

# Fish Oils and Angina/Heart Attack

## Summaries of the latest research concerning fish oils and angina/heart attack

### Antiarrhythmic properties of fish oils

CHIETI, ITALY. Several large clinical trials have confirmed the ability of fish oils to prevent sudden cardiac death in both presumably healthy subjects as well as in patients having suffered a heart attack (myocardial infarction). Considering that sudden cardiac death, largely caused by ventricular fibrillation, accounts for somewhere between 250,000 and 300,000 deaths every year in the US alone, it is clearly highly significant that a diet rich in oily fish or fish oil supplements may reduce the incidence of sudden cardiac death by up to 45%. Researchers at the universities of Chieti and Pisa recently published a review of the current "state-of-the-art" in regard to fish oils and arrhythmias. Highlights are: \* Supplementation with fish oils shows its beneficial effect within a few weeks. \* It is unlikely that the biological effects of fish oils would vary depending on source (oily fish or fish oil supplement). \* Animal experiments have shown that fish oils act on individual myocytes (heart cells) to inhibit the excitatory Na<sup>+</sup> current, stabilize the inactivated state of the Na channel, and prolong the effective refractory period of the cardiac cycle. The L-type Ca<sup>++</sup> current is also inhibited by fish oils and the outward flow of K<sup>+</sup> is reduced. All effects which would reduce the tendency to arrhythmia either by decreasing automaticity or by interfering with re-entry circuits. \* Two small trials have shown a reduction in PVCs (premature ventricular complexes) with fish oil supplementation. In one of these trials 34 participants with frequent PVCs, but no life-threatening arrhythmias were given 2.4 grams/day of fish oils while the control group was given sunflower seed oil which is rich in linoleic acid (an omega-6 fatty acid). PVCs decreased by 48% in the fish oil group as compared to 25% in the sunflower seed group. \* Fish oils have been shown to decrease heart rate variability and there is some suggestion that they may also reduce sympathetic and increase parasympathetic (vagal) activity in the autonomic nervous system. \* Prostaglandins and thromboxane A<sub>2</sub>, produced from arachidonic acid, are mostly proarrhythmic so a high intake of omega-6 fatty acids may be detrimental. Although most research, so far, has focused on the effect of fish oil on life-threatening ventricular arrhythmias it is likely that many of the findings may also be applicable to atrial fibrillation. *De Caterina, Raffaele, et al. Antiarrhythmic effects of omega-3 fatty acids: from epidemiology to bedside. American Heart Journal, Vol. 146, September 2003, pp. 420-30/*

### Fish oils benefit the heart

SOUTHAMPTON, UNITED KINGDOM. It is well established that populations with a high consumption of oily fish have a lower incidence of heart disease and several studies have confirmed that fish oils (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) are the protective components. There is also impressive evidence that they help prevent atherosclerosis, lower blood pressure, reduce triglyceride levels, and are highly protective against both fatal and non-fatal heart attacks. Fish oils also have antiarrhythmic effects and help prevent blood clotting. Recent research concludes that perhaps the most important effect of fish oils, when it comes to preventing cardiovascular disease, is their ability to stabilize atherosclerotic plaque by reducing the infiltration of inflammatory and immune cells (lymphocytes and macrophages) into the plaque. Heart attacks are now believed to involve the rupture of an atherosclerotic plaque. These plaques come in two main varieties, those with a thin, unstable fibrous cap and those with a thick, stable fibrous cap. A recent study showed that supplementation with 1.4 grams/day of fish oil significantly reduced macrophage infiltration and resulted in a substantial shift towards a preponderance of stable, thick-capped plaques. At least two studies have shown that the beneficial effects of fish oils on heart health become clear after about 2 months. *Calder, Philip C.*

*New evidence in support of the cardiovascular benefit of long-chain n-3 fatty acids. Italian Heart Journal, Vol. 4, July 2003, pp. 427-29 /*

