The Great Fish Oil Experiment

From the original article in 2007. Author: Ray Peat.

Reading medical journals and following the mass media, it's easy to get the idea that fish oil is something any sensible person should use. It's rare to see anything suggesting that it could be dangerous.

During the recent years in which the U.S. government has gone from warning against the consumption of too much of these omega-3 oils *("to assure that the combined daily intake of two fatty acids that are components" "(i.e., eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) would not exceed 3 grams per person per day (g/p/d)")* to sponsoring biased industry claims, there has been considerable accumulation of information about the dangers of fish oils and omega-3 fatty acids. But there has been an even greater increase in the industry's promotional activities.

The US government and the mass media selectively promote research that is favorable to the fish oil industry. The editorial boards of oil research journals often include industry representatives, and their editorial decisions favor research conclusions that promote the industry, in the way that editorial decisions in previous decades favored articles that denied the dangers of radiation and reported that estrogen cures almost everything. Marcia Angell, former editor of the NEJM, has observed that the "significant results" reported in published studies can be properly interpreted only by knowing how many studies reporting opposite results were rejected by the editors.

One way to evaluate published studies is to see whether they tell you everything you would need to know to replicate the experiment, and whether the information they provide is adequate for drawing the conclusions they draw, for example whether they compared the experimental subjects to proper control subjects. With just a few minimal critical principles of this sort, most "scientific" publications on nutrition, endocrinology, cancer and other degenerative diseases are seen to be unscientific. In nutritional experiments with fish oil, controls must receive similar amounts of vitamins A, D, E, and K, and should include fat free or "EFA" deficient diets for comparison.

In declaring EPA and DHA to be safe, the FDA neglected to evaluate their antithyroid, immunosuppressive, lipid peroxidative (Song et al., 2000), light sensitizing, and antimitochondrial effects, their depression of glucose oxidation (Delarue et al., 2003), and their contribution to metastatic cancer (Klieveri, et al., 2000), lipofuscinosis and liver damage, among other problems.

> “Houston-based Omega Protein Inc.'s bottom line may get a little fatter.
>
> The publicly traded company, which produces an Omega-3 fatty acid product called OmegaPure, has signed an agreement to provide its fish oil in school lunches in 38 school districts in South Texas beginning this month.
>
> The 500-person company, which has ties to former President George Bush's Zapata Corp., will distribute the product through an agreement with Mercedes-based H&H Foods.
>
> Although the dollar amount of the contract between Omega Protein and H&H Foods hinges on future sales, the company is poised to cash in as school administrators and parents refocus their attention on the nutritional content of student diets.
>
> Omega Protein President and CEO Joseph von Rosenberg says the company's recent investment of $16.5 million for a fish oil refinery in Reedville, Va., scheduled for completion in May, and an increased awareness of the benefits of Omega-3 in human food, positions Omega to capitalize on predicted demand.”
>
> Jenna Colley
> Houston Business Journal

Andrew Weil was on the radio recently recommending DHA (usually found in fish oil*) to treat depression, and I think that means that a lot of people are buying it and eating it. A few years ago the government declared that it was "generally regarded as safe" and approved its use in baby formula, and a few months ago Texas school districts contracted with Omega Protein (which grew out of the Bush family's Zapata Corporation) to provide menhaden fish oil for school lunches. Between the 1950s and the 1970s, people were assured that eating polyunsaturated seed oils would protect them against heart disease. There's no evidence that the bad outcome of that campaign decreased the gullibility of the public. They are happily joining in the latest public health experiment.

**Weil recommends eating "oily fish"--"wild Alaskan salmon, mackerel, sardines, or herring"--. "If you do take supplements, fish oil is a better source of DHA than algae"*

When a group of people in government and industry decide on a policy, they can use carrots (good jobs, grants, and prestige) and sticks (loss of jobs and grants, organized slander, and worse) to make their guidelines clear, and most people will choose to follow those cues, even if they know that the policy is wrong. Historically, policy makers have told the public that "radiation is good for you," "estrogen will make you fertile (or safely infertile) and feminine and strong and intelligent," "starchy foods will prevent diabetes and obesity," "using diuretics and avoiding salt will make pregnancy safer," and that the polyunsaturated fatty acids are "nutritionally essential, and will prevent heart disease."

