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Long Chain Polyunsaturated Fatty Acids: The New Frontier in Nutrition

Introduction

The past two decades have witnessed considerable advances in researchers' understanding of the role that fats play in health and nutrition. Increased disease risk has been associated with high saturated fat consumption, while a growing body of research has linked the consumption of polyunsaturated fatty acids (PUFA) to improved health. Research into long chain omega-3 PUFA has shown that they are critical for development of brain and vision in infants and may play an important role in long term health, such as protecting against cardiovascular disease and reducing symptoms of inflammatory diseases. Studies have also suggested that low intakes of PUFA may be involved in the neurological disorders of depression, aggression and possibly Alzheimer's disease.

Studies suggest that while total fat levels in the typical Western diet are too high, the intake of long-chain omega-3 PUFA is too low. A commensurate reduction in omega-6 fatty acids is also needed to redress the balance generally seen as beneficial for optimal health in man. Recommendations from government and nutrition groups for long chain omega-3 fatty acids in diets are slowly forthcoming. Intakes of about one gram per day of long- chain omega-3 PUFA are required for proper development, well above current intakes.

Concern over high fat intake can often obscure the fact that fat serves crucial metabolic purposes, not just providing energy but also permitting the proper functioning of tissues. It helps maintain the health of the skin and hair, and it protects the body organs from temperature extremes and mechanical shock. As a component of cell membranes, fat helps maintain cell

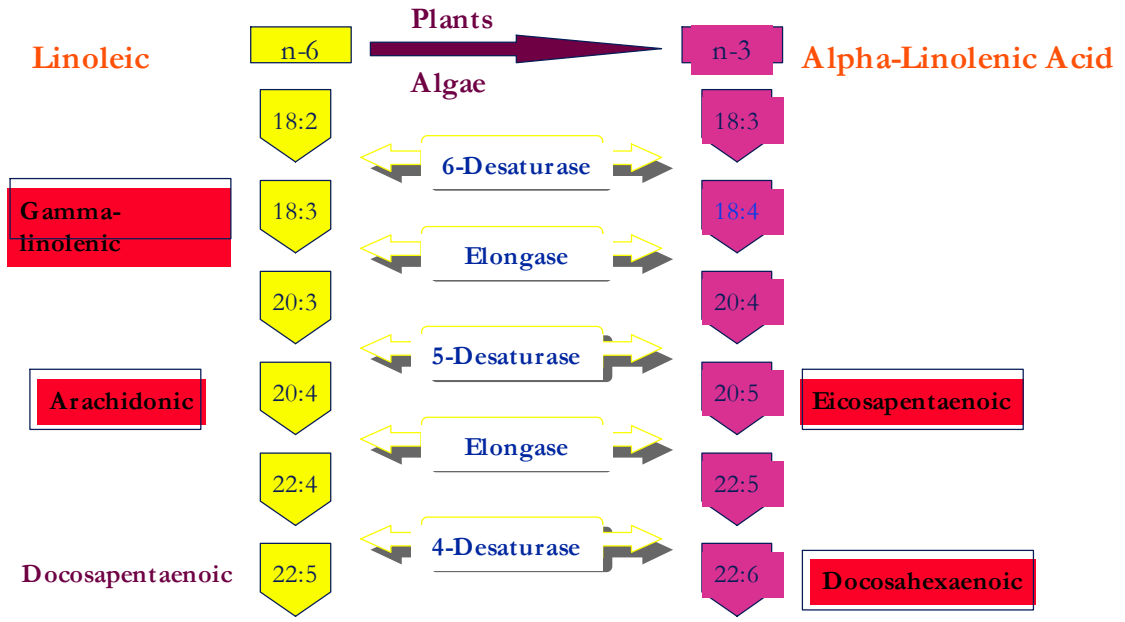
shape and flexibility and controls the passage of substances into and out of the cell. It also acts as the carrier for vitamins A, D, E and K and helps in their absorption.