## **Fish oils benefit women with diabetes**

BOSTON, MASSACHUSETTS. Several studies have found a clear inverse association between the consumption of fish and fish oils and the risk of coronary heart disease (CHD) and sudden cardiac death. However, it is not known whether this protective effect extends to diabetes patients. Researchers at the Harvard Medical School have just concluded a study to examine this. Their study included 5103 female nurses with diabetes, but free of cardiovascular disease and cancer at entry. Between 1980 and 1996 there were 362 cases of CHD (7.1%) and 468 deaths from all causes in the study group (9.2%). The causes of death were CHD or stroke ? 161, cancer ? 172, and other causes ? 135. Study participants completed detailed food frequency questionnaires in 1980, 1984, 1986, 1990 and 1994. The researchers noted a strong correlation between the risk of CHD and fish intake. Women who consumed fish once a week had a 40% lower risk of CHD than did women who consumed fish less than once per month. Eating fish 5 times per week reduced CHD risk by 64% and overall mortality by 52%. Only dark-meat fish (mackerel, salmon, sardines, bluefish, and swordfish) and shrimp, lobster and scallops showed a beneficial effect. The researchers also calculated the amount of fish oils (eicosapentaenoic acid and docosahexaenoic acid) obtained from the diet and found that study participants with an average intake of just 250 mg/day had a 31% reduction in CHD and a 37% reduction in death from all causes compared to participants with a low (40 mg or less) daily intake. The researchers note that fish oil supplementation does not impair glycemic control and suggest that regular fish consumption should be considered as an integral part of a healthy diet for the management of diabetes. *Hu, Frank B., et al. Fish and long-chain omega-3 fatty acid intake and risk of coronary heart disease and total mortality in diabetic women. Circulation, Vol. 107, April 15, 2003, pp. 1852-57 Grundy, Scott M. N-3 fatty acids: priority for post-myocardial infarction clinical trials. Circulation, Vol. 107, April 15, 2003, pp. 1834-36 (editorial)/*

## **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/*

## Older people benefit from fish oils

SEATTLE, WASHINGTON. There is abundant evidence that a diet rich in fatty fish is highly protective against death from heart disease in people 65 years of age and younger. Now researchers at the University of Washington and the Fred Hutchinson Cancer Research Center have extended the evidence to include people with an average age of 78 years. Their study included 54 men and women who had suffered a fatal heart attack or other fatal ischemic heart disease event, 125 people who had suffered a non-fatal heart attack, and 179 matched controls. All study subjects had blood samples drawn about 2 years prior to the cardiovascular event. The phospholipid phase of the blood plasma was isolated and analyzed for its contents of the fatty acids eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), alpha-linolenic acid (ALA), and linoleic acid (LA). EPA and DHA are the main constituents of fish oil, ALA is found in canola, flax and soybean oils, and LA is a main constituent of safflower and cottonseed oils. The researchers found that subjects with a high phospholipid content of EPA + DHA had a 70% lower incidence of fatal heart disease than did those with a lower level (4.1% versus 3.3% of total fatty acids). Participants with a high level of ALA had a 50% reduced risk of fatal heart disease. Subjects with a high level of LA, on the other hand, had a 2.4 times higher incidence of fatal heart disease than did those with a lower level. There was no association between the levels of the fatty acids and the incidence of non-fatal heart attacks. The researchers ascribe this to the fact that EPA and DHA (and perhaps ALA) are known to prevent ventricular arrhythmias ? the main factor in sudden cardiac death. Ventricular arrhythmias are not involved in non-fatal heart attacks. The researchers conclude that their findings lend further support to the recommendation from the American Heart Association to consume 2 fish meals (preferably fatty fish) per week. Dr. William Harris of the University of Missouri, in commenting on the results, suggests that a combined daily intake of 1 gram of EPA + DHA is both safe and prudent, but that supplementation with fish oil capsules may be required to achieve this goal. *Lemaitre, RN, et al. n-3 polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study. American Journal of Clinical Nutrition, Vol. 77, February 2003, pp. 319-25 Harris, WS. n-3 long-chain polyunsaturated fatty acids reduce risk of coronary heart disease death: extending the evidence to the elderly. American Journal of Clinical Nutrition, Vol. 77, February 2003, pp. 279-80 (editorial)/*

