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More Research Highlights the Broad Health Benefits of Omega-3 Fish Oils and Fatty Fish

Research on omega-3 fish oils keeps looking better and better: new studies have found that omega-3s fish oils can help with three catastrophic diseases – Alzheimer's, heart failure, and cancer.

Ernst J. Schaefer, MD, of the USDA's nutrition research center at Tufts University, Boston, analyzed levels of omega-3s and the risk of dementia, including Alzheimer's disease. He and his colleagues measured blood levels of docosahexaenoic acid (DHA, one of the principal omega-3s in fish) in 899 elderly men and women. More than half of the subjects also completed dietary questionnaires, which were used to assess intake of DHA and fish.

Over nine years, 99 of the subjects developed dementia. Schaefer determined that people with the highest blood levels of DHA were about half as likely to develop dementia, compared with people who consumed little DHA. They were also 39 percent less likely to develop Alzheimer's disease.

People with the highest DHA levels consumed about three servings of fish each week, which provided the equivalent of 180 mg of DHA daily.

Fats form about 50 percent of the brain's nonwater weight, and DHA is the predominant fat found in cell membranes of the brain's gray matter.

In a separate study, Alberto U. Ferrari, MD, of the University of Milano-Bicocca, Milan, Italy, treated 25 heart failure patients with beta-blocker and ACE-inhibitor drugs. All of the patients had previously suffered a heart attack that left them with a weakened ability to pump blood.

Fifteen of the patients were also given 2 grams of omega-3 fish oils daily, and 10 received placebos daily for four months. The fish oil supplements contained about three-fifths DHA and two-fifths eicosapentaenoic acid (EPA, another omega-3 fat).

The omega-3s improved the patients' "baroflex sensitivity," leading to a more stable heart rate, less variability in heart rate, and lower resting heart rate. The benefits, Ferrari noted, were above and beyond the improvements achieved with the medications.

Finally, Alicja Wolk, DMSc, of the Karolinska Institute, Stockholm, Sweden, and her colleagues analyzed the relationship between consumption of fish rich in omega-3 fats and the risk of kidney cancer in women. They drew on data from an ongoing study of more than 61,000 middle-age and elderly women whose health was tracked for an average of 15 years.

Women who consumed one or more servings of fatty fish per week were 44 percent less likely to develop kidney cancer, compared with women who did not eat fish. Women who consumed one or more servings of fatty fish per week for at least 10 years were 74 percent less likely to develop kidney cancer.

References: Schaefer EJ, Bongard V, Beiser AS, et al. Plasma phosphatidylcholine docosahexaenoic acid content and risk of dementia and Alzheimer's disease. *Archives of Neurology*, 2006;63:1545-1550. Radaelli A, Cazzaniga M, Viola A, et al. Enhanced baroreceptor control of the cardiovascular system by polyunsaturated fatty acids in heart failure patients. *Journal of the American College of Cardiology*, 2006; 48:1600-1606. Wolk A, Larsson SC, Johansson JE, et al. Long-term fatty fish consumption and renal cell carcinoma incidence in women. *JAMA*, 2006;296:1371-1376. □

Perspectives...

Trans Fats at Root of Health Problems

If you had asked me, 20 years ago, about the single most harmful food ingredient, I would have said it was sugar. Today, I say it's trans fats.

Trans fats are found in partially hydrogenated vegetable oils, which are used to make french fries, chicken nuggets, other deep fried foods, nondairy creamers, cakes, cookies, crackers, many brands of margarine, and other processed foods. The average American consumes five pounds of trans fats each year.

Trans fats are a major reason why millions of people have high cholesterol, suffer from inflammatory arthritis, and have erectile dysfunction.

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To explain, trans fats are far worse than saturated fats when it comes to increasing blood levels of the "bad" low-density lipoprotein (LDL) cholesterol. Most doctors prescribe statins to lower LDL, but it would make more sense to simply avoid foods containing trans fats.

Trans fats also inhibit enzymes called desaturases and elongases, which help the body convert omega-3 fats to powerful anti-inflammatory compounds. When inflammation gets out of control, doctors commonly prescribe Cox-2 inhibitor drugs, such as Celebrex and other powerful analgesic drugs. Again, it would be more sensible to avoid trans fats and Cox-2 inhibitor drugs, while increasing intake of anti-inflammatory omega-3 fish oils.

