

Fish Oils and Stroke/Blood Coagulation

Summaries of the latest research concerning fish oils and stroke and blood coagulation

Review supports benefits of omega-3 fatty acids for prevention of heart disease

ATLANTA, GEORGIA. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) have been linked to lower mortality from coronary heart disease (CHD) in several, but not all, observational studies on the topic. Prevention trials of n-3 PUFAs have also supported a role in CHD prevention, but several different varieties of n-3 PUFAs were used. Now, researchers from Emory University School of Medicine have reviewed the data from randomized controlled clinical trials on n-3 PUFAs and CHD. The studies were divided into those using plant-based n-3 PUFAs (alpha-linolenic acid, ALA), fish-based n-3 PUFAs (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA), and fish consumption in the diet. Fourteen randomized clinical trials were included in the review, six of which were of fish oil, including one large trial of 10,000 participants. The researchers report a clear trend suggesting that there are important differences in CHD outcomes when using fish-based EPA or DHA compared with plant-based ALA. Most of the fish oil trials suggest a significant reduction in total mortality and CHD deaths and a possible strong antiarrhythmic effect. The dietary fish trials also suggest a reduction in mortality and reduced arrhythmia, supporting the theory that fish-based n-3 PUFAs may impart their cardioprotective effect by acting as an antiarrhythmic agent. They may do so by stabilizing the electrical activity of heart muscle cells or by decreasing the heart rate. The trials of ALA supplements and ALA-enriched diets, including walnut, soybean, or flaxseed oil, were less reliable, but showed possible benefits in reducing mortality. The review concludes that the evidence suggests a role for fish oil (EPA, DHA) or fish in secondary prevention, as clinical trial data demonstrate a significant reduction in total mortality, coronary heart disease death, and sudden death. However the data on ALA is limited by studies of limited quality. Several previous studies have suggested that n-3 PUFAs reduce heart attack risk through benefiting endothelial function (cells of blood vessel walls), reducing inflammation, and the risk of thrombosis (blood clotting). The American Heart Association has published guidelines for patients with CHD recommending a consumption of fish and fish oil, totaling 1g/day of EPA and DHA. *Harper, C.R. and Jacobson, T.A. Usefulness of Omega-3 Fatty Acids and the Prevention of Coronary Heart Disease. American Journal of Cardiology, Vol. 96, December 2005, pp. 1521-29/*

Fish oils recommended for heart disease prevention

DALLAS, TEXAS. The American Heart Association has reviewed the benefits of regular consumption of fish and fish oils. The review concludes that fish and fish oils help prevent cardiovascular disease including fatal and non-fatal heart attacks, strokes, sudden cardiac death, and coronary artery disease (angina). The reviewers believe that the mechanisms by which fish oils exert their protective effect include: * Reduction in susceptibility to ventricular arrhythmia * Decrease in platelet aggregation * Reduction in triglyceride levels * Retardation of atherosclerosis * Lowering of blood pressure * Promotion of nitric oxide induced endothelial relaxation * Anti-inflammatory effects. Fish and fish oils contain long-chain polyunsaturated omega-3 fatty acids, more specifically, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The average American diet contains only about 100-200 mg/day of EPA and DHA. The diet also contains about 1.4 grams/day of alpha-linolenic acid mainly from canola and soybean oils. Alpha-linolenic acid can be converted in the body to EPA and DHA, but not in amounts sufficient to make a significant impact. Some studies have shown that alpha-linolenic acid, on its own, may have heart-protective effects, but other studies have failed to confirm this. NOTE: Flax seed oil is a

particularly rich source of alpha-linolenic acid. The American Heart Association recommends that people increase their intake of long-chain polyunsaturated omega-3 oils from fish or directly from fish oil supplements. Healthy people should consume oily fish at least twice a week. Patients with heart disease should eat enough oily fish on a daily basis to obtain about 1 gram per day of EPA and DHA combined or take a fish oil supplement providing 1 gram per day of EPA + DHA. Patients with high triglyceride levels should receive 2-4 grams/day of EPA+DHA under the care of a physician. The reviewers point out that many fish species contain significant amounts of methylmercury, polychlorinated biphenyls (PCBs), dioxins, and other environmental contaminants and therefore must be consumed in moderation, if at all, especially by children and pregnant and lactating women. Poorer quality fish oils may also contain these contaminants, so it is important to only supplement with highly purified, pharmaceutical grade oils. *Kris-Etherton, PM, et al. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation, Vol. 106, November 19, 2002, pp. 2747-57/*