## Fish, mercury, and heart disease

BALTIMORE, MARYLAND. Several studies have shown that regular fish consumption protects against cardiovascular disease. Other studies have shown that consuming mercury-contaminated fish increases the risk of coronary heart disease. The beneficial effect of fish consumption is believed to be due to the presence of the omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in the tissue of fish and shellfish. Two recent studies have attempted to answer the question "Are the beneficial effects of fish oils (EPA and DHA) outweighed by the negative effects of mercury"? The first study, carried out by a team of researchers from eight European countries, Israel and the United States, involved 684 men who had suffered a first non-fatal heart attack and 724 matched controls. All participants had their mercury level measured in toenail clippings and their level of DHA measured in a fat tissue sample taken from the buttock. Participants with a mercury level of 0.66 mcg/gram were found to

have twice (odds ratio of 2.16) the risk of having a first heart attack when compared with participants having a mercury level of 0.11 mcg/gram. This risk assessment was arrived at after adjusting for age, DHA level in adipose tissue, body-mass index, waist:hip ratio, smoking status, alcohol intake, HDL cholesterol level, diabetes, history of hypertension, family history of heart attack, blood levels of vitamin E and beta-carotene, and toenail level of selenium. The research team also found that participants with a high (0.44% of total fatty acids) fat tissue content of DHA had a 41% lower risk of having a first heart attack than did those with a low (0.10% of total fatty acids) fat tissue level of DHA. This risk assessment was arrived after adjusting for all other known risk factors including toenail mercury level. The researchers point out that the main sources of mercury are occupational exposure (dentists), exposure to silver-mercury amalgam in dental fillings, and fish consumption. They conclude that the health benefit of fish consumption is significantly diminished if the fish is high in mercury. They also confirm the cardioprotective effect of fish oils (DHA). The second study was part of the Health Professionals Follow-Up Study begun in 1986 as a cooperative venture between the Harvard School of Public Health, the Brigham and Women's Hospital, and Harvard Medical School. The study involved 33,737 male health professionals who had toenail clippings analyzed for mercury in 1987. After 5 years of follow-up 470 participants had been diagnosed with coronary heart disease. The researchers observed that dentists, who are habitually exposed to mercury, had toenail mercury levels (0.91 mcg/gram) that were twice as high as the levels found in non-dentists (0.45 mcg/gram). They also found a direct relationship between fish consumption and mercury level with participants consuming an average of 357 grams (3/4 lb) of fish per week having a level of 0.75 mcg/gram while those who consuming 145 grams (1/3 lb) per week had a level of 0.29 mcg/gram. After adjusting for age, smoking and other risk factors for heart disease the researchers conclude that there is no clear association between total mercury exposure and the risk of coronary heart disease, but that a weak relation cannot be ruled out. / Guallar, E, et al. Mercury, fish oils, and the risk of myocardial infarction. *New England Journal of Medicine*, Vol. 347, November 28, 2002, pp. 1747-54  
Yoshizawa, K, et al. Mercury and the risk of coronary heart disease in men. *New England Journal of Medicine*, Vol. 347, November 28, 2002, pp. 1755-60  
Bolger, PM and Schwetz, BA. Mercury and health. *New England Journal of Medicine*, Vol. 347, November 28, 2002, pp. 1735-36/  
\*Editor's comment:\* The two studies clearly do not agree as to whether high mercury levels are associated with an increased risk of coronary heart disease. I am inclined to believe that they are. Furthermore, there is compelling evidence of significant associations between high mercury levels and Alzheimer's disease, Parkinson's disease, congestive heart failure, kidney damage, hearing loss, and high blood pressure. So definitely, mercury, from whatever source, is a very bad actor and should be avoided. The joint European/Israeli/US study clearly confirms that DHA (fish oil) is protective against a first heart attack, so regular consumption of low-mercury-level fish is still a healthy option. An alternative approach to obtaining DHA (and EPA) on a regular basis is to supplement with 1 gram/day of a high quality, molecular distilled, non-rancid fish oil containing a minimum of 220 mg EPA and 220 mg DHA. Reliable sources of such fish oils can be found at [www.coromega.com](http://www.coromega.com) and at [www.consumerlab.com/results/omega3.asp](http://www.consumerlab.com/results/omega3.asp) To be on the safe side it is best to eat fish and shellfish with an average mercury content of less than 0.10 ppm. Unfortunately, there are not too many species left that fulfill this requirement. King crab, scallops, catfish, salmon (fresh, frozen and canned), oysters, shrimp, clams, saltwater perch, flounder, and sole are all good choices. Salmon is my favourite because of its combination of a low mercury content with a high level of beneficial EPA and DHA. The following fish species should be avoided: tilefish, swordfish, king mackerel, shark, grouper, tuna, American lobster, halibut, pollock, sablefish, and Dungeness and blue crab. Limited sampling of the following also indicated high mercury levels: red snapper, marlin, orange roughy, saltwater bass. Atlantic cod, haddock, mahi mahi, and ocean perch have mercury levels around 0.18 ppm, so should be eaten in moderation. For more on mercury content of fish see [www.cfsan.fda.gov/~frf/sea-mehg.html](http://www.cfsan.fda.gov/~frf/sea-mehg.html)

