Council for Responsible Nutrition

WHITE PAPER

Long Chain Omega-3 Fatty Acids in Human Health

HEART HEALTH: The Role of Eicosapentaenoic, Docosahexaenoic, & Alpha-Linolenic Acids (EPA, DHA, and ALA)

Council for Responsible Nutrition.
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Summary: Increased intakes of all three of the main omega-3 fatty aids alpha-linolenic acid (ALA), eicosapantaenoic acid (EPA) and docosahexaenoic acid (DHA) have been shown to have multiple health benefits. The strongest evidence for cardiovascular benefit is related to increased intakes of EPA and DHA. The U.S. Food and Drug Administration (FDA) has permitted a qualified health claim for foods and dietary supplements containing EPA and DHA, saying: "Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease." (FDA 2004 a,b).

Reviews of the evidence for cardiovascular benefit of omega-3 fatty acids

FDA reviewed the clinical data supporting cardiovascular benefits of EPA and DHA in 2000 when considering a qualified health claim. FDA noted that four randomized, controlled, clinical intervention trials conducted in populations with CHD or high risk factors for CHD found substantial benefits (GISSI 1999, von Schacky 1999, Singh 1997, Burr 1994). All four studies "reported significant reductions in CHD risk with increased consumption of omega-3 fatty acids, predominantly EPA and DHA, with one study also noting ALA. The largest study, the GISSI trial, conducted in patients who had survived a recent myocardial infarction (MI), reported a 15 percent decrease in relative risk of CHD (defined as death, non-fatal MI, and non-fatal stroke) in the intervention group that consumed 850-882 mg/d of ethyl esters of EPA and DHA…" (FDA 2000). On the basis of these studies, FDA permitted a qualified health claim for dietary supplements containing EPA and DHA.

In 2004, FDA again reviewed the data on cardiovascular benefits of EPA and DHA, especially recent observational studies relevant to dietary intakes of EPA and DHA from conventional foods. These included data from two large prospective cohorts, the Nurses Health Study (Hu 2002) and the Physicians Health Study (Albert 1998, Albert 2002). On the basis of these studies, FDA extended the omega-3 qualified health claim to include conventional foods that are sources of EPA and DHA (FDA 2004 a,b).

The Agency for Healthcare Research and Quality (AHRQ), a division of the U.S. Department of Health and Human Services, also recently reviewed the evidence on omega-3s and cardiovascular disease, at the request of the National Institutes of Health (NIH) Office of Dietary Supplements (ODS). The report concluded: "Overall, the evidence from the primary and secondary prevention studies supports the hypothesis that consumption of omega-3 fatty acids (EPA, DHA, ALA), fish, and fish oil reduces all-cause mortality and various CVD outcomes such as sudden death, cardiac death (coronary or MI death), and MI, although the evidence is strongest for fish or fish oil." (ARHQ 2004).

The American Heart Association's Nutrition Committee issued a statement on fish, omega-3s and heart disease in 2002 and concluded that "omega-3 fatty acids have been shown in epidemiological and clinical trials to reduce the

incidence of CVD. Large-scale epidemiological studies suggest that individuals at risk for CHD benefit from the consumption of plant-and marine-derived omega-3 fatty acids, although the ideal intakes presently are unclear. Evidence from prospective secondary prevention studies suggests that EPA and DHA supplementation ranging from 0.5 to 1.8 g/d (either as fatty fish or supplements) significantly reduces subsequent cardiac and all-cause mortality. For alpha-linolenic acid, total intakes of about 1.5 to 3 g/d seem to be beneficial." (AHA 2002).

Dietary intakes and dietary recommendations

For heart health, the public has been urged for many decades to reduce consumption of saturated fats and replace them with unsaturated fats. Saturated fats are the solid fats that can be seen in many meat products, such as beef, pork, poultry and some plants such as coconut, palm fruit and palm kernel oil. Seed oils like cottonseed also have relatively high levels of saturated fat. In contrast, unsaturated fats are fluid at room temperature. They include monounsaturated fats (also known as omega-9 or oleic acid) that are present in olive oil, and the polyunsaturated fatty acids (PUFAs) present in many grains, nuts, plant oils, and fish. PUFAs fall into two classes, the omega-6 and the omega-3 fatty acids. The names indicate the chemical structure of these fatty acids, which have their first unsaturated bond (double bond) at carbon number 6 or carbon number 3, respectively, from the end of the chain.