The original "essential fatty acids" were linoleic, linolenic, and arachidonic acids. Now that the toxic effects of those are coming to be recognized, new "essential fatty acids," the omega-3 fatty acids, including those with long chains, found in fish oils, are said to make babies more intelligent, to be necessary for good vision, and to prevent cancer, heart disease, obesity,

arthritis, depression, epilepsy, psychosis, dementia, ulcers, eczema and dry skin.

With just a normal amount of vitamin E in the diet, cod liver oil is certain to be highly oxidized in the tissues of a mammal that eats a lot of it, and an experiment with dogs showed that it could increase their cancer mortality from the normal 5% to 100%. Although fish oils rapidly destroy vitamin E in the body, some of them, especially the liver oils, can provide useful vitamins, A and D. In studies comparing fish oil diets with standard diets, these nutrients, as well as any toxins besides fatty acids (Huang, et al., 1997; Miyazaki, et al., 1998) in either type of oil, should be taken into account, but they seldom are.

Despite the nutritional value of those vitamins, fish oils are generally much more immunosuppressive than the seed oils, and the early effects of fish oil on the "immune system" include the suppression of prostaglandin synthesis, because the more highly unsaturated long chain fats interfere with the conversion of linoleic acid into arachidonic acid and prostaglandins. The prostaglandins are so problematic that their suppression is helpful, whether the inhibition is caused by aspirin or vitamin E, or by fish oil.

Some of the important antiinflammatory effects of fish oil result from the oxidized oils, rather than the unchanged oils (Sethi, 2002; Chaudhary, et al., 2004). These oils are so unstable that they begin to spontaneously oxidize even before they reach the bloodstream.

In experiments that last just a few weeks or months, there may not be time for cancers to develop, and on that time scale, the immunosuppressive and antiinflammatory effects of oxidized fish oil might seem beneficial. For a few decades, x-ray treatments were used to relieve inflammatory conditions, and most of the doctors who promoted the treatment were able to retire before their patients began suffering the fatal effects of atrophy, fibrosis, and cancer. (But a few people are still advocating x-ray therapy for inflammatory diseases, e.g., Hildebrandt, et al., 2003.) The fish oil fad is now just as old as the x-ray fad was at its peak of popularity, and if its antiinflammatory actions involve the same mechanisms as the antiinflammatory immunosuppressive x-ray treatments, then we can expect to see another epidemic of fibrotic conditions and cancer in about 15 to 20 years.

Around 1970 researchers reported that animals given fish oil in their food lived longer than animals on the standard diet. Alex Comfort, who was familiar with the research showing that simple reduction of food intake increased longevity, observed that the animals were very reluctant to eat the food containing smelly fish oil, and were eating so little food that their longevity could be accounted for by their reduced caloric intake. Even when "fresh" deodorized fish oil is added to the diet, its spontaneous oxidation before it reaches the animal's tissues reduces its caloric value. Without antioxidants, fish oil is massively degraded within 48 hours, and even with a huge amount of antioxidant there is still considerable degradation (Gonzalez, 1988; Klein, et al., 1990).

Fish oil has been used for hundreds of years as varnish or for fuel in lamps, and the fatty fish have been used as fertilizer and animal feed, and later the hydrogenated solid form of the oil, which is more stable, has been used in Europe as a food substitute for people. When whale hunting was reduced around 1950, fish oil was substituted for whale oil in margarine production. Like the seed oils, such as linseed oil, the fish oils were mostly replaced by petroleum derivatives in the paint industry after the 1960s.

Although by 1980 many animal diseases were known to be caused by eating oily fish, and the unsaturated oils were known to accelerate the formation of the "age pigment," lipofuscin, many "beneficial effects" of dietary fish oil started appearing in research journals around that time, and the mass media, responding to the industry's public relations campaign, began ignoring studies that showed harmful effects from eating fish oil.