## **Fish oils protect women against heart disease**

BOSTON, MASSACHUSETTS. There is ample evidence that frequent fish consumption or supplementation with fish oils markedly reduces the risk of coronary heart disease, sudden

cardiac death, and heart attacks in men. Up until now there has been little work done to see if the same holds true for women. Researchers at the Harvard Public School of Health have just released the results of a major study aimed at remedying this situation. The study involved 84,688 female nurses who were enrolled in 1970. All participants completed food frequency questionnaires in 1980, 1984, 1986, 1990 and 1994. In the 16-year period between 1980 and 1996 a total of 1513 women either died from coronary heart disease (484) or suffered a non-fatal heart attack (1029). After adjusting for age, smoking and other known cardiovascular risk factors the researchers conclude that women who eat fish once a week have a 34 per cent lower incidence of death from heart disease and a 25 per cent lower incidence of non-fatal heart attacks. They also conclude that the protective effect of fish consumption is entirely due to the content of omega-3 fatty acids (fish oils) in the fish. They also note that both fish and fish oil consumption were associated with a decreased risk of dying from any cause. The researchers believe that fish oils reduce the incidence of heart disease through their antiarrhythmic effects and their reduction of platelet aggregability and triglyceride levels. They conclude that their findings lend further support to the benefits of twice weekly fish consumption. *Hu, Frank B., et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. Journal of the American Medical Association, Vol. 287, April 10, 2002, pp. 1815-21/*

## **Fish oils: a must for heart attack survivors**

SANTA MARIA IMBARO, ITALY. A group of Italian researchers (GISSI) reported in 1999 that supplementation with fish oil reduces the mortality among patients who have survived a first heart attack. Their study involved over 11,000 heart attack survivors who supplemented with 1 gram/day of fish oil (580 mg of eicosapentaenoic acid [EPA] and 290 mg of docosahexaenoic acid [DHA]) for 3.5 years. The researchers have now re-analyzed their data in an attempt to determine how the fish oil exerts its protective effect. The reduced mortality was apparent after only three months of supplementation (1.1 per cent versus 1.6 per cent in the placebo group) and continued for the duration of the study. The reduction in the incidence of sudden cardiac death accounted for about 57 per cent of the total improvement in mortality rates. At the end of the study 2.7 per cent of the placebo group participants had died from sudden cardiac death as compared to only 2.0 per cent in the fish oil group. Overall, cardiovascular death (including stroke) at the end of the study was 6.5 per cent in the placebo group versus 5.5 per cent in the fish oil group. There was no statistical significant difference in the incidence of non-fatal heart attacks between the fish oil and placebo groups. The researchers conclude that fish oils exert their protective effect by preventing fatal ventricular arrhythmias rather than through an improvement in cholesterol profile. They did note a small (4.6 per cent) drop in triglyceride levels in the fish oil group, but found no significant differences in LDL (low-density lipoprotein) and HDL (high-density lipoprotein) cholesterol between the two groups. They also point out that the number of lives (per 1000 patients) which could be saved every year by giving heart attack survivors fish oil exceeds the number of lives (per 1000 patients) estimated to be saved by treating heart disease patients with high cholesterol levels with pravastatin. This puts fish oils squarely in the category of highly effective heart "drugs". *Marchioli, Roberto, et al. Efficacy of n-3 polyunsaturated fatty acids after myocardial infarction: results of GISSI-Prevenzione trial. Lipids, Vol. 36, Supplement 2001, pp. S119-S126 Marchioli, Roberto, et al. Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of GISSI-Prevenzione. Circulation, Vol. 105, April 23, 2002, pp. 1897-1903 Leaf, Alexander. On the reanalysis of the GISSI-Prevenzione. Circulation, Vol. 105, April 23, 2002, pp. 1874-75 (editorial)/*