The parent fatty acid for both classes is the 18-carbon fatty acid, called linoleic acid (LA) for the omega-6 series and alpha-linolenic acid (ALA) for the omega-3 series. These are the two "essential" fatty acids, in nutritional terms, because they cannot be made by the body but must be obtained from food sources. These can be elongated by human, animal and marine life metabolism to produce longer-chain fatty acids such as arachidonic acid (ARA) in the omega-6 series or EPA and DHA in the omega-3 series (Figure 1). The Institute of Medicine states "ALA is not known to have any specific functions other than to serve as a precursor for synthesis of EPA and DHA." (IOM 2002). However, the conversion of ALA to EPA and DHA occurs only at a very low rate (Emken 1994, Pawlosky 2001). Such conversion will not be sufficient to produce the levels of EPA and DHA believed to have heart health benefits. The optimal approach to ensuring optimum intakes of omega-3 fatty acids for heart health is to directly increase consumption of EPA and DHA via frequent fish consumption or supplementation. Note however, that women of childbearing age should follow FDA guidelines on fish consumption to limit exposure to environmental contaminants.

Omega-6 PUFAs are present in the most commonly consumed oils, including cottonseed, corn oil, soybean and peanut oil. In contrast, the major source of omega-3 fatty acids is dietary intake of fish, fish oil, vegetable oils (principally canola and soybean), some nuts including walnuts, and dietary supplements (ARHQ 2004). ALA is also found in abundance in flaxseed oil. In North American diets, omega-6 PUFAs make up 89 percent of the total consumption of polyunsaturated fatty acids, while

omega-3 PUFAs make up only about 9 percent. Because omega-6 PUFAs are consumed in such relatively large quantities, "maintaining a sufficient intake of omega-3 fatty acids is particularly important since many of the body's physiologic properties depend upon their availability and metabolism." (ARHQ 2004). Many experts have recommended that Western industrialized nations should significantly reduce overall omega-6 PUFA intake and increase omega-9 and omega-3 PUFA intake in order to improve cardiovascular health and brain function (Simopoulos 2000).

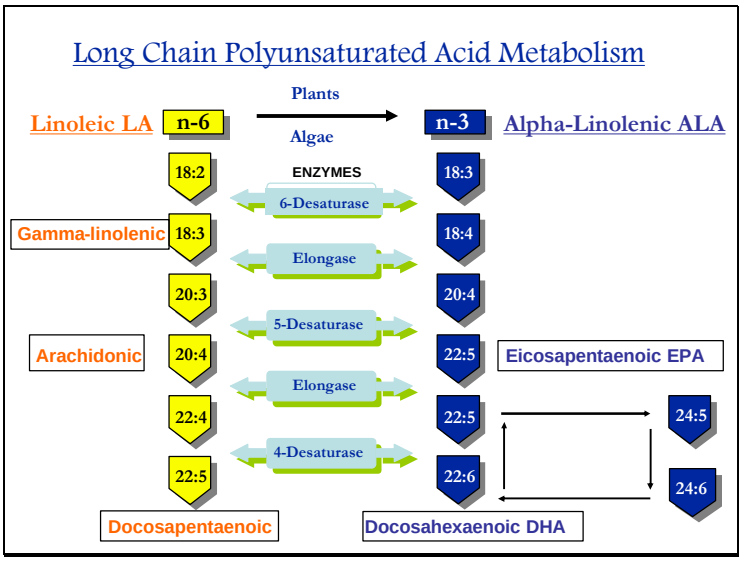

Figure 1. The metabolism of Alpha Linolenic Acid (ALA) to the longer chain fatty acids, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA).

According to the Institute of Medicine report on Dietary Reference Intakes for macronutrients, the omega-3 fatty acids "play an important role as structural membrane lipids, particularly in nerve tissue and the retina." (IOM 2002). ALA cannot be synthesized in the human body, and the lack of it results in clinical symptoms including neurological abnormalities and poor growth. Therefore, ALA is considered to be essential in the diet. ALA can be elongated to EPA and DHA, whose metabolic products "have been shown to have beneficial effects in preventing coronary heart disease, arrhythmias, and thrombosis." (IOM 2002). Specifically, EPA and DHA and their byproducts are metabolic regulators that tend to reduce inflammation, prevent heart arrhythmias, reduce platelet aggregation, dilate the blood vessels, and lower blood triglyceride levels (ARHQ 2004).

