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MARINE N-3 POLYUNSATURATED FATTY ACIDS AND CORONARY HEART DISEASE: COME A LONG WAY BUT EXPECT MORE

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Nearly 40 years have passed since Bang, Dyerberg, and their colleagues from the Department of Clinical Chemistry in Aalborg, Denmark, started their investigations in traditionally living Greenland Eskimos to explore anecdotal reports of a reduced incidence of coronary heart disease (CHD) in this population living nearly exclusively on seafood. Based on findings from several expeditions to Greenland (8,1), Dyerberg and Bang, in a seminal paper from 1978, suggested that intake of marine n-3 polyunsaturated fatty acids (PUFA), notably eicosapentaenoic acid (EPA), might prevent atherosclerosis and thrombosis (10).

Since then, the hypothesis has been explored intensely, and a vast number of epidemiological studies, animal and laboratory experiments, studies on the effect of n-3 PUFA on risk factors for CHD, and large randomized clinical trials have been published. Results have not been uniform, but evidence is emerging that n-3 PUFA may reduce CHD (9,3,2,12,11). Still, there are many issues that remain to be clarified with respect to n-3 PUFA and prevention of CHD. Among these, some important (but not the only) ones are:

Mechanisms of action?

Studies have suggested several mechanisms by which intake of marine n-3 PUFA may reduce the risk of CHD including a reduction in plasma triglycerides, a reduction in platelet reactivity, a slight blood pressure lowering effect, and antiinflammatory and antiarrhythmic effects (9,3,2,12,11,4). While the latter two mechanisms have been in focus recently, it is conceivable that the overall effect is derived from a combination of the abovementioned and other less documented and, most likely, hitherto unknown effects. In addition, my personal view is that diet-gene interactions may be of major importance. A better understanding of mechanisms is crucial to determine which type (EPA and/or docosahexaenoic acid (DHA)) and dose of n-3 PUFA should be advocated for the prevention of CHD.

EPA or DHA?

Fish contain both EPA and DHA, and both n-3 PUFA are present in fish oil capsules, although in varying proportions in different preparations. Little is known about the effects of docosapentaenoic acid (DPA), and the effects of n-3 PUFA are generally attributed to EPA and DHA. Studies using highly purified preparations of EPA and DHA have suggested differences in their effects (9,3,2,12,11,4). EPA and DHA also differ in their relative concentrations in cells and tissues, but in the human body EPA can be elongated and desaturated to DHA (with the opposite conversion also being possible) further complicating matters. Initially, focus was almost entirely on EPA (10), but recent data have suggested that DHA may be equally or perhaps even more important. However, it is likely that the effects of EPA and DHA may complement each other and together account for the clinical effects observed.

What is the optimal dose of n-3 PUFA for prevention of CHD?

Clinical intervention trials have suggested that a dose of approximately 1 g per day reduces CHD (7,6,5), but none of the abovementioned

mechanisms has been convincingly documented to occur at such a low intake of n-3 PUFA. Actually, the biochemical effects are generally more beneficial with (much) higher doses of n-3 PUFA (9,3,2,12,11,4), and it is tempting to speculate that higher doses (13) may lead to greater reductions in CHD. This hypothesis obviously needs to be substantiated by findings from clinical trials, and in practice higher doses will be difficult to achieve by fish consumption alone.

Fish vs fish oil concentrates?

Apart from EPA, DPA, and DHA, fish also contain active and potentially cardioprotective substances such as iodine, selenium, vitamin D, and peptides. On the other hand, fish may also contain pollutants eg mercury and other toxic compounds (which can be removed during processing of fish oil concentrates) with potential adverse effects on CHD. Importantly, however, randomized clinical trials have reported similar effects of fatty fish and fish oil capsules suggesting that the main active substances actually are n-3 PUFA present in both fish and fish oil concentrates.

Although further clarification and documentation are needed, at present it makes good sense to follow the recommendation by several health organizations that the public, and in particular patients with CHD, should eat fish, preferably fatty, at least twice weekly to obtain an intake of marine n-3 PUFA of at least 1 g per day (7 g per week).

The present special issue of CMB contains new insights and thoughtful reviews that should update the reader and hopefully stimulate interest in the effects of n-3 PUFA on vascular disease.

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