Deficiencies or inadequacies of most fatty acids are rare because the body can synthesize them from other food components to meet its needs. The exceptions are the two families of PUFA, designated omega-3 and omega-6, which are essential fatty acids that must be obtained from dietary sources. Furthermore, the body cannot convert the fatty acids in one family of PUFA into those in the other.

There is little concern about low intakes of the omega-6 family because dietary sources are widely available. Most notably, vegetable oils provide a rich source of linoleic acid, the precursor or parent PUFA. The body then converts this into longer-chain omega-6 PUFA, mainly gamma-linolenic acid (GLA) and arachidonic acid (AA). Figure 1.

Figure 1. Schematic Diagram of the Metabolism of Long Chain Fatty Acids

PUFA Families
and Metabolism of LC Omega Fatty Acids

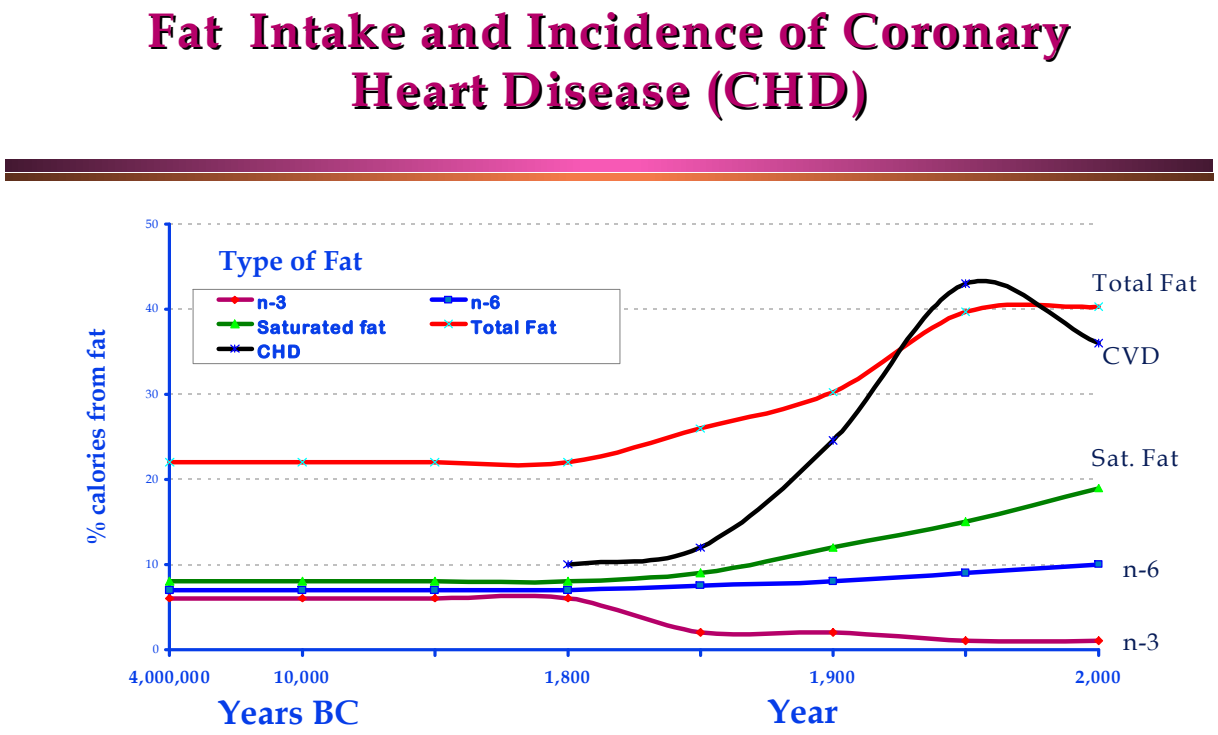


Sources of the omega-3 family of PUFA – the subject of most of the current research into PUFA and health – are far rarer in modern diets, however. Leafy green vegetables provide the precursor, alpha-linolenic acid, for conversion into longer-chain omega-3 PUFA, principally eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). However, the richest sources of EPA and DHA are fish oil and fatty fish such as mackerel, herring and sardines. Leaf and Weber reported that the average intake of the omega-3 PUFA is now only 4 to 10 percent of the intake of omega-6 PUFA, compared to an estimated ratio of roughly 1:1 about 150 years ago (1) (Figure 2.)