## **New risk factor for sudden death**

PARIS, FRANCE. Sudden cardiac death is a common occurrence in industrialized countries. There is evidence that a high level of free fatty acids in the blood plasma is an independent risk factor for ventricular arrhythmias and sudden death in people who have suffered a heart attack.

Medical researchers at the University of Paris now report that a high level of circulating free fatty acids (non-esterified) is also a potent risk factor for sudden death in men without cardiovascular disease. The study involved 5250 men, aged 42 to 53 years at the start of the study in 1967-72. All participants were free of cardiovascular disease at the time of entry. The men were followed for an average of 22 years during which 1601 deaths occurred ? 91 of them were classified as sudden cardiac deaths and 145 as fatal heart attacks. Analysis of test data showed that the level of free fatty acids circulating in the blood plasma is a potent risk factor for sudden death. Men with a high level had a 70 per cent higher risk than did men with a low level. Surprisingly, high fatty acid levels were not a risk factor for fatal heart attack. Other prominent risk factors for sudden death were parental sudden death, parental heart attack, smoking, high systolic blood pressure, and high body mass index (obesity). High cholesterol levels increased the risk of sudden death by a relatively modest 18 per cent. The researchers and Dr. Alexander Leaf, MD of the Harvard Medical School point out that not all fatty acids are detrimental. There is ample evidence that the omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the main components of fish oil are actually highly protective against sudden cardiac death. Dr. Leaf believes that it is the omega-6 fatty acids found in vegetable oils (corn, safflower, sunflower, and peanut) that are responsible for initiating the arrhythmias leading to sudden death. Fish oils, on the other hand, exert a protective effect in amounts as low as 600-1000 mg/day (EPA+DHA). Dr. Leaf points out that government agencies and heart associations have long been advocating an increased intake of polyunsaturated fatty acids without making any distinction between omega-6 essential fatty acids which appear to promote sudden death and omega-3 fatty acids (EPA and DHA) which prevent it. *Jouven, Xavier, et al. Circulating nonesterified fatty acid level as a predictive risk factor for sudden death in the population. Circulation, Vol. 104, August 14, 2001, pp. 756-61* Leaf, Alexander. *Plasma nonesterified fatty acid concentration as a risk factor for sudden cardiac death: the Paris prospective study. Circulation, Vol. 104, August 14, 2001, pp. 744-45 (editorial)*

## **Fish oils and heart disease**

AALBORG, DENMARK. It is increasingly clear that atherosclerosis is, at least partially, an inflammatory disease. There is also growing evidence that high blood levels of C-reactive protein (CRP) are associated with an increased risk of coronary heart disease and heart attacks. Danish researchers now report a direct correlation between CRP levels and severity of atherosclerosis. They also suggest that CRP levels can be kept in check by frequent consumption of fish or fish oils. Their study involved 269 patients referred for angiography because of suspected coronary artery disease. Besides undergoing angiography the patients had their CRP levels measured and were also tested for the level of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in their granulocytes (a type of white blood cell). They also filled out a questionnaire about their fish consumption. The researchers found that patients with one or more coronary arteries blocked by 50 per cent or more had significantly higher CRP levels in their blood than had patients with no significant blockages. They also observed an inverse correlation between CRP levels and the level of DHA in granulocytes. The level of DHA in granulocytes, in turn, was closely related to fish consumption. The researchers conclude that DHA has an anti-inflammatory effect which results in lower CRP levels and suggest that fish consumption may decrease the risk of coronary artery disease. *Madsen, Trine, et al. C-reactive protein, dietary n-3 fatty acids, and the extent of coronary artery disease. American Journal of Cardiology, Vol. 88, November 15, 2001, pp. 1139-42/*