In addition, trans fats affect blood vessel tone and flexibility, leading to a heart-disease risk factor known as endothelial dysfunction. Trans fats induce endothelial dysfunction by interfering with the activity of nitric acid, one of the body's most important regulatory molecules. Impaired nitric acid activity also causes erectile dysfunction. Again, avoiding trans fats would be more prudent than taking medications for erectile dysfunction.

Finally, trans fats increase the chances of becoming overweight – another significant concern, given that two-thirds of American adults are now overweight. Based on all the evidence, trans fats fundamentally change how the body deals with fats, with far-reaching consequences.

Trans fats should be banned, but that's not likely to happen. Companies that make processed foods or sell fast foods want to keep using trans fats, even though they're damaging the health of millions of people. Foods containing less than 0.5 grams of trans fats per serving – that is, up to 449 mg – can be labeled as having zero trans fats per serving. Read the fine print and don't buy any food containing "partially hydrogenated vegetable oils" or shortening. – JC

Long-Term and High-Dose Metformin Use Can Compromise B12 Levels

Metformin, a glucose-lowering drug, is one of the most widely prescribed drugs for type-2 (adult-onset) diabetes. But the longer a person takes the drug, especially at high dosages, the more likely he will develop a deficiency of vitamin B12.

Researchers have known since the early 1970s that almost one-third of patients taking metformin have problems absorbing vitamin B12. Studies have found that metformin reduces blood levels of the vitamin by 14 to 30 percent.

In the most recent study along these lines, Kai Ming Chow, MRCP, a physician at the Prince of Wales Hospital, Hong Kong, investigated 155 diabetic

patients who developed vitamin B12 deficiency after taking metformin. Chow also studied 310 diabetic patients taking metformin but with no signs of vitamin B12 deficiency.

Patients taking metformin for three or more years were almost two and one-half times more likely to develop vitamin B12 deficiency. Furthermore, each 1-gram increase in the daily dosage almost tripled the risk of vitamin B12 deficiency.

Vegetarians, who are at particular risk of vitamin B12 deficiency, were about eight times more likely to have a deficiency when taking metformin.

Some evidence indicates that metformin may interfere with absorption of vitamin B12 in the ileum, the last part of the small intestine.

Reference: Teng RZW, Szeto CC, Chan MHM, et al. Risk factors of vitamin B12 deficiency in patients receiving metformin. *Archives of Internal Medicine*, 2006;166:1975-1979. □

Supplemental GABA Combats Stress, Helps Promote Sense of Relaxation

Supplements of gamma aminobutyric acid (GABA), can promote relaxation, buffer stress, and may strengthen immunity, according to a recent study by Japanese researchers.

GABA is both an amino acid and neurotransmitter. Previous research has shown that it helps the brain filter out extraneous information – background static, so to speak – and improve mental focus.

In the latest study, Adham M. Abdou, PhD, a researcher at Pharma Foods, Japan, along with colleagues at two Japanese universities, tested the effects of supplemental GABA on 13 healthy men and women. The subjects were given a glass of distilled water (placebo), water containing 100 mg of GABA, and water containing 200 mg of L-theanine on three different days. L-theanine is an amino acid that boosts GABA levels.

The researchers recorded brain-wave patterns of the subjects while they were resting quietly. After 60 minutes, supplemental GABA led to significant increases in brain alpha waves, which reflect a "relaxed and effortless alertness." At the same time, brain beta waves decreased, indicating less stress and better mental focus. L-theanine had a beneficial effect, but it wasn't as great as with GABA.

In a separate experiment, the researchers measured immunoglobulin A (IgA) levels in the saliva of eight men and women with acrophobia, who were asked to walk across a high, narrow suspension bridge. Before walking across the bridge, they were given either GABA or a placebo.

Stress lowers levels of IgA, whereas relaxation increases its concentration. IgA also protects against

viral and bacterial infection.

The subjects who took supplemental GABA had higher IgA levels after crossing the bridge. In contrast, those who took placebos had lower IgA levels, indicative of greater stress.