Figure 2.

Cardiovascular Disease* Expressed as a percentage of total mortality

Source: Leaf and Weber, 1987

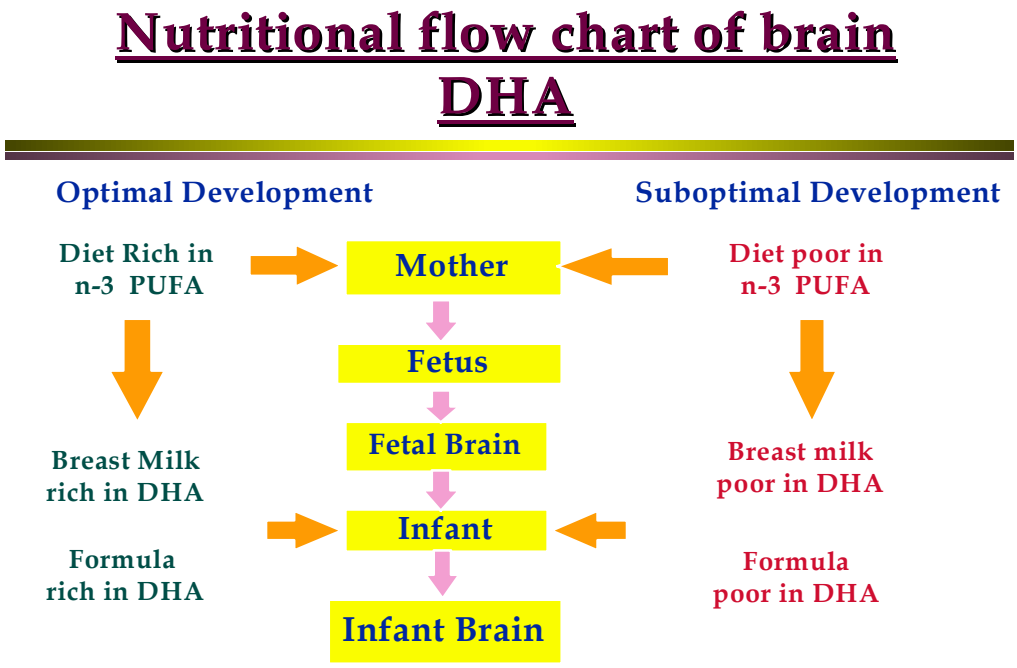


Scientists first identified roles for PUFA in the 1920s, but it wasn't until the 1980s that new work expanded that knowledge considerably, especially regarding the long-chain PUFA.

Maternal and Infant Nutrition

Omega-3 PUFA's role in neural development during gestation and infancy is well established. DHA and AA, supplied first through the placenta and then in human milk, are incorporated into the phospholipid membranes of the brain and retina, and they continue to accumulate there from gestation through the first two years after birth. Since these nutrients are not produced by the developing embryo, the fetus and placenta are fully dependent on the mother's intake and stores of essential fatty acids. Pregnant women, infants and toddlers are among the most likely groups to have deficient levels of PUFA. (Figure 3)

Figure 3. Flow of Long Chain Fatty Acids to Infant Brain from Maternal and Infant Formula Sources



Studies have shown slower visual development in babies who received conventional infant formula, which includes alpha-linolenic acid but not the longer-chain DHA. While babies have a limited capacity to convert the parent compound alpha-linolenic acid to the longer-chain DHA, the efficiency and rate of the conversion appears to be inadequate to supply the necessary levels for optimal retinal and neural development.

Premature babies are especially at high risk of DHA deficiency because the placental transfer of DHA is most marked during the third trimester. The deficiency could have a serious impact on neurodevelopment because it is during this last trimester that DHA is being incoporated into the tissues of the brain and retina. However, Bendich has reported that when premature babies fed formula also received supplemental DHA as fish oil, their sight developed as quickly as breast-

fed babies. (2). Leading researchers and authoritative scientific groups such as the World Health Organization have called for direct addition of DHA and AA to infant formulas.