When reviewers in professional journals begin to ignore valid research whose conclusions are harmful to the fish oil industry, we can see that the policy guidelines set by the industry and its agents in government have become clear. Around the end of the century, we begin to see a strange literary device appearing, in which research reports on the toxic effects of omega-3 oils are prefaced by remarks to the effect that "we all know how great these oils are for good health." I think I detect groveling and shuffling of the feet by authors who want to get their work published. If you are willing to say that your work probably doesn't mean what it seems to mean, maybe they will publish it.

For more than 50 years, the great majority of the medical publications on estrogen were part of the drug industry's campaign to fraudulently gain billions of dollars, and anyone who cared to analyze them could see that the authors and editors were part of a cult, rather than seekers of useful knowledge. Likewise, the doctrine of the harmlessness of x-rays and radioactive fallout was kept alive for several decades by demonizing all who challenged it. It now looks as though we are in danger of entering another period of medical-industrial-governmental cultism, this time to promote the universal use of polyunsaturated fats as both drugs and foods.

In 2004, a study of 29,133 men reported that the use of omega-3 oil or consumption of fish didn't decrease depression or suicide, and in 2001, a study of 42,612 men and women reported that after more than 9 years the use of cod liver oil showed no protective effect against coronary heart disease (Hakkarainen, et al., 2004; Egeland, et al., 2001).

The most popular way of arguing that fish oil will prevent heart disease is to show that it lowers blood lipids, continuing the old approach of the American Heart Association's "heart protective diet." Unfortunately for that argument, it's now known that the triglycerides in the blood are decreased because of the fish oil's toxic effects on the liver (Hagve and Christophersen, 1988; Ritskes-Hoitinga, et al., 1998). In experiments with rats, EPA and DHA lowered blood lipids only when given to rats that had been fed, in which case the fats were incorporated into tissues, and suppressed mitochondrial respiration (Osmundsen, et al., 1998).

The belief that eating cholesterol causes heart disease was based mainly on old experiments with rabbits, and subsequent experiments have made it clear that it is ***oxidized*** cholesterol that damages the arteries (Stapran, et al., 1997). Since both fish oil and oxidized cholesterol damage rabbits' arteries, and since the lipid peroxides associated with fish oil attack a great

variety of biological materials, including the LDL lipoproteins carrying cholesterol, the implications of the rabbit experiments now seem very different.

Another way of arguing for the use of fish oil or other omega-3 fats is to show a correlation between disease and a decreased amount of EPA, DHA, or arachidonic acid in the tissues, and to say "these oils are deficient, the disease is caused by a deficiency of essential fatty acids." Those oils are extremely susceptible to oxidation, so they tend to spontaneously disappear in response to tissue injury, cellular excitation, the increased energy demands of stress, exposure to toxins or ionizing radiation, or even exposure to light. That spontaneous oxidation is what made them useful as varnish or paint medium. But it is what makes them sensitize the tissues to injury. Their "deficiency" in the tissues frequently corresponds to the intensity of oxidative stress and lipid peroxidation; it is usually their presence, rather than their deficiency, that created the disposition for the disease.

One of the earliest harmful effects of polyunsaturated fatty acids, PUFA, to be observed was their acceleration of the formation of lipofuscin or ceroid, the "age pigment," during oxidative stress or vitamin E deficiency. Associated with the formation of lipofuscin, the PUFA were discovered to cause degeneration of the gonads and brain, and the fact that vitamin E could prevent some of their toxic effects led to the idea that vitamin E was essentially an antioxidant. Unfortunately, the protective effect of vitamin E against the PUFA is only partial (Allard, et al., 1997).

The degenerative diseases are all associated with disturbances involving fat metabolism and lipid peroxidation. Alzheimer's disease, alcoholic and nonalcoholic liver disease, retinal degeneration, epilepsy, AIDS, diabetes, and a variety of circulatory problems involve breakdown products of the PUFA. The products of PUFA decomposition include acrolein, malondialdehyde, hydroxynonenal, crotonaldehyde, ethane, pentane, and the neuroprostanes, which are prostaglandin-like molecules formed from DHA by free radical lipid peroxidation products, especially in the brain and at a higher level in Alzheimer's disease.

