

## **Omega-3 fatty acids and cardiovascular disease**

### **Current Opinion in Clinical Nutrition and Metabolic Care Volume 7(2) March 2004 pp 131-136**

Clemens von Schacky,

FROM ABSTRACT

Omega-3 fatty acids are gaining acceptance in the cardiovascular field. The present review describes the most recent studies and developments in the field.

Recent findings:

Marine n-3 fatty acids, that is eicosapentaenoic and docosahexaenoic acids, prevent fatal myocardial infarction and sudden cardiac death by their antiarrhythmic effects and presumably also by their effect on infarct size, the latter mediated by plaque stabilization, improvements in endothelial function and other mechanisms.

In contrast, a cardioprotective effect of alpha-linolenic acid, a plant-derived n-3 fatty acid, remains to be clearly demonstrated in adequate intervention trials.

Other forms of applications, like parenteral use or other indications, like in the psychiatric field, are currently being actively investigated.

Summary:

Eicosapentaenoic and docosahexaenoic acids, but not alpha-linolenic acid, prevent sudden death and other cardiovascular catastrophies, and have therefore been recently incorporated into the pertinent guidelines of European and American cardiologic societies.

THIS AUTHOR ALSO NOTES:

"Current guidelines from various nutritional and cardiologic societies recommend intake of n-3 fatty acids to prevent cardiovascular disease."

Unsaturated fatty acids (n-9, n-6, n-3) are defined by the position of the first double bond in the carbon chains from the methyl end carbon.

In humans, double bonds cannot be inserted into the methyl end of a fatty acid; therefore, humans cannot interconvert fatty acid families.

“Conventional textbook wisdom has it that, within a family, unsaturated fatty acids can be chain elongated and desaturated to their longer, and more highly desaturated, derivatives. This is true in rodents. In humans, however, this process does not occur at a quantitatively or biologically relevant degree: alpha-linolenic acid (LNA) is chain elongated/desaturated to eicosapentaenoic acid (EPA) in small amounts in adult humans.” **[Very Important for strict vegetarians]**

Ingestion of alpha-LNA [plant source 18 carbon long n-3 with 3 double bonds] cannot replicate the biological action of purified EPA.

**[Again, Important for strict vegetarians]**

EPA is poorly elongated/desaturated to docosahexaenoic acid (DHA).

DHA is retroconverted to EPA, but this does not have great biological relevance.

“In comparative studies of pure EPA and DHA in humans, DHA, but not EPA, was found to lower blood pressure, improve endothelial function, and increase high-density and low-density lipoproteins.”

Therefore, “not only alpha-LNA, but probably also EPA, and definitely DHA, thus appear as essential fatty acids by themselves for humans.” **[Very Important]**

“Plant sources of n-3 fatty acids (flaxseed, soy, nuts) contain alpha-LNA, while EPA plus DHA are found in fish and fish oils.”

“Thus, recommending intake of n-3 fatty acids from plant sources to achieve the cardiovascular benefit demonstrated for EPA plus DHA is unfounded.” **[Important]**

Alpha-Linolenic acid occurs in plants.

“Higher consumption of alpha-LNA is associated with less coronary and carotid atherosclerosis.”

“EPA plus DHA have consistently decreased plasma triglyceride concentrations.”

In one study, a small increase in EPA, but not in DHA, was noted after ingestion of up to 9.5 g alpha-LNA per day for 6 months. **[Important]**

In another study, alpha-LNA increased inflammation, while DHA had the opposite effect.

6.3 g/day alpha-LNA for 2 years increased total cholesterol, lowered high-density lipoprotein and increased triglycerides as compared with linolenic acid. [Bemelmans WJ, Broer J, Feskens EJ, *et al.* Effect of an increased intake of alpha-linolenic acid and group nutritional education on cardiovascular risk factors: the Mediterranean Alpha-linolenic Enriched Groningen Dietary Intervention (MARGARIN) study. *Am J Clin Nutr* 2002; 75:221-227]

Very little evidence in terms of mechanisms of action, animal studies, clinical studies in humans with surrogate or intermediate endpoints exists to support a potential cardiovascular benefit of alpha-LNA [18 carbon plant derived omega-3]. A host of epidemiologic studies have been published recently on fish, n-3 fatty acids and cardiovascular morbidity and mortality.

"Fried fish or fish sandwich consumption was not of any benefit, while consumption of tuna or other broiled or baked fish was associated with lower risk of ischemic cardiac death, especially arrhythmic ischemic cardiac death."

[Mozaffarian D, Lemaitre RN, Kuller LH, *et al.* Cardiac benefits of fish consumption may depend on the type of fish meal consumed: the Cardiovascular Health Study. *Circulation* 2003; 107:1372-1377.]

There is a significant antiarrhythmic effect of EPA and DHA.

