
| | Herring (2-3%) |
| | Freshwater fish (1-5%) |

Note: Values in parentheses represent percent of total fatty acid, Lee(44).

## PUFA Metabolism

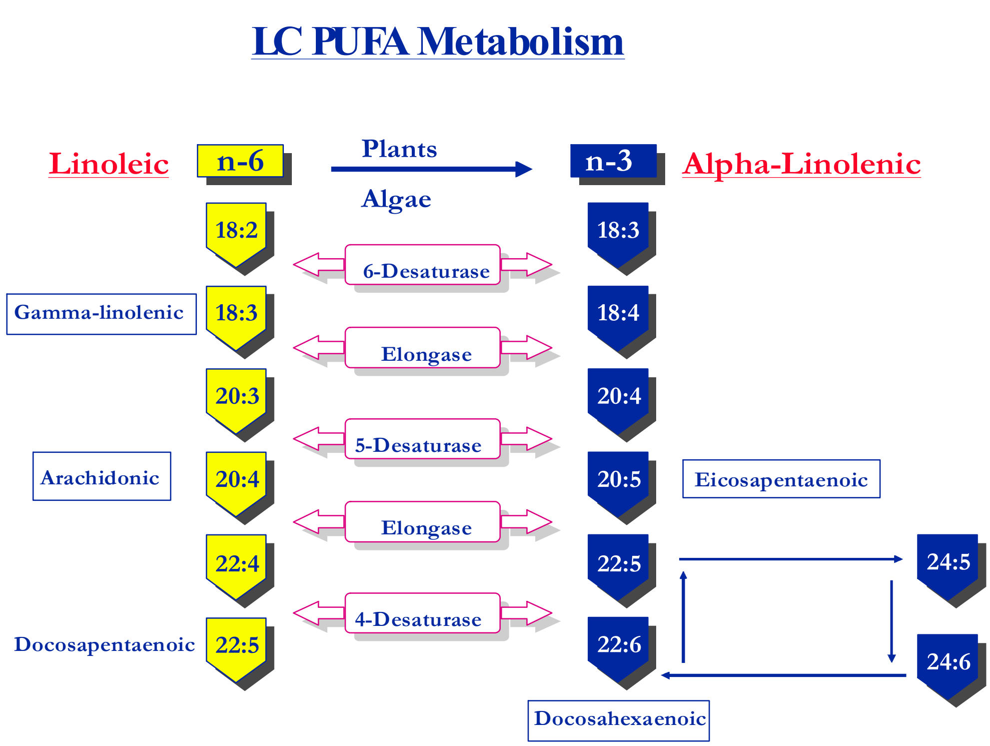
Though the human body is able to produce saturated and monounsaturated fatty acids from food components, it cannot synthesize PUFAs. Without such compounds, deficiencies can develop leading to symptoms such as skin damage, excessive loss of water through the skin, and disturbances of growth and hormonal balance.

The metabolic process that converts linoleic acid to GLA and AA and alpha-linolenic acid to EPA and DHA involves elongation of the carbon chain through the addition of carbon atoms and desaturation of the molecule through the addition of double bonds. This requires a series of special enzymes called elongases and desaturases which convert these two essential fatty acids into longer-chain and more unsaturated PUFAs which proceed to intervene in various ways in the body's biological processes. They regulate the body's delicate chemistry, maintain important hormone-like substances such as prostaglandins, thromboxanes and leukotrienes at the required levels, and play a key role in preventing certain diseases and keeping us generally healthy. According to our present state of knowledge, GLA, AA, EPA and DHA and their metabolites are critically important physiologically. It is no coincidence that all four of these valuable fats are present in the mother's milk.

Chain elongation and desaturation occurs only at the carboxyl end (COOH) of the fatty acid molecule in all biological organisms. (57) The same group of enzymes are responsible for metabolizing both omega-6 and omega-3 PUFA, resulting in competition between the two PUFA families for these enzymes (64). The relative oversupply of omega-6 PUFA in the diet may impair the transformation of omega-3 PUFA into its longer chain metabolites, EPA and DHA This can lead to a relative imbalance of the metabolic end products (64,44,12,17).

## Metabolism of Omega-3 and Omega-6 PUFA

Figure 2.



## Omega-3 PUFA in the Food Chain

Marine plants are the primary source of omega-3 PUFA in the food chain. Fish and other marine animals who feed on these plants are able to elongate and desaturate the parent essential fatty acid into longer chain PUFA. Therefore, most fish have quite high levels of both EPA and DHA (Table 2).

**Table 2. Total EPA and DHA content of selected fish**

| Fish | gram/100gram* |
|---|---|
| Atlantic mackerel | 2.5 |
| Atlantic salmon,farmed | 1.8 |
| Pacific herring | 1.7 |
| Atlantic herring | 1.6 |
| Lame trout | 1.6 |
| Bluefin tuna | 1.6 |
| Sturgeon | 1.5 |
| Anchovy | 1.4 |
| Sprat | 1.3 |
| Sardines, canned,drained | 1.1 |

Nettleton (52).