Cardiovascular Health

Research into cardiovascular health and PUFA intake has also advanced considerably during the past decade. There seem to be a number of different areas where omega-3 PUFA may influence cardiovascular outcomes.

By far, the strongest data is the area of triglycerides, a component (like cholesterol) of lipoproteins. Growing evidence suggests that triglycerides are associated with an increased risk for coronary heart disease. Studies have consistently found that in patients receiving omega-3 supplementation, there were significant reductions in serum levels of the triglycerides and very low density lipoproteins that promote clogging of the arteries. Connor (3) reported that the triglyceride-lowering effect was seen in patients with either high or normal triglyceride levels, and decreases of up to 50 percent were frequently observed. A recent meta analysis summarised the wealth of data on triglycerides. (4)

Siscovick *et al*. (5) reported that consuming small amounts of EPA and DHA, equivalent to one meal of fatty fish per week, was associated with a 50 percent reduction in the risk of cardiac arrest. Placebo-controlled studies by Christensen *et al.* and Sellmayer *et al*. (6,7) confirmed the initial data.

In four studies analyzed by Gapinski *et al*. (8), omega-3 supplementation also significantly reduced restenosis, or the reclogging of arteries, in patients undergoing angioplasty.

Several studies have also suggested that increased consumption of long-chain omega-3 PUFA can reduce blood pressure in mildly hypertensive individuals. In work such as Knapp (9) and Weber and Leaf (10), the reductions in both the systolic and diastolic blood pressure levels have

ranged from 3 to 10 points. One reason appears to be increased formation of nitric oxide, a blood vessel dilator that lowers blood pressure and lessens the work required of the heart.

Other work, such as that by Abbey *et al*. (11), has reported reductions in the clotting agents that cause heart attacks, as well as reductions in cardiac arrhythmias, which are believed to be one of the major causes of sudden death in patients with heart disease. The mechanisms behind these results remain uncertain, but the work to date suggests effects that are individually small but collectively significant, especially in concert with standard therapy and lifestyle changes.

Other Health Effects

Research into other health effects with increased omega-3 consumption is less extensive but also promising. Among the subjects of current interest are rheumatoid arthritis, psoriasis, ulcerative colitis, Crohn's disease and a number of neurological conditions. Studies such as Fortin (12) suggest that long chain omega-3 PUFA may modify and provide modest therapeutic benefits for inflammatory and autoimmune diseases. Research into neuronal dysfunction leading to adrenoleukodystrophy (ALD), depression, aggression and attention-deficit hyperactivity disorder may be a result of a deficiency of long chain omega-3 fatty acids. Additionally, this deficiency may be exacerbated through the chronic use of alcohol.

Dietary Intake Recommendations Urgently Needed

This body of work has prompted a reevaluation of dietary requirements for omega-3 PUFA. Although the U.S. still does not have recommended dietary allowances (RDA) for either omega-3 or omega-6 PUFA, the Food and Nutrition Board noted in 1989 that "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."

The review of lipids and in particular long chain fatty acids by the Food and Nutrition Board in the development of new RDAs will occur in the near future as a part of the current update of recommendations in the United States.

Dietary Intakes Found to be at Low Levels in Most Developed Countries

In discussing dietary recommendations on PUFA consumption, it is important to distinguish between omega-3 and omega-6 fatty acids because they are metabolically and functionally distinct and have opposing physiological functions. Canada began issuing separate recommendations in 1990. For omega-3 PUFA, these range from 0.5 g per day for infants to 1.8 g per day for adolescent boys or roughly one sixth the Canadian recommendation for omega-6 PUFA. In the United Kingdom, the British Nutrition Foundation recommends a daily intake of omega-3 PUFA ranging from 0.5 to 2.5 percent of energy. This amount would be obtained by 3 to 4 g of fish oil or two to three servings of fatty fish per week.