Fish oils help prevent stroke and heart attacks

SOUTHAMPTON, UNITED KINGDOM. Atherosclerosis increases the risk of stroke and heart attack because part of the atherosclerotic buildup (plaque) on the inner wall of arteries may dislodge and block smaller arteries in the brain and heart respectively and thus cut off the vital supply of oxygenated blood. Depending on its tendency to break loose from the artery wall plaque is classified as either stable or unstable with the stable form being the least likely to cause problems. Researchers at the University of Southampton have just completed a clinical trial to see if fish oil supplementation would improve plaque stability and thus help prevent heart attack and stroke. Their study involved 162 patients who were awaiting carotid endarterectomy (an operation involving the removal of atherosclerotic deposits from the carotid artery feeding the brain). The patients were randomly allocated to receive a placebo, fish oil (omega-3 polyunsaturated fatty acid) or sunflower oil (omega-6 polyunsaturated fatty acid) daily from the time they entered the study until the endarterectomy during which atherosclerotic plaque was removed for analysis. The placebo capsules contained an 80:20 blend of palm and soybean oils (a composition which closely matches that of the average UK diet); the sunflower oil capsules contained 1 gram of sunflower oil plus 1 mg of vitamin E (alpha-tocopherol); the fish oil capsules contained 1 gram of fish oil and 1 mg of vitamin E. The participants took 6 capsules daily providing a total to 3.6 grams linoleic acid (in the sunflower oil capsules) or 850 mg EPA (eicosapentaenoic acid) + 500 mg of DHA (docosahexaenoic acid) in the fish oil capsules. The duration of supplementation varied between 7 and 189 days with the median being 42 days. Upon analysis of the removed plaque the researchers found that the supplemented fish oil (EPA and DHA) had been readily incorporated into the plaques and had resulted in favourable changes. Plaque from fish oil treated patients tended to have thick fibrous caps and no signs of inflammation indicating more stability. Plaques from the control and sunflower oil groups, on the other hand, tended to have thin fibrous caps and signs of inflammation indicating less stability. The number of macrophages (large scavenger cells) in the plaque of fish oil treated patients was also significantly less than the number observed in the control and sunflower oil groups. The researchers conclude that the increased plaque stability observed in the fish oil treated patients could explain the reduction in fatal and non-fatal heart attacks and strokes associated with an increased intake of fish oils. *Thies, Frank, et al. Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomised controlled trial. The Lancet, Vol. 361, February 8, 2003, pp. 477-85/*

Fish prevents stroke

BOSTON, MASSACHUSETTS. Several studies have shown that regular fish consumption helps protect against stroke. It is not clear, however, whether fish consumption protects against both ischemic stroke (stroke caused by a blood clot) and hemorrhagic stroke (stroke caused by a burst blood vessel). Researchers at the Harvard School of Public Health have now released the results

of a major study designed to answer this question. The study involved 43,671 male health professionals aged 40 to 75 years when enrolled in 1986. During a 12-year follow-up period 608 strokes occurred (377 ischemic, 106 hemorrhagic, and 125 strokes of unknown origin). The annual stroke rate in this group is clearly remarkably low at 0.1% overall and 0.07% for ischemic stroke. The participants completed food frequency questionnaires in 1986, 1990 and 1994. Men who consumed fish at least once a month had a 44% lower risk of having an ischemic stroke than did men who consumed fish less than once per month. No significant associations were found between fish or long chain omega-3 PUFA (polyunsaturated fatty acid) intake and the risk of hemorrhagic stroke, but a possible association could not be ruled out due to the relatively small number of hemorrhagic strokes that occurred in the group. The optimum protection was achieved at fish consumption once per week and more frequent fish consumption (5 or more times per week) did not reduce stroke risk further. The protective effect of fish consumption was not significantly affected by the use of aspirin or vitamin E supplements (about 25% of participants used aspirin for stroke protection and about 20% supplemented with vitamin E). The researchers calculated the intake of PUFAs (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) from fish and found that significant protection against ischemic stroke was achieved at a daily fish oil intake of between 50 mg and 200 mg. The level of daily intake of alpha-linolenic acid did not affect stroke risk. Additional fish oil supplementation did not reduce risk of ischemic stroke any further. *He, K, et al. Fish consumption and risk of stroke in men. Journal of the American Medical Association, Vol. 288, December 25, 2002, pp. 3130-36/ *Editor's comment:* The observed reduction of ischemic stroke risk of 44% compares to a stroke risk reduction of 21% by taking a daily aspirin and a risk reduction (in atrial fibrillation patients) of 64% by taking high-dose warfarin. High-dose warfarin, unfortunately, confers a significant risk for serious internal bleeding.*