The Institute of Medicine has established an Adequate Intake level of 1.1 to 1.6 g/d for ALA. Median population intake of ALA, as shown by a 24-hour

recall in NHANES III, was only 0.9 g/d, so increased intakes would be desirable. In the same NHANES III data, the median intakes of EPA and DHA were zero, since only about 25 percent of the population consumed any EPA or DHA on the survey day. Mean intakes of EPA and DHA were only 40 and 70 mg/d, respectively (ARHQ 2004), suggesting that a significant increase in intake is needed to meet recommended levels for heart health.

The Institute of Medicine did not establish an Adequate Intake level for EPA and DHA. However, a number of other countries (Canada, Sweden, United Kingdom, Australia, and Japan) have made dietary recommendations for omega-3 fatty acids, and these typically suggest 0.3 to 0.5 g/d of EPA and DHA (AHA 2002). The American Heart Association recommends two fish meals a week to provide this level of intake. The Dietary Guidelines for Americans issued in January 2005 echo this advice (Dietary Guidelines 2005). However, typical North Americans consume very little fish. For those whose diets fall short, dietary supplements of EPA and DHA would be highly beneficial in optimizing intakes for heart health.

The American Heart Association notes that, for secondary prevention, higher levels of EPA and DHA ranging from 0.5 to 1.8 g/d have been shown to reduce cardiac and all-cause mortality, and that intakes of ALA in the range of 1.5 to 3 g/d appear to be beneficial (AHA 2002). For most people, dietary changes plus supplementation will be required to reach protective levels of intake for EPA and DHA.

Conclusion

Omega-3 polyunsaturated fatty acids are important to overall health and have a special role to play in promoting heart health, especially the very long chain fatty acids EPA and DHA. Dietary intakes are typically very low. Frequent fish consumption or supplementation with EPA and DHA are the best ways to achieve a protective intake level of about 0.5 g/d.

References:

AHA 2002. American Heart Association Scientific Statement: Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation 2002; 106:2747-2757.

Albert CM, Hennekens CH, O'Donnell CJ, et al. Fish consumption and risk of sudden cardiac death. JAMA 1998; 279:34-38.

Albert CM, Campos H, Stampfer MJ, et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. NEJM 2002; 346:1113-1118.

ARHQ 2004. Agency for Healthcare Research and Quality, Evidence Report Number 94. Effects of omega-3 fatty acids on cardiovascular disease. March 2004. Available from ARHQ website.

Burr ML, Sweetham PM, Fehily AM. Letters to the Editor. Diet and reinfarction. European Heart Journal 1994;15:1152-1153.

Dietary Guidelines for Americans. 2005 report of the Dietary Guidelines Advisory Committee. Chapter 4, Fats. Available from the Dietary Guidelines website.

Emken EA, Adlof RO, Gulley RM. Dietary linoleic acid influences desaturation and acetylation of deuterium-labeled linoleic and linolenic acids in young adult males. Biochim Biophys Acta 1994; 1213:277-288.

FDA 2000. Letter regarding dietary supplement health claim for omega-3 fatty acids and coronary heart disease, October 31, 2000. Available from FDA website.

FDA 2004 (a). Letter responding to health claim petition dated June 23, 2003 (Wellness petition): Omega-3 fatty acids and reduced risk of coronary heart disease. Available from FDA website.

FDA 2004 (b). Letter responding to health claim petition dated November 3, 2003 (Martek petition): Omega-3 fatty acids and reduced risk of coronary heart disease. Available from FDA website.

GISSI Prevenzione Investigators (Gruppo Italiano per lo Studio della Sopravivenza nell'Infarto miocardico). Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-prevenzione trial. Lancet 1999; 66:649-659.

Hu FB, Bronner L, Willett WC, et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. JAMA 2002; 288:2569-2578.

IOM 2002. Institute of Medicine: Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. The National Academies Press, Washington, D.C., 2002.

Pawlosky RJ, Hibbeln JR, Novotny JA, Salem N Jr. Physiological compartmental analysis of alpha-linolenic acid metabolism in adult humans. J Lipid Res 2001; 42:1257-1265.

Simopoulos AP, Leaf A, Salem N Jr. Workshop statement on the essentiality of and recommended dietary intakes for omega-6 and omega-3 fatty acids. Prostaglandins, leukotrienes and essential fatty acids 2000; 63:119-121.

Singh RB, Niaz MA, Sharma JP, et al. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction. Cardiovascular Drugs and Therapy 1997; 11:485-491.

von Schacky C, Angerer P, Kothny W, et al. The effect of dietary omega-3 fatty acids on coronary atherosclerosis - A randomized double-blind, placebo-controlled trial. Annals of Internal Medicine 1999; 130:554-562.