As a part of total recommended fat intake, these recommendations are quite modest. However, Simopoulos (13) found that the average intake of omega-3 PUFA in North America is only a third to a half of these levels. The importance of this shortfall may be especially pronounced in those with a predisposition to cardiovascular disease, hypertension, arthritis or psoriasis.

Changes in both diet and the methods of food production explain the low consumption rates of long chain omega-3 polyunsaturated fatty acids (PUFA), which researchers have linked to various illnesses in Western societies. Certainly the most obvious reason is the low average intake of fish oil or fatty fish that are rich sources of DHA and EPA, the main long-chain omega-3 fatty acids. However, secondary sources, including meat and eggs, also provide less of the omega-3 fatty acids than they once did. The decrease in secondary sources is due to the predominance of grain in livestock and poultry feed. Green vegetation is a rich source of alpha-linolenic acid, the omega-3 precursor that animals convert to DHA and EPA. Grain, on the other hand, is rich in omega-6 but poor in omega-3 fatty acids.

Furthermore domestic beef from farm-finished animals contains little or no detectable amounts of omega-3 PUFA. Newton (14) further noted that feeding practices in modern aquaculture now produce fish that contain less omega-3 PUFA than those that feed on plankton. At the same time, consumption of the omega-6 PUFA has risen. Not only has vegetable oil technology popularized the use of cooking oils from sunflowers, peanuts and corn – all good sources of linoleic acid – it has also increased their use in processed foods.

Increasing the Dietary Sources of Omega-3 PUFA

Researchers now suggest that the balance between different types of fat is important for good health and estimate that the dietary ratio of omega-6 to omega-3 PUFA in North America ranges between 10:1 and 20:1, compared to a ratio of 1:1 until 150 years ago (Figure 2)

Rebalancing that ratio has always presented a challenge because many people find fish, particularly fatty fish, either inconvenient or unpalatable. Furthermore, strong tastes and odors have also limited the use of fish oil in processed foods that include fat for flavor or texture. As a result, Roche has developed a range of omega-3 PUFA products under the trade name "Ropufa" for use in supplementation and food enrichment programs.

Figure 4. Special refining and purification of Ropufa Omega-3 oils.

ROPUFA EPA Oil Processing Steps

- Neutralizing (NaOH)
  - Removes Free Fatty Acids
  - Prevents formation of soaps
  - Removes pesticides, pigments
- Bleaching (Diatomaceous Earth)
  - Removes chlorophyll/pigments
  - Removes peroxides
  - Removes heavy metals, pesticides
- Adsorption (Silica/ Carbon)
  - Removes polymers, volatiles, improves stability
- Deodorisation (High Vacumn./Low Temp Steam)
  - Removes peroxides, aldehydes, ketones
- Stabilization (Antioxidant Mixture)
  - Protects against oxidation in storage

Although obtained from fish oil, the "Ropufa" omega-3 products are specially refined to provide neural taste and odor. Figure 4. Food manufacturers may simply add these products to their current list of ingredients, but will more often use them to replace some of the other fats and improve a product's nutritional profile. In European markets, "Ropufa" oils and powders are now being added to bread, margarine, mayonnaise, salad dressings and milk drinks. In development are combinations of cardioprotective substances such as vitamin E, vitamins B6, B12 and folic acid for lowering homocysteine, plus cholesterol lowering oats to provide truly functional foods as RTE breakfast cereals or cereal bars. Generally 10-20% of recommended intakes can be incorporated in many foods at typical serving sizes. These fish-based oils were developed because these natural sources have the backing of years of scientific research and have been the material used by leading researchers. Novel oil sources such as those from single cell fermentation of algae have fatty acid profiles significantly differing from fish oils, in particular a lack of EPA. Researchers believe that a balance of both EPA and DHA are both critically important in human health and metabolism.

Increased dietary intakes of long-chain fatty acids from the omega-3 family appear crucial for optimal development of infants and adults. The reduction of cardiovascular disease and other neurological disorders appears a promising area. Incorporation of new highly refined oils and powders into a variety of products by food companies is a step forward in providing these essential nutrients to consumers.

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