## **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 prevent heart attacks**

KUOPIO, FINLAND. Finnish researchers provide additional evidence of the protective effects of fish oils. Their recently completed study involved 1871 Finnish men aged 42 to 60 years who were free of coronary heart disease at the beginning of the study in 1984. Ten years later 194 of the men had suffered an acute coronary event (160 heart attacks among them). The men had their blood analyzed for fatty acids at the start of the study. Men with a high level (more than 3.58% of total fatty acids) of the polyunsaturated fatty acids found in fatty fish, docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA), were found to have a 44% lower risk of suffering an acute coronary event than did men with a low level (less than 2.38% of total fatty acids). There was no correlation between the level of eicosapentaenoic acid (EPA) and heart attack risk. Fish caught in Finnish waters tends to have a high level of mercury so the researchers also measured the hair content of mercury in the study participants. They found that men with a high DHA+DPA level and a low mercury level (less than 2 micrograms/gram) had a 67% lower risk of a coronary event than did men with a low DHA+DPA level and a high mercury content (greater than 2.0 micrograms/gram). The researchers speculate that mercury may contribute to the risk of coronary events by binding selenium in an inactive form so that it cannot support the synthesis of the important antioxidant glutathione peroxidase. They conclude that fish oils reduce the risk of acute coronary events, but caution that mercury in fish could reduce this protective effect. \*Editor's Note\*: The best way to avoid mercury and still obtain the benefits of fish oils is by supplementing with a high quality fish oil (molecular distilled). *Rissanen, Tiina, et al. Fish oil-derived fatty acids, docosahexaenoic acid and docosapentaenoic acid, and the risk of acute coronary events. Circulation, Vol. 102, November 28, 2000, pp. 2677-79/*

## **Bypass patients may benefit from fish oils**

MUNICH, GERMANY. There is considerable evidence that supplementation with fish oils helps prevent or slow down atherosclerosis. Some studies have shown that fish oil supplementation may help prevent restenosis (reclosing) of the arteries after angioplasty, but more recent studies have found no such effect. A recent study found that coronary bypass patients who supplemented their diet with 4 grams/day of an 83% fish oil concentrate had less reclosings (distal anastomosis occlusions) of their bypass grafts than did the controls. After one year the patients taking fish oils had a reclosing (occlusion) rate of 27% while the control patients had a reclosing rate of 33% (a 23% relative improvement). Eating fatty fish once or more each week or supplementing with fish oils (0.5 g/day) has been found to increase the survival of heart attack patients by 29%. A recent

experiment showed that cardiac transplant patients who supplemented with 5 grams/day of fish oils after their operation had normal endothelium- dependent coronary vasodilation when tested after three weeks whereas it was abnormal in matched control patients. It is not known whether fish oil supplementation will increase the survival time for heart transplant patients. [34 references] *von Schacky, Clemens. n-3 fatty acids and the prevention of coronary atherosclerosis. American Journal of Clinical Nutrition, Vol. 71 (suppl), January 2000, pp. S224-275/*

