

FISH OIL

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Long Bottom Line At The top: Fish oil contains long chain fatty acids EPA and DHA which do good things. One or two fish servings weekly or 1 gram fish oil daily inhibit clotting and reduce risk of heart attack and sudden death from arrhythmia. Higher doses lower lipid levels, temper inflammation, and help some adults with depression. DHA is essential for normal infant brain and eye development. Read and take seriously the side effects described at the end of this article.

Fish oil contains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), two long-chain omega-3 fatty acids. They constitute a large proportion of the fat in fish, seafood and the oils pressed from them. They are **elongated versions of an essential fatty acid, α -linolenic acid (ALA)**.

Theoretically we don't need to consume EPA and DHA from fish, because our bodies can make them from ALA. But we aren't very efficient at making long chain omega-3 fatty acids, and the longer the chain, the less we make. In spite of DHA being the major omega-3 fatty acid in the brain, we make less DHA, at a length of 26 carbons, than we do 25-carbon EPA.

The other essential fatty acid, linoleic, is an omega-6 fatty acid. In spite of linoleic and linolenic acids being almost identical, they follow very different paths in the body, leading to or against inflammation, clotting and immune activation.

Non-fish oil omega-3 fatty acids: People unjustifiably lump all the omega-3 fatty acids, from ALA to DHA, together as a class of do-good fats. ALA substitutes only as a weak version of DHA and EPA when it comes to preventing cardiac problems. The data that supports ALA as preventing heart disease suffers from poor study design and confounding by other dietary changes.

DHA's role in brain and nerves far surpass those of EPA or ALA. Limited conversion of EPA and ALA to DHA guarantee that the former won't work as well as the latter.

We believe that EPA and DHA act together to lower triglycerides (fat in the blood) and reduce heart disease and inflammation, but no one has evaluated them separately. Other sources of omega-3 fatty acids, such as nuts, reduce cardiovascular disease, but other good things in nuts might be responsible.

Neurological effects: Infants and small children absolutely require tiny amounts of DHA for brain and eye growth and development. Without it, their ability to see, think and behave normally suffers. In spite of turning some ALA into DHA, most of the DHA they need comes from the maternal womb and breast milk. Mothers' bodies accommodate by packing breast milk with linolenic acid, EPA and DHA, at almost 5 times the omega-6 fatty acid concentration.

N-3 fatty acids may be involved in brain speech-center development. In a small study in which each child served as their own control, as little as 250 mg per day of EPA + DHA benefitted children with speech apraxia.

Fish oil has helped some adults with neurological and behavioral disorders, ranging from depression and bipolar disorder to schizophrenia and dyslexia. We lack good studies to tell us which patients will benefit most and which dose works best. Depression requires a higher dose (more than 3 grams) than does heart disease.

Japanese students who took 1.5-1.8 grams of DHA daily, scored better on tests of stress and aggression during final exams, compared to those who took soybean oil capsules. Don't get too excited – it didn't make them smarter, just more relaxed.

Cancer Omega-3 fatty acids have suppressed cancer growth in animals. No epidemiological data have yet linked dietary fish with less cancer in humans.

Inflammation The body converts omega-3 fatty acids into predominantly *anti*-inflammatory molecules. Omega-6 fatty acids originating in vegetable oils often generate *pro*-inflammatory substances. EPA competes for the cyclooxygenase enzyme to block omega-6 fatty acids conversion to pro-inflammatory substances

Doctors have toyed with fish oil to treat inflammatory diseases for a long time. What we know so far is: When someone lands in the hospital with severe enough infection that it causes diffuse lung disease, feeding omega-3 fats may reduce inflammatory damage. The same is true in the lab with animals.

Large EPA + DHA doses (2.7 grams daily) halve the relapse rate in Crohn's disease, an inflammatory disease of the colon. Large amounts of EPA + DHA (> 9 grams of standard fish oil capsules) alleviate pain and swelling to some extent in rheumatoid arthritis patients. Whopping doses of 12 grams fish oil daily can help heal an chronic overuse musculoskeletal injury.

Cholesterol & Triglycerides: Since the 1950's we have known that fish oil is superior to other fats in lowering cholesterol. The first study to reduce heart attacks with fish diets was published in 1972. However, in the 1970's and 1980's, as Americans increasingly focused on cholesterol, public health officials and dietitians demonized saturated fat and told us to eat vegetable oils rich in omega-6 fatty acids. The fact that EPA + DHA is 6 to 7 times more potent than omega-6 fatty acids was lost on the American dietary scene.