The reactions of three types of cell--vascular endothelium, nerve cells, and thymus cells--to the PUFA will illustrate some of the important processes involved in their toxicity.

When the body doesn't have enough glucose, free fatty acids are released from the tissues, and their oxidation blocks the oxidation of glucose even when it becomes available from the breakdown of protein caused by cortisol, which is released during glucose deprivation. Cells of the thymus are sensitive to glucose deprivation, and even in the presence of glucose, cortisol prevents them from using glucose, causing them to take up fatty acids. The thymic cells die easily when exposed either to excess cortisol, or deficient glucose. The polyunsaturated fatty acids linoleate, arachidonate, and eicosapentaenoic, are especially toxic to thymic cells by preventing their inactivation of cortisol, increasing its action. (Klein, et al., 1987, 1989, 1990). Lymphocytes from people with AIDS and leukemia are less able to metabolize cortisol. An extract of serum from AIDS patients caused lymphocytes exposed to cortisol to die 7 times faster than cells from healthy people. AIDS patients have high levels of both cortisol and free polyunsaturated fatty acids (Christeff, et al., 1988).

The cytotoxicity caused by EPA and its metabolites (15 mg. of EPA per liter killed over 90% of a certain type of macrophage) isn't inhibited by vitamin E (Fyfe and Abbey, 2000). Immunological activation tends to kill T cells that contain PUFA (Switzer, et al., 2003).

When animals are fed fish oil and then exposed to bacteria, their immunosuppressed thymic (T) cells cause them to succumb to the infection more easily than animals fed coconut oil or a fat free diet. Natural killer cells, which eliminate cancer cells and virus infected cells, are decreased after eating fish oil, and T suppressor cells are often increased. More subtle interference with immunity is produced by the actions of PUFA on the "immune synapse," a contact between cells that permits the transmission of immunological information. The immunosuppressive effect of fish oil is recognized as a useful aid in preventing the rejection of transplanted organs, but some studies are showing that survival a year after transplantation isn't improved.

Polyunsaturated fatty acids, especially those that can be turned into prostaglandins, are widely involved in causing inflammation and vascular leakiness. EPA and DHA don't form ordinary prostaglandins, though the isoprostanes and neuroprostanes they produce during lipid peroxidation behave in many ways like the more common prostaglandins, and their enzymically formed eicosanoids have some functions similar to those of the common prostaglandins. The brain contains a very high concentration of these unstable fatty acids, and they are released in synapses by ordinary excitatory process.

Chan, et al., 1983, found that polyunsaturated fats caused brain swelling and increased blood vessel permeability. In 1988, Chan's group found that DHA and other polyunsaturated fatty acids added to cultured cells from the cerebral cortex produced free radicals and stimulated production of malondialdehyde and lactate, and inhibited the uptake of glutamic acid, which suggests that they would contribute to prolonged excitation of the nerves (Yu, et al., 1986). In brain slices, the polyunsaturated fatty acids caused the production of free radicals and swelling of the tissue, and the saturated fatty acids didn't (Chan and Fishman, 1980). The PUFA inhibited the respiration of mitochondria in brain cells (Hillered and Chan, 1988), and at a higher concentration, caused them to swell (Hillered and Chan, 1989), but saturated fatty acids didn't produce edema. Free radical activity was shown to cause the liberation of free fatty acids from the cellular structure (Chan, et al., 1982, 1984). The activation of lipases by free radicals and lipid peroxides, with the loss of potassium from the cells, suggests that excitation can become a self-stimulating process, leading to cellular destruction.

DHA itself, rather than its decomposition products, facilitates excitatory (glutamate) nerve transmission (Nishikawa, et al., 1994), and that excitatory action causes the release of arachidonic acid (Pellerin and Wolfe, 1991).

Considering just one of the products of fish oil peroxidation, acrolein, and a few of its effects in cells, we can get an idea of the types of damage that could result from increasing the amount of omega-3 fats in our tissues.