Fish oils prevent stroke in women

BOSTON, MASSACHUSETTS. A 1995 study concluded that men who ate fish five or more times per week had a 40 per cent lower risk of having a stroke than did men who ate fish less than once a week. Researchers at the Harvard Medical School and the Brigham and Women's Hospital now report that the benefits of fish consumption are even more spectacular for women. Their just completed study involved 79,839 female nurses who were between the ages of 34 and 59 years at the start of the study in 1980. After 14 years of follow-up a total of 574 strokes had occurred in the group. Most of the strokes (303) were ischemic, i.e. caused by a blood clot. There were also 181 hemorrhagic strokes, i.e. caused by a ruptured artery and 90 strokes of undetermined origin. After adjusting for age, smoking and other cardiovascular risk factors the researchers concluded that women who ate fish once a week lowered their risk of having a stroke of any kind by 22 per cent and those who consumed fish five or more times per week reduced their risk by 52 per cent. They ascribe the protective effect of fish consumption to the commensurate intake of fish oils (omega-3 fatty acids). They estimate that women whose intake of fish oils is 0.5 gram/day or more have a 30 per cent lower risk of suffering a stroke than do women whose intake is below about 0.1 gram/day. There was no evidence that women with a high fish or fish oil consumption have an increased risk of hemorrhagic stroke. The researchers believe that the protective effects of fish oils are due to their ability to inhibit platelet aggregation, lower blood viscosity, suppress the formation of leukotrienes, reduce fibrinogen levels and reduce blood pressure levels and insulin resistance. They also note that the beneficial effects of fish consumption were substantially more pronounced among women who did not take aspirin on a regular basis. *Iso, Hiroyasu, et al. Intake of fish and omega-3 fatty acids and risk of stroke in women. Journal of the American Medical Association, Vol. 285, January 17, 2001, pp. 304-12 [40 references]*

Fish oils recommended for diabetes and hypertension

TROMSO, NORWAY. Fish and fish oils help protect against the development of atherosclerosis and heart disease. It is believed that fish oils exert their protective effect by lowering blood pressure and the levels of triglycerides and very-low-density lipoprotein (VLDL). Fish oils are also

believed to reduce *platelet aggregation* and to suppress the growth of smooth-muscle cells in the arterial walls. Many people with hypertension also suffer from diabetes and there has been concern that fish oil supplementation may aggravate problems with glucose intolerance. Researchers at the University of Tromso now report that fish oil supplementation lowers blood pressure significantly in people with hypertension and has no effect on glucose control even in people with mild diabetes. The study involved 78 obese volunteers with essential hypertension. The participants were randomly assigned to one of two equal-sized groups. The fish oil group received four fish oil capsules a day (containing a total of 3.4 grams of a mixture of eicosapentaenoic acid and docosahexaenoic acid) for a period of 16 weeks. The control group received four corn oil capsules a day. At the end of the test period the average (mean) systolic blood pressure had dropped by 4.4 mm Hg and the diastolic pressure by 3.2 mm Hg in the fish oil group. The average blood pressure in the control group did not change. The researchers also found that plasma triglyceride and VLDL levels in the fish oil group decreased significantly (by about 9 per cent) while they increased significantly (by about 12 per cent) in the control group. There were no changes in total or low-density-lipoprotein levels in either group. Extensive tests (oral glucose tolerance, hyperglycemic and hyperinsulemic clamps) were done to evaluate the effect of fish oil supplementation on glucose control. No adverse effects were found. An editorial accompanying the research report concludes that fish or fish oil is useful in the prevention of vascular disease in diabetics. Patients with diabetes should eat fish two to three times a week or, as an alternative, supplement with two to three one gram capsules of fish oil per day. *Toft, Ingrid, et al. Effects of n-3 polyunsaturated fatty acids on glucose homeostasis and blood pressure in essential hypertension. Annals of Internal Medicine, Vol. 123, No. 12, December 15, 1995, pp. 911- 18 Connor, William E. Diabetes, fish oil, and vascular disease. Annals of Internal Medicine, Vol. 123, No. 12, December 15, 1995, pp. 950-52/*