"The higher the percentage of EPA plus DHA in red cell phospholipids, the lower the heart rate."

"In a case-control study, toenail mercury levels were directly associated with the risk of myocardial infarction, and the adipose-tissue DHA level was inversely associated with the risk. The authors interpreted this finding by stating that high mercury content may diminish the cardioprotective effect of fish intake."

[Guallar E, Sanz-Gallardo MI, van't Veer P, *et al.* Mercury, fish oils, and the risk of myocardial infarction. Heavy Metals and Myocardial Infarction Study Group. *N Engl J Med* 2002; 347:1747-1754]

"Concerns about n-3 fatty acids increasing the number of strokes do not seem warranted in the 1 g/day dosage range."

The mechanisms of action of n-3 fatty acids include:

- 1) An antiarrhythmic effect can be demonstrated.
- 2) Omega-3 fatty acids inhibit the fast, voltage-dependent sodium currents and the calcium currents in excitable cardiac tissue.
- 3) There is an antiinflammatory effect of EPA plus DHA.
- 4) There is histologic evidence for plaque stabilization only in those supplemented with n-3 fatty acids.
- 5) Supplementation with 1.65 g/day n-3 fatty acids modestly mitigates the course of coronary atherosclerosis, as assessed by coronary angiogram.

"EPA plus DHA might therefore prevent both arrhythmias and pump failure brought about by large myocardial infarctions - the two major pathologies underlying sudden cardiac death."

"In a scientific statement issued in November 2002, the American Heart Association recommended that patients with documented coronary heart disease take about 1

g/day EPA + DHA, preferably in the form of oily fish, or a EPA + DHA supplement in consultation with the treating physician.”

[Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. American Heart Association. Nutrition Committee. Circulation 2002; 106:2747-2757. First statement of the American Heart Association differentiating between plant-derived and marine n-3 fatty acids]

The European Society for Cardiology has issued three different guidelines, in which n-3 fatty acids are recommended:

- 1) European guidelines on cardiovascular disease prevention state that “oily fish and omega-3-fatty acids have particular protective properties.”
- 2) European guidelines on management of acute myocardial infarction recommend “supplementation with 1 g fish oil n-3 poly-unsaturated fatty acids” for secondary prevention of myocardial infarction.
- 3) European guidelines on prevention of sudden cardiac death recommend n-3 supplementation for all patients after a myocardial infarction for primary prophylaxis of sudden death.

“In psychiatric disorders, EPA plus DHA currently show promising results.”

**[IMPORTANT]**

Because of environmental reasons, EPA and DHA need to be introduced into the diet from sources other than fish. **[IMPORTANT]**

## CONCLUSIONS

“Taken together, EPA plus DHA are now firmly established in the therapy after a myocardial infarction and in prevention of cardiovascular disease.”

“In general, a dose of 1 g/day of EPA plus DHA is recommended, be it in the form of fish or fish oil capsules.”

## KEY POINTS FROM DAN MURPHY

- 1) Marine n-3 fatty acids, eicosapentaenoic and docosahexaenoic acids, prevent fatal myocardial infarction and sudden cardiac death by their antiarrhythmic effects, by their effect on infarct size, by plaque stabilization, and by improvements in endothelial functions.
- 2) A cardioprotective effect of alpha-linolenic acid, a plant-derived n-3 fatty acid, has not been clearly demonstrated.
- 3) Eicosapentaenoic and docosahexaenoic acids, but not alpha-linolenic acid, prevent sudden death and other cardiovascular catastrophes.
- 4) Rodents can convert alpha-linolenic acid (18:3n-3 from plants) to EPA (20:5n-3 from fish) and EPA to DHA (22:6n-3 from fish) through desaturation and elongation; but in humans, this process does not occur at a quantitatively or biologically relevant degree.
- 5) Humans cannot obtain an adequate amount of EPA or DHA from dietary alpha-LNA, even if they take 6.3 g/day alpha-LNA for 2 years.
- 6) Because of their poor interconversion, alpha-LNA, EPA, and definitely DHA are each essential fatty acids by themselves for humans, and each need to be ingested separately.
- 7) Plant sources of n-3 fatty acids does not achieve the cardiovascular benefit noted for EPA plus DHA.
- 8) Fried fish or fish sandwich consumption is not associated with improved cardiovascular benefit.
- 9) Consuming n-3 fatty acids in the range of 1 g/day does not increase stroke risk.
- 10) EPA plus DHA are anti-inflammatory.
- 11) In November 2002, the American Heart Association recommended that patients with documented coronary heart disease take about 1 g/day EPA + DHA.
- 12) EPA plus DHA ingestion is showing promising results in psychiatric disorders.
- 13) Because of environmental reasons, EPA and DHA need to be introduced into the diet from sources other than fish, i.e. from supplementation.