Dietary fish oil is especially good at lowering triglyceride levels. It also dials down the liver's production of apoB, the major LDL protein. Fish oil is one of the few things that lowers Lp(a), a particularly bad form of LDL. Fish oil decreases lipids in people with a wide range of starting cholesterol and triglyceride levels. The higher the triglycerides, the better it works, even in the face of high dietary cholesterol intake.

In the process of lowering triglycerides EPA + DHA may raise LDL-C levels. As the body disposes of the triglyceride-carrying VLDL particles, they evolve into LDL particles. If the liver can effectively clear LDL from the blood, LDL-C blood levels fall along with triglycerides. If not, they rise.

Blood Pressure: Large EPA+DHA doses (6 grams of 85% EPA + DHA) lower systolic pressure (top number) by 4.6 and the diastolic pressure (bottom number) by 3. For reference, EPA + DHA constitutes only 40-50% of natural fish oil.

Eskimos Ground-breaking studies of Greenland Eskimos attributed the scarcity of heart attacks to their diet. Studies in the 1950's through the 1970's found that they consumed enough seal, whale and fish to provide 14 g/day of omega-3 fatty acids, a huge load, and had lower than predicted cholesterol and triglyceride levels. If Eskimos move to another country and forsake their seal and whale diet, their heart attack rate approximates the rate in the new country, confirming that genetics don't play a role.

Controversy: Fish oil doesn't necessarily protect against death: Eskimos have low heart attack rates, but have short life expectancy. People in both Japan and eastern Finland eat fish frequently but Finns' heart disease rate far exceeds that of Japanese. What if the Eskimos' protective agent, instead of omega-3 fatty acids, is living in an igloo or not having a corporate boss?

To address this question, further observational diet trials were done. They confirm the high fish → low heart attack theory. The Diet and Reinfarction Trial showed a 29% reduction in overall mortality in survivors of a first heart attack who consumed fatty fish at least twice weekly for two years. Japanese-American men who ate 2 or more fish meals per week in the Honolulu Heart study had 1/3 the risk of heart attacks as those who ate less than that. The Chicago Western Electric Study of middle age men followed for up to 31 years showed an inverse association between fish consumption and death from coronary heart disease. Investigators found similar results in middle-aged men and elderly men and women in a Netherlands trial and part of the Multiple Risk Factor Intervention Trial.

The Health Professionals Follow-up Study confirmed that people who ate 1-2 fish servings weekly incurred 25% less coronary risk than those who ate none at all. But they debunked the more-fish-is-better idea, finding no further benefit from high levels of fish intake, especially in those most worried about a heart attack. If a person thinks he will surely die of heart disease, he may clean up his entire lifestyle, not just fish, destroying any conclusions one might make about fish alone.

Some observational studies are not so positive. After 11 follow-up years, the Physicians' Health Study (all males) concluded that eating fish at least once a week did not affect heart attack rate or cardiac mortality. It did cut the sudden and all-cause death rate.

Analyses of lumped together studies generally find 10-24% fewer fatal and 22-29% fewer non-fatal heart attacks, 12-46% fewer strokes and 23% improved total mortality. Both patients who have never had heart disease and those with prior heart attacks accrue benefit from 1-2 fish meals per week. These numbers seem relatively consistent, but do vary somewhat, probably because of not being able to control all variables.

The best way to prove that fish oil rather than fish (which may work by displacing something worse) keeps people free from heart disease, is to test it directly against placebo. In one such study 6 grams (a high dose) of EPA-enriched fish oil daily for two years partially reversed coronary patients' arterial narrowing. In another, 4 grams of fish oil per day reduced the risk of clogging a coronary artery graft by 25%. A few scientists have measured body tissue concentrations of omega-3 fatty acids after supplementation, and found that levels correlate with reduced heart attack rates.

The GISSI-Prevenzione trial of 11,324 subjects drives the argument for supplementation. With 1 gram per day of EPA+DHA (not fish oil), fewer people died in the two years after a heart attack, compared to those ingesting no fish or fish oil. The sudden death rate plummeted, presumably from a reduction of abnormal heart rhythms. Compared to people taking no supplement, the benefit was immediate and progressively widened to statistical significance within 4 months. Fish oil did this without lowering LDL-cholesterol - In fact, it increased slightly.

Some have proposed that fish oil or EPA + DHA supplements prevent the most deaths if started within days after a heart attack. Ongoing studies are now looking at optimal timing.

Fish oil should supplement statins in high risk patients, not replace them. Statins lower LDL-C much more effectively and have non-cholesterol effects that reduce vascular disease.

Stroke: Nine studies of fish oil and stroke incidence varied widely, from 6% *more* to 21% *fewer* strokes in people consuming any fish compared to those who eat none. Unlike heart disease, as the number of fish meals per week increases, they seem to proportionately increase protection, reducing stroke by 12-46%.