## **Fish oils help prevent sudden cardiac death**

AALBORG, DENMARK. Sudden cardiac death (SCD) is now the most common cause of death in the Western world. SCD is often caused by ventricular arrhythmias in patients with heart disease, but may also occur among previously healthy people. The risks of arrhythmias and SCD are closely tied in with heart rate variability (HRV) with a high variability index corresponding to a lower risk. It would also appear that the risk of SCD can be substantially reduced by an increased consumption of fish. Some very recent research has shown that survivors of a first heart attack can avoid having a second one by supplementing with fish oils. An obvious question is whether there is a connection between heart rate variability and fish oil intake. Danish researchers at the Aalborg Hospital are convinced that there is indeed a very close connection - at least in men. Their recently released study involved 25 women and 35 men who were generally healthy and took no medications. The participants were randomized into three groups. Group 1 was given 10 fish oil capsules daily providing a total of 6.6 grams of n-3 polyunsaturated fatty acids (3.0 g eicosapentaenoic acid [EPA] and 2.9 g docosahexaenoic acid [DHA]); group 2 was given three fish oil capsules (0.9 g EPA and 0.8 g DHA) plus seven olive oil capsules daily, and group 3, the control group, was given 10 olive oil capsules daily. The study participants gave fasting blood samples and had their HRV measured with a Holter recorder for 24 hours at the start of the study and after 12 weeks of supplementation. The researchers found that fish oil supplementation significantly increased the concentration of EPA and DHA in both blood platelets and granulocytes and that this increase was highly dose-dependent. They also found a significant, dose-dependent reduction in triacylglycerols, but no significant changes in total, LDL or HDL cholesterol levels. The 24-hour Holter recordings showed a correlation between heart rate (pulse rate) and blood level of EPA and DHA with a higher level corresponding to a lower pulse rate in both men and women. There was also a very significant association between DHA level in men and SDNN. SDNN (the standard deviation of all normal R-R intervals during the 24-hr Holter recording) is an important index of HRV with higher values indicating greater heart rate variability. The researchers conclude that supplementation with fish oils, especially DHA, may help prevent arrhythmias and sudden cardiac death in healthy men. They found no association between EPA/DHA levels in women and HRV, but urge further studies to confirm this seeming lack of effect. *Christensen, Jeppe Hagstrup, et al. Heart rate variability and fatty acid content of blood cell membranes: a dose-response study with n-3 fatty acids. American Journal of Clinical Nutrition, Vol. 70, September 1999, pp. 331-37/*

## **Fish oils protect against death from heart disease**

SANTA MARIA IMBARO, ITALY. There is clear evidence that a diet rich in oily fish confers considerable protection against heart disease. What is less clear is whether concentrated fish tissue oils in capsule form confer similar benefits. A very large group of Italian researchers (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico) has just completed a major study which shows the benefits of fish oil supplementation in patients who have survived a first heart attack. Their study involved over 11,000 heart attack survivors who were randomly assigned to one of four groups. Group one received a one-gram gelatin capsule containing about 580 mg of eicosapentaenoic acid (EPA) and 290 mg of docosahexaenoic acid (DHA) as ethyl esters every day. Group two received 300 mg of synthetic vitamin E daily; group three both fish oil and vitamin E; and group four served as the control group. All participants ate a largely

Mediterranean diet and continued to take their prescribed medications (beta-blockers, aspirin, and ACE-inhibitors). After 3.5 years of follow-up it was clear that the participants who had received fish oil or fish oil plus vitamin E had lowered their risk of dying or having another heart attack or a stroke by 10 to 15 per cent. The group who had taken vitamin E alone derived no statistically significant benefit from doing so. (Editor's note: The 300 mg of synthetic vitamin E used in the study corresponds to about 150 IU of natural vitamin E. This would be much less effective than the 200-400 IU/day of \*natural\* vitamin E used in studies which have shown a benefit of vitamin E in regard to heart disease and stroke). The researchers conclude that daily supplementation with fish oils (equivalent of consuming 100 grams of fish per day) is beneficial for patients who have survived a first heart attack. They suggest that the role of vitamin E needs further exploration. (Editor's note: Other studies have shown that vitamin E protects fish oils from going rancid so it is a good idea to take a combination of the two). NOTE: This study was funded in part by Bristol-Myers Squibb, Pharmacia-Upjohn, Societa Prodotti Antibiotici, and Pfizer. / Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *The Lancet*, Vol. 354, August 7, 1999, pp. 447-55 Brown, Morris. Do vitamin E and fish oil protect against ischaemic heart disease? *The Lancet*, Vol. 354, August 7, 1999, pp. 441-42 (commentary)/