Fish oils help prevent cardiac arrest

SEATTLE, WASHINGTON. Cardiac arrest is a serious, usually fatal condition in which the heart stops pumping. Cardiac arrest most commonly occurs in connection with ventricular fibrillation and its primary cause is a heart attack. Researchers at the University of Washington now report that the risk of cardiac arrest can be significantly lowered by an increased intake of seafood rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Their study involved 334 patients who had suffered cardiac arrest during the period 1988 to 1994 and 493 controls matched for age and sex. None of the study participants had had any indication of heart disease prior to the beginning of the study. Interviews with survivors or their spouses were used to determine the participant's fish intake in the month preceding the cardiac arrest. The researchers found that the intake of just one portion of fatty fish per week lowered the risk of cardiac arrest by an impressive 50 per cent after adjusting for age, smoking, family history of heart attacks, hypertension, diabetes, obesity, physical activity, education, and cholesterol level. The researchers believe that consumption of fish increases the level of EPA and DHA in the membranes of the red blood cells which in turn reduces *platelet aggregation* and coronary spasm. This belief was confirmed by finding that blood samples taken from 95 cardiac arrest patients and 133 controls showed that a high blood content of EPA and DHA (five per cent of total fatty acids) corresponded to a 70 per cent reduction in the risk of cardiac arrest when compared to study participants with a low EPA and DHA content in their blood (3.3 per cent of total fatty acids). Other studies have shown that patients who have already suffered a heart attack can reduce their risk of future life-threatening arrhythmias and sudden cardiac death by increasing their intake of fish, fish oils or linolenic acid (flax seed oil). The researchers conclude that a modest intake of EPA and DHA from seafood may reduce the risk of ventricular fibrillation and death from coronary heart disease. NOTE: Fresh salmon is one of the best sources of fish oils; it contains twice as much per serving as does albacore tuna and six times more EPA and DHA than a serving of cod. / Siscovick, David S., et al. Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. *Journal of the American Medical Association, Vol. 274, No. 17, November 1, 1995, pp. 1363-67/* *Fish oil supplementation does not increase bleeding tendency* OSLO, NORWAY. A group of Norwegian

medical researchers reports that fish oil supplementation does not increase the bleeding tendency in heart disease patients receiving aspirin or warfarin. The study involved 511 patients who had undergone coronary artery bypass surgery. On the second day after the operation half the patients were assigned in a random fashion to receive 4 grams of fish oil per day (providing 2 g/day of eicosapentaenoic acid, 1.3 g/day of docosahexaenoic acid, and 14.8 mg/day of vitamin E). At the same time the patients were also randomized to receive either 300 mg of aspirin per day or warfarin aimed at achieving an INR of 2.5-4.2. The patients were evaluated every 3 months and questioned about bleeding episodes for the duration of the 9-month study. The researchers concluded that fish oil supplementation did not result in a statistically significant increase in bleeding episodes in either the aspirin group or in the warfarin group. They also found no significant long-term effects of fish oil on common parameters of coagulation and fibrinolysis. They noted that the blood levels (serum phospholipid levels) of eicosapentaenoic acid and docosahexaenoic acid increased by 140% and 14% respectively in the patients taking fish oil. The serum triglyceride levels decreased by 19.1% in the fish oil group while no significant change was observed in the remainder of the patients. NOTE: This study was partially funded by Pronova Biocare AS (a fish oil manufacturer) and Nycomed Pharma AS. *Eritsland, J., et al. Long-term effects of n-3 polyunsaturated fatty acids on haemostatic variables and bleeding episodes in patients with coronary artery disease. Blood Coagulation and Fibrinolysis, Vol. 6, 1995, pp. 17-22*