“Under stress conditions certain metabolites, like GABA, are depleted, therefore, additional nutrients are required to replace these metabolites,” Abdou and the other researchers wrote.

Reference: Abdou AM, Higashiguchi S, Horie K, et al. Relaxation and immunity enhancement effects of gamma-aminobutyric acid (GABA) administration in humans. *BioFactors*, 2006;26:201-208. □

Turmeric, an Herbal Extract, May Prevent Progression of Rheumatoid Arthritis

Turmeric, an extract of the spice curry, may help reduce symptoms of rheumatoid arthritis, according to an experiment using laboratory rats.

The herbal extract has been used for centuries in southern Asian medicine to treat inflammation. It is rich in curcuminoids, a family of antioxidant compounds that includes curcumin, demethoxycurcumin, and bis-demethoxycurcumin.

Janet L. Funk, MD, of the University of Arizona Health Sciences Center, Tucson, and her colleagues tested a turmeric extract that was comparable to commercial products. She administered it to the rats before or after they developed laboratory-induced arthritic symptoms.

The turmeric blocked joint inflammation and the destruction of joint cartilage and bone, with higher dosages having greater effects. It worked, at least in part, by inhibiting nuclear factor kappa beta (NFkB), a protein that activates pro-inflammatory genes. Turmeric also reduced the activity of genes that regulate NFkB.

Reference: Funk JL, Frye JB, Oyarzo JN, et al. Efficacy and mechanism of action of turmeric supplements in the treatment of experimental arthritis. *Arthritis & Rheumatism*, 2006;54:3452-3464. □

Higher Blood Levels of Vitamin E Linked to Lower Risk of Death from Disease

Vitamin E has taken a beating by both researchers and the press in the past several years, even though most clinical trials have shown benefits from supplements. In the latest long-term study, researchers found that men with the highest blood levels of vitamin E were the least likely to die from disease.

Margaret E. Wright, PhD, of the National Cancer Institute, Bethesda, Maryland, and her colleagues analyzed data from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study after 19 years of follow up. The study focused on 29,000

middle-age Finnish men who smoked tobacco and often consumed alcohol. More than 13,000 of the subjects have died since the study began.

Wright reported that men with the highest blood levels of vitamin E at the beginning of the study had a 21 percent lower risk of cancer, a 19 percent lower risk of cardiovascular disease, and a 30 percent lower risk of dying from other diseases. Deaths from accidents were not related to vitamin E intake.

Blood levels of vitamin E were roughly equivalent to consuming 22 IU daily, mostly from food. Only 10 percent of the subjects were taking supplemental vitamin E when the study began.

Reference: Wright ME, Lawson KA, Weinstein SJ, et al. Higher baseline serum concentrations of vitamin E are associated with lower total and cause-specific mortality in the alpha-tocopherol, beta-carotene cancer prevention study. *American Journal of Clinical Nutrition*, 2006;84:1200-1207. □

Silymarin, an Herbal Extract, Help Diabetic Patients Control Blood Sugar

Silymarin, an extract from the seeds of the herb milk thistle (*Silybum marianum*) can greatly benefit people with type-2 (adult-onset) diabetes.

Hassan Fallah Huseini, PhD, of the Institute of Medicinal Plants, Tehran, Iran, and colleagues asked 51 diabetic patients to take either 200 mg of silymarin three times daily or placebos for four months. The patients did not know which they were taking.

By the end of the study, patients taking silymarin had striking improvements in almost every indicator of glucose tolerance and cardiovascular disease. Fasting blood sugar decreased from an average of 156 mg/dl to 133 mg/dl, a decline of almost 15 percent. Glycated hemoglobin (HbA1c), a marker of average glucose levels over about six weeks, went from 7.8 to 6.8 percent, a drop of almost 13 percent. Patients taking placebos had increases in fasting blood sugar and glycated hemoglobin.

In addition, patients taking silymarin benefited from a 25 percent decline in insulin levels. In addition, their total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels declined significantly. Even though the patients' high-density lipoprotein (HDL) cholesterol decreased, their overall cholesterol to HDL and HDL to LDL ratios remained the same. Liver enzymes, a marker of liver function, improved slightly.