* amounts specified may vary slightly according to season, and food availability

## Roles in Human Health

Both classes of PUFA are important for normal biological function and are involved in a variety of physiological processes. Most clinical studies on the protective and therapeutic effects of omega-3 PUFA have used preformed EPA and DHA in the form of fish oil. The potential health benefits of fish oil include reduced risk of coronary vascular disease, hypertension and atherosclerosis as well as inflammatory and autoimmune disorders (28,21,67,42,36,39,61,22).

**Coronary Vascular Disease**: Omega-3 fatty acids have been extensively studied for their effect upon coronary vascular disease (CVD). Although the exact mechanism remains unclear, research suggests that omega-3 PUFA in fish oil may prevent CVD by lowering serum triglycerides, reducing the occurrence of arrythmia and acting as antiatherogenetic and antithrombotic agents.(1) Studies investigating the effects of omega-3 PUFA on blood lipid and lipoprotein levels have consistently demonstrated that omega-3 PUFA supplementation lowers blood triglyceride and VLDL concentrations in a dose dependent fashion (60,16,10,62) .

The triglyceride lowering effect is seen both in patients with high triglycerides and those with normal levels. The magnitude of this effect is large; decreases of 50% or more are frequently observed (16). In patients with hypertriglyceridemia substantial reductions have been observed with a daily fish oil intake as would be found in 200g of fatty fish (31).

Cardiac arrhythmias are believed to be one of the major causes of sudden death in patients with coronary heart disease. Animal experiments have shown that omega-3 PUFA can reduce susceptibility to heart arrthymia (59,1,46,56,50,32,23,51,45,30,29,6,68,38,43). The effect of omega-3 PUFA in model systems occurs very rapidly, with protection being observed within minutes after the addition of the fatty acid to the system. Observational and other studies indicate that small amounts of omega-3 PUFA, equivalent to one fatty fish meal per week was associated with a 50% reduction in risk of cardiac arrest (65). Placebo controlled trials confirm the initial data (13,63)

**Mild Hypertension**: Several studies have suggested that high doses of fish oil can reduce blood pressure in mildly hypertensive individuals. Mean reductions range between 3 and 10 mm Hg for both systolic and diastolic pressure (67,40,27).

**Restenosis:** Omega-3 fatty acids have been shown to be helpful in preventing restenosis—the reclogging of arteries—in patients undergoing angioplasty. Restenosis commonly occurs in 30 to 45% of the dilated lesions approximately 6 months after the procedure (26). In approximately half of the reported studies, a benefit has been reported when omega-3 fatty acid supplementation was provided (18,49,66). In none of the studies were any negative effects of omega-3 fatty acid supplementation reported. Meta-analysis of seven trials showed that in four trials omega-3 supplementation was of significant benefit and reduced the likelihood of restenosis by 13.9% (26).

**Inflammatory and Autoimmune Disorders**: Many experimental studies have provided evidence that omega-3 PUFA may modify and provide modest therapeutic benefits by reducing inflammatory and autoimmune disorders including rheumatoid arthritis, psoriasis, and ulcerative colitis (64,21,25).

**Aggression and Depression:**The well known correlation between depression and cardiovascular disease, multiple sclerosis and postpartum depression may be linked to low levels of omega-3 PUFA in neural membranes. Changing patterns of dietary fat consumption and the increasing rates of depression during the last one hundred years are also consistent with this theory. In cross-national studies comparing diets, scientists found that in countries where fish are a prominent part of the diet rates of depression were lower than North America. Similarly, meta-analysis of six studies has found a high incidence of depression in patients with multiple sclerosis compared to other disabilities. Several studies have found a depletion of omega-3 PUFA in the neuronal tissues of multiple sclerosis patients (34,31,24,39,40).

**Neurological Dysfunction:** Peroxisomal disorders including Zellweger syndrome, Adrenoleukodystrophy (ALD) and others disorders of peroxisome biogenesis have significant tissue deficiencies of DHA. In the brain, DHA levels are only 20-30% of normal and in the retina DHA may be virtually absent. Based on these findings significant on-going research using fish oil concentrates appears to improve both the visual symptoms and neuronal dysfunction (47) .

**Infant Development**: During intrauterine life DHA and AA are incorporated into the phospholipid membranes of the retina and brain and continue to accumulate during the first two years of life after birth (35,48)

Therefore, adequate intake of DHA and AA is critical during pregnancy, lactation and infancy for proper development of these tissues.