People who eat fish are usually in a higher socio-economic class, exercise more, and smoke and weigh less, so can't give all the credit for reducing strokes to fish. This must be the case, since more Greenland Eskimos succumb to strokes than do fish-eating Japanese. So eat fish, optimize overall lifestyle and go light on the seal and whale meat.

Arterial disease in legs: The limited data available concerning omega-3 fatty acids and peripheral arterial disease doesn't look promising, in spite of decreased blood viscosity.

Heart Rhythm: Those who consume fish or fish oil capsules have lower risk of sudden cardiac arrest. The most common causes of cardiac arrest are massive heart attack and arrhythmia (irregular, rapid heart rate). Fish oil seems to stabilize heart rhythms, as seen in animal models, cell culture and cardiac bypass patients. Fish oil may not block all arrhythmias: EPA+DHA seem to work their anti-arrhythmic magic best in survivors of heart attacks and by reducing atrial fibrillation and PVC's, rather than ventricular tachycardia or fibrillation.

Dose: People who eat any fish fare better than those who eat none. Most evidence points to no added benefit from taking more than 1 gram EPA+DHA daily or eating more than 1-2 fish servings (3-4 ounces each) per week. As little as 30 g (one ounce) of lean fish per day lowered mortality by 50% in the Zutphen heart/diet study, without further benefit in those who ate much more. I wonder how many fish servings it takes to off-set a string of bacon/baloney/ribs days.

Mechanisms for vascular effects: EPA and DHA probably reduce heart disease and stroke through their effect on platelets. Platelets are bits of cells that form clot when activated by injury. Clot and cholesterol plug arteries, causing tissue to die from lack of a blood supply.

Scientists believe that omega-3 fatty acids insinuate themselves into platelet membranes, inhibiting platelet aggregation and prolonging bleeding time. This probably involves effects on prostaglandins. If platelets can't aggregate, arteries are less likely to close off. The effect is not as strong as that of 81 mg of aspirin.

EPA and DHA also work in many other ways: They reduce clot by reducing levels of some clotting proteins and inducing an activator of clot dissolution. They enhance blood vessel relaxation by nitric oxide. They reduce activity of the special nervous system involved in the 'flight or fight' response. By depositing in cell membranes, EPA and DHA reduce blood thickness and increase blood cell fluidity. Through other mechanisms (SRBP & PPAR's), they block fat generation and stimulate fat burning.

Diabetes: Scientists differ with respect to fish oil's effect on blood glucose. Insulin sensitivity improves in rats fed omega-3 fatty acids, probably by influencing cellular regulation of fat and sugar metabolism. Greenland Eskimos and Alaskan Indians have much less diabetes than would be expected from their obesity. These data seem promising, but we are long way from recommending fish oil for sugar control.

With all the heart disease that afflicts diabetics, one would think they should all take fish oil. I'm not aware of a study that singles out diabetics to see if they have fewer heart attacks or deaths on fish oil.

Sources: Only marine sources supply EPA and DHA in quantities sufficient to influence health. Fatty deep sea fish are the most concentrated dietary sources of EPA and DHA. Rich sources include mackerel, all types of salmon, sablefish, eel, yellowfin tuna, Maine lobster, Pacific oysters and herring.

Flaxseed oil and English walnuts are rich in ALA. Other oils, like soybean, canola and olive, and plants like chia, hemp, purslane, kiwi seeds and lingonberry contain some ALA, but omega-6 fatty acids predominate.

Wild plant leaves contain appreciable omega-3 fatty acids, while cultivated plants are poor sources. Wild animal meat contains small amounts of omega-3 fatty acids because the animals feed on wild plants. Feeding domesticated animals omega-6 fatty acid rich corn yields meat with only saturated and omega-6 fatty acids.

Side effects: The very effects that keep arteries from clotting off can cause problems. Greenland Eskimos have prolonged bleeding times and easy bruisability, presumably as a result of fish oil's platelet effects.

Mercury may contaminate fish, particularly farmed fish. Be sure to choose a fish oil supplement from non-farmed fish that has been purified of any PCB's, dioxin and mercury. Besides making someone loony, mercury may predispose to CHD.

Omega-3 fatty acids have a 4% rate of mostly gastrointestinal side effects. People may burp fish, bloat and/or have loose stool. Fish oil might make psoriasis worse, whereas omega-6 fats seem to improve it, for unclear reasons.

Though EPA and DHA become anti-inflammatory prostaglandins and reduce inflammation, their many double bonds might peroxidize prior to such conversion. Adding vitamin E to fish oil capsules keeps them from oxidizing while sitting on the shelf, but may not be sufficient to prevent doses greater than 3 grams daily from increasing blood peroxides.