The researchers wrote that high levels of blood sugar and free fatty acids, both characteristic of diabetes, lead to increased levels of harmful free radicals. These free radicals are involved in many of

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Quick Reviews of Recent Research

• Benefits of eating fish outweigh potential risks

Researchers at Harvard University analyzed the benefits and risks of eating fish, a potential source of mercury and dioxin contamination. They calculated that eating one to two fish meals per week, especially fish high in omega-3 fats, reduced the risk of death from heart disease by 36 percent and death from other causes by 17 percent. The researchers wrote that women of childbearing age and nursing mothers should consume two seafood meals per week, but limit their consumption of high-mercury fish, such as shark, king mackerel, swordfish, and golden bass. Docosahexaenoic acid (DHA), one of the omega-3s, is important in the development of fetal and infant brains. The researchers noted that consuming 250 mg daily of DHA and eicosapentaenoic acid (EPA) may be sufficient for heart protection. They concluded that, "for major health outcomes among adults...the benefits of fish intake exceed the potential risks. For women of childbearing age, benefits of modest fish intake, except for a few selected species, also outweigh risks."

Mozaffarian D, et al. *JAMA*, 2006;296:1885-1899.

• Resveratrol has striking anti-aging effects in mice

Resveratrol, an antioxidant found in red wine, has a pronounced anti-aging effect in obese laboratory mice, according to a study by American researchers. High supplemental doses of resveratrol prevented nearly all negative health changes caused by eating high-calorie diets. The mice received the human equivalent of almost 1,700 mg of resveratrol daily – the amount that would be in roughly a thousand glasses of red wine. Compared with untreated mice, those getting resveratrol maintained higher activity of SIRT1, considered an anti-aging gene. The mice also maintained normal liver function

Silymarin and Diabetes...

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the complications of diabetes, as well as insulin resistance and impaired insulin secretion. Silymarin, which is an antioxidant, neutralizes those free radicals and may also help normalize insulin secretion.

A previous study, published by Italian researchers in 1997, found that silymarin supplements helped diabetic patients who also had cirrhosis of the liver.

Reference: Huseini HF, Larijani B, Heshmat R, et al. The efficacy of *Silybum marianum* (L.) Gaertn. (Silymarin) in the treatment of type II diabetes: a randomized, double-blind, placebo-controlled, clinical trial. *Phytotherapy Research*, 2006;20:1036-1039. □

and had relatively low levels of glucose, insulin, and insulin-like growth factor-1. The average lifespan of the mice increased by about 15 percent, and they also maintained a higher quality of life, with more physical activity and improvements in motor skills.

Baur JA, et al. *Nature*, 2006:epub ahead of print.

• Green tea associated with low cardiovascular deaths

Japanese researchers analyzed green tea consumption and the risk of death in a study of more than 40,000 middle-age and elderly men and women. Drinking three or more cups of green tea was associated with substantially lower risks of death from cardiovascular disease in both men and women. Women benefited more than men from green tea, with consumption of five or more cups daily related to a 31 percent reduction in cardiovascular-related deaths. Green tea had the greatest benefit in reducing the risk of stroke.

Kuriyama S, et al. *JAMA*, 2006;296:1255-1265.

• Vitamin D may lower risk of pancreatic cancer

American researchers analyzed vitamin E intake and the risk of pancreatic cancer among more than 47,000 men and 75,000 women. They found that higher intakes of vitamin D were related to lower risks of developing pancreatic cancer. People who consumed more than 600 IU of vitamin D daily were 41 percent less likely to develop that type of cancer.

Skinner HG, et al. *Cancer Epidemiology, Biomarkers and Prevention*, 2006;15:1688-1695.

• Tomato extract improves blood clotting

Scottish researchers investigated the effects of tomato extract on blood clotting in 90 healthy subjects. The tomato extract prevented blood clots, which could contribute to a reduced risk of heart attack. The tomato extract had the greatest effect in people with high levels of either homocysteine or C-reactive protein, both markers of cardiovascular risk.

O'Kennedy N, et al. *American Journal of Clinical Nutrition*, 2006;84:561-569.

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