Fish oils reduce cardiovascular risk factors

OSLO, NORWAY. High blood levels of triglycerides and fibrinogen are known risk factors for cardiovascular disease. Fibrinogen is a large protein molecule which is a key factor in blood coagulation. High levels of fibrinogen aggravate the symptoms of intermittent claudication and speeds up the progression of atherosclerosis. Recent research has shown that fibrinogen level is a more reliable indicator of heart disease risk than is total cholesterol level. Researchers at the University of Oslo now report that fish oil supplementation is effective in lowering both triglyceride and fibrinogen levels. Their study involved 64 healthy men between the ages of 35 and 45 years. The participants were randomly assigned to receive either 14 1-gram capsules of fish oils or 14 1-gram capsules of olive oil every day for six weeks. The fish oil capsules contained 25.7% eicosapentaenoic acid (EPA) and 20.5% docosahexaenoic acid (DHA) and the olive oil capsules contained about 80% oleic acid. Blood samples were taken and analyzed at the start of the study, 3 and 6 weeks into the study, and 3 weeks after stopping supplementation. The red blood cell (phospholipid phase) content of EPA increased markedly after supplementation; DHA level increased slightly and the level of both linoleic acid and arachidonic acid decreased significantly. Blood level of fibrinogen dropped an average of 13% (from 2.73g/L to 2.37 g/L) after 3 weeks, but returned to baseline 3 weeks after stopping fish oil supplementation. There were no changes in fibrinogen levels in the olive oil group. Triglyceride levels decreased by an average of 22% (from 1.58 mmol/L to 1.23 mmol/L) after 6 weeks in the fish oil group, but increased by about 19% in the olive oil group. Values in both groups reverted to baseline 3 weeks after ceasing supplementation. Total cholesterol level and the level of LDL cholesterol (low-density lipoprotein) did not change with supplementation in either group, but a small transient decrease in the level of HDL (high-density lipoprotein) cholesterol was noted in the fish oil group. Blood pressure fell slightly in both groups after 3 and 6 weeks of supplementation, but reverted to baseline once supplementation was discontinued. The researchers conclude that the anti-thrombotic (blood clot preventing) effect of fish oils may be due to their ability to lower fibrinogen levels. *Flaten, Hugo, et al. Fish-oil concentrate: effects of variables related to cardiovascular disease. American Journal of Clinical Nutrition, Vol. 52, 1990, pp. 300-06/*

Consuming freshwater fish may lower risk of heart disease

KUOPIO, FINLAND. A 15-week experiment involving 62 students was carried out to determine if a regular diet of freshwater fish affects coronary heart disease risk factors. The students were

divided into three groups: a fish eating group who made no other changes to their diet, a fish eating group who also decreased their overall fat intake and a control group (19 students) who ate a typical western diet. The special diet consisted of one fish meal a day (in addition to the regular diet) and provided about 0.25 g/day of eicosapentaenoic acid and 0.55 g/day of docosahexaenoic acid. Serum cholesterol was found to decrease in fish eaters who also decreased their lipid intake but not in the other groups. Blood triglyceride levels decreased significantly in the fish eating groups, but not in the control group. Levels of apolipoproteins A1 and B were lowered in both fish eating groups as was the formation of *thromboxane B2* during incubation of whole blood. In the fish eating groups, the proportion of omega-3 fatty acids increased significantly in erythrocyte ghosts and platelets at the expense of omega-6 fatty acids. The results of the study support the contention that moderate fish consumption has a protective effect against coronary heart disease. / Agren, J.J., et al. Boreal freshwater fish diet modifies the plasma lipids and prostanoids and membrane fatty acids in man. LIPIDS, Vol. 23, No.10, October 1988, pp. 924-929/ Coromega *Additional References* 1. Mori, T.A., et al. Interactions between dietary fat, fish, and fish oils and their effects on platelet function in men at risk of cardiovascular disease. *Arterioscler Thromb Vasc Biol*, Vol. 17, February 1997, pp. 279-86 *Conclusion:* Fish oil supplementation reduces platelet aggregation in men with increased risk of cardiovascular disease. *OILOFPISCES.COM* *INTERNATIONAL HEALTH NEWS* Copyright © 2006 by Hans R. Larsen Oilofpisces.com does not provide medical advice. Do not attempt self- diagnosis or self-medication based on our reports. Please consult your health-care provider if you wish to follow up on the information presented.