The "barrier" between the brain and blood stream is one of the most effective vascular barriers in the body, but it is very permeable to oils, and lipid peroxidation disrupts it, damaging the ATPase that regulates sodium and potassium

(Stanimirovic, et al., 1995). Apparently, anything that depletes the cell's energy, lowering ATP, allows an excess of calcium to enter cells, contributing to their death (Ray, et al., 1994). Increasing intracellular calcium activates phospholipases, releasing more polyunsaturated fats (Sweetman, et al., 1995) The acrolein which is released during lipid peroxidation inhibits mitochondrial function by poisoning the crucial respiratory enzyme, cytochrome oxidase, resulting in a decreased ability to produce energy (Picklo and Montine, 2001). (In the retina, the PUFA contribute to light-induced damage of the energy producing ability of the cells [King, 2004], by damaging the same crucial enzyme.) Besides inhibiting the ability of nerve cells to produce energy from the oxidation of glucose, acrolein inhibits the ability of cells to regulate the excitatory amino acid glutamate (Lovell, et al., 2000), contributing to the excitatory process. High levels of acrolein (and other products of PUFA degradation) are found in the brain in Alzheimer's disease (Lovell, et al., 2001).

The "prion" diseases, CJD and TSE/BSE (mad cow disease) have many features in common with Alzheimer's disease, and several studies have shown that the "prion" protein produces its damage by activating the lipases that release polyunsaturated fatty acids and produce lipid peroxides (Bate, et al., 2004, Stewart, et al., 2001).

Acrolein reacts with DNA, causing "genetic" damage, and also reacts with the lysine in proteins, for example contributing to the toxicity of oxidized low density lipoproteins (LDL), the proteins that carry cholesterol and that became famous because of their involvement in the development of atherosclerosis that was supposedly caused by eating saturated fats.

My newsletter on mad cow disease discussed the evidence incriminating the use of fish meal in animal feed, as a cause of the degenerative brain diseases, and earlier newsletters (glycemia, and glycation) discussed the reasons for thinking that inappropriate glycation of lysine groups in proteins, as a result of a lack of protective carbon dioxide/carbamino groups, produces the amyloid (or "prion") proteins that characterize the dementias. Acrolein, produced from the decomposing "fish oils" in the brain, is probably the most reactive product of lipid peroxidation in the brain, and so would be likely to cause the glycation of lysine in the plaque-forming proteins.

These toxic effects of acrolein in the brain are analogous to the multitude of toxic effects of the omega-3 fatty acids and their breakdown products in all of the other organs and tissues of the body. Cancer cells are unusual in their degree of resistance to the lethal actions of the lipid peroxides, but the inflammatory effects of the highly unsaturated fatty acids are now widely recognized to be essentially involved in the process of cancerization (my newsletters on cancer and leakiness discuss some of the ways the fats are involved in tumor development).

The fats that we synthesize from sugar, or coconut oil, or oleic acid, the omega-9 series, are protective against the inflammatory PUFA, in some cases more effective even than vitamin E.

In Woody Allen's 1973 movie, ***Sleeper,*** the protagonist woke up after being frozen for 200 years, to find that saturated fats were health foods. At the time the movie was made, that had already been established (e.g., Hartroft and Porta, 1968 edition of *Present Knowledge in Nutrition*, who showed that adequate saturated fat in the diet helped to protect against the formation of lipofuscin).

PS:

Royal Society for the Protection of Birds says 2004 has been the most catastrophic breeding season on record for seabirds along UK coasts. It says industrial fishing to supply fish meal and oil is barely sustainable and imperils the whole marine food web.

"The UK has suffered serious seabird disasters this year already. In Shetland and Orkney, entire colonies of birds failed to produce any young because of severe food shortages. "On top of that, hundreds of seabirds have been washing ashore having perished at sea. Again, lack of food is thought to be one of the reasons." The report, Assessment Of The Sustainability Of Industrial Fisheries Producing Fish Meal And Fish Oil, was compiled for the RSPB by Poseidon Aquatic Resource Management Ltd and the University of Newcastle-upon-Tyne.

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