## Eat fish and live longer

BOSTON, MASSACHUSETTS. There is a growing consensus that regular fish consumption protects against heart disease. There is, however, still controversy as to whether this protection applies to all forms of heart disease and it is also not clear how fish exerts its protective effect. Some studies have found that fish consumption protects only against sudden cardiac death while others have found that it protects only against nonsudden death. Now researchers at the Harvard Medical School and the Brigham and Women's Hospital weigh in with a comprehensive new study which concludes that even modest fish and shellfish consumption protects against sudden cardiac death in men and significantly reduces total mortality. The study involved over 20,000 male American physicians who were between the ages of 40 and 84 years in 1982 when the study commenced. Food frequency questionnaires were administered after 12 and 18 months and again in 1988. By December 1995 133 of the participants had died from a sudden cardiac event (death occurring within one hour from onset of symptoms). Analysis of the collected data showed that the men who consumed fish once or more each week had a 52 per cent lower risk of dying from a sudden cardiac event than did the men who ate fish less than once a month. This lower risk applied after adjusting for all other known risk factors. The estimated dietary intake of marine n-3 fatty acids also correlated well with the risk of sudden cardiac death with an intake of more than 300 mg/month providing significant protection. The extent of protection did not increase significantly with greater fish or marine n-3 fatty acid intake indicating that eating fish once a week is sufficient to provide worthwhile protection. Fish consumption was not associated with the risk of nonsudden death, total myocardial infarction or total deaths from cardiovascular diseases. There was, however, a 30 per cent decrease in the overall mortality among the men consuming fish once or more each week as compared to the men eating fish less than once per month. The researchers speculate that fish consumption may exert its protective effect by preventing fatal arrhythmias. They suggest that the n-3 fatty acids found in fish and shellfish (eicosapentaenoic acid and docosahexaenoic acid) are responsible for the antiarrhythmic properties and point out that alpha-linolenic acid, an n-3 fatty acid found in flax oil and nuts, also has antiarrhythmic properties. They did not investigate the benefits of fish oil supplements and purposely excluded 777 physicians from the study who were taking fish oil supplements. The researchers conclude that eating fish once per week may substantially reduce the risk of sudden cardiac death. In an accompanying editorial Dr. Daan Kromhout of the Dutch National Institute of Public Health concurs with this conclusion and adds that patients already suffering from cardiac disease should be advised to eat fish twice a week. *Albert, Christine M., et al. Fish consumption and risk of sudden cardiac death. Journal of the American Medical Association, Vol. 279, January 7, 1998, pp. 23-28 Kromhout, Daan. Fish consumption and sudden cardiac death. Journal of the American Medical Association, Vol. 279, January 7, 1998, pp. 65-66 (editorial)/*

## **Fish oils and heart attack**

OSLO, NORWAY. There is now substantial evidence that fish and fish oil consumption protects against sudden death from coronary heart disease. There is also evidence that fish consumption reduces the risk of dying from a heart attack (acute myocardial infarction). Researchers at the University of Oslo now report that heart attack patients who had supplemented with cod liver oil (providing approximately 950 mg of eicosapentaenoic acid and 800 mg of docosahexaenoic acid per day) or fish oil capsules (providing approximately 700-1100 mg of eicosapentaenoic acid and 500-750 mg of docosahexaenoic acid per day) for at least 4 weeks prior to their attack tended to have substantially milder attacks than did patients who did not supplement. The study involved 753 patients who were admitted to hospital with a heart attack and discharged alive. The researchers found that patients who had taken cod liver oil or fish oil tended to have smaller infarcts (small localized areas of dead tissue resulting from a disruption of the blood supply to the areas) than did non-supplementing patients. The researchers conclude that fish oils may reduce infarct size and the incidence of large (more debilitating) infarcts and also seem to enhance the effect of thrombolysis (the dissolution of blood clots by the infusion of an enzyme such as streptokinase). NOTE: This study was supported in part by Zeneca AS, Pfizer AS, Astra Norge AS and Pharmacia AS. *Landmark, Knud, et al. Use of fish oils appears to reduce infarct size as estimated from peak creatine kinase and lactate dehydrogenase activities. Cardiology, Vol. 89, 1998, pp. 94-102 [68 references] /*

## **Eating fish prevents death of heart attack patients**

AALBORG, DENMARK. A low degree of heart rate variability (HRV) is a very strong predictor of sudden death among survivors of a heart attack (myocardial infarction). Danish researchers now report that a high fish consumption increases the concentration of n-3 polyunsaturated fatty acids (PUFAs) in cell membranes and that this increase is associated with a significant beneficial increase in HRV. Their study involved 52 patients who had suffered a heart attack and had a left ventricular ejection fraction of 40 per cent or less. The researchers found that patients who ate fish once a week had an 18 per cent higher HRV than non-fish eaters. Fish eaters were also found to have a higher content of DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid) in their blood platelets. Patients with more than 3.14 per cent DHA in their platelets were found to have a 43 per cent higher