The unborn child needs an adequate supply of docosahexaenoic acid (DHA) if the gray matter in its brain and the tissue and cell membranes of the retina are to develop fully and properly. For this reason, the necessary amount of this member of the n-3 PUFA family is provided through the mother's placenta between the twenty-sixth and fortieth weeks of pregnancy and accumulates in the brain and retina of the fetus. Premature babies are affected particularly badly by DHA deficiency because they miss the vital phase before birth during which DHA is supplied and they are not able to synthesize enough of this PUFA to ensure the normal development of the brain and retina. However, DHA (like all the other PUFAs in the n-3 and n-6 families) is also present in the mother's milk since the development of these organs is not completed until several weeks after birth. It has been shown that sight develops more slowly in bottle-fed babies since there is no DHA in artificial milk or conventional baby and infant formulas. If premature babies and babies that are not breast-fed are given a diet enriched with DHA in the form of fish-oil concentrates, their sight develops as satisfactorily as that of breast-fed babies (11).

## **Recommended Intakes**

Many omega-3 and omega-6 fatty acids are essential for normal growth and development throughout the life cycle and should be included in the diet, especially of pregnant women, premature infants and full-term infants. Because they are metabolically and functionally distinct and have opposing physiological functions, a differentiation should be made between these two classes of essential fatty acids when dietary recommendations are made. In 1990, Canada issued separate dietary recommendations for omega-6 and omega-3 PUFA. Table 3.

Table 3. Summary of recommended nutrients based on energy expressed as daily rates (Canadian Recommendations PUFA)

| **Category** | | **Omega-3 PUFA (g)** | **Omega-6 PUFA (g)** |
|---|---|---|---|
| Children | 1-6 Yrs. | 0.6-1.0 | 4-6 |
| | 7-15 Yrs. | 1.0-1.4 | 7-9 |
| Adults | 16-75 Yrs. | 1.0-1.8 | 7-11 |
| Pregnancy (additional) | | 0.05-0.16 | 0.3-0.9 |
| Lactation (Additional) | | 0.25 | 1.5 |

From Simopoulos (1)

In the United Kingdom, the Department of Health recommends an omega-3 PUFA intake of a minimum of 0.2 percent of energy (19). In addition, the Task Force of the British Nutrition Foundation proposes a daily omega-3 PUFA intake ranging from 0.5 to 2.5 percent of energy in the form of alpha-linolenic acid, which corresponds to 1-6 grams linolenic acid for men and 1-5 grams for women. The Task Force additionally indicates 2 percent of total energy as a safe upper limit for the intake of EPA and DHA. For example, the resulting recommended mean intake of 1.25 grams of EPA plus DHA can be covered with 3-4 grams of fish oil or 2-3 servings of fatty fish per week (28).

No specific Recommended Dietary Allowances for either omega-6 or omega-3 PUFA have been established in the United States. However, according to the most recent RDA text, “rapid developments in the field of fat-soluble dietary factors, and their physiological role will require periodic reappraisal of their significance in nutrition and the regulation of metabolic functions. The possibility of establishing RDAs for these fatty acids should be considered in the near future (24).

Currently the dietary intake of omega-3 fatty acids in the USA is estimated at 150-200mg per day similar to other western industrialized countries (4,9,20). This would indicate a significant “dietary gap” from generally regarded prudent intakes.

**Enteral Formulas**

Most enteral nutrition formulas contain omega-6 PUFA, primarily in the form of corn oil, sunflower oil or safflower oil, which are rich in linoleic acid. Less consideration has been given to the inclusion of omega-3 PUFA, even though prolonged tube feedings with formulas lacking these essential nutrients have been shown to produce deficiency symptoms such as blurring of vision and neurological impairment (5). Today, only about half of the enteral nutrition formulas contain omega-3 PUFA, primarily from soybean oil (36). Because the conversion of alpha-linolenic acid to DHA and EPA can be slow, unreliable and in the case of the seriously ill, inhibited, many experts recommend that preformed EPA and DHA in the form of fish oil be included in enteral formulas (28).

**Infant Formula**:Several researchers have suggested that infant formula should contain DHA and AA at a ratio that mimics human milk from well-nourished women in the range of 4:1 to 10:1 (53,33). Although most infant formulas now provide the parent compounds, the capacity of newborns to convert alpha-linolenic acid and linoleic acid to their long chain metabolites, DHA and AA, may be limited (14,15,7,54). Therefore, in addition to individual researchers, a number of authoritative scientific groups, including the European Society for
Pediatric Gastroenterology and Nutrition, the British Nutrition
Foundation and the WHO/FAO Expert Committee on Fats and Oils in

Human Nutrition, recommend that DHA and AA be added directly to infant formulas.

**Supplementation**

Whereas health officials recommend two to three servings of fish per week, per capita consumption remains at approximately one serving (64). Therefore, most North Americans fail to obtain adequate amounts of EPA and DHA from dietary sources. Higher intakes of fish or fish oils may be advisable for individuals with a predisposition to CHD, hypertension, arthritis, psoriasis and cancer. For those who do not like fish or can not get enough omega-3 PUFA from dietary sources, nutritional supplementation in the form of fish oil capsules may be indicated.

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