DHA for Hearts and Minds

by Ben Best

Sixty percent of heart attacks occur without warning due to irregular heartbeats which DHA can prevent. Although DHA is contained in fish oil, DHA is superior to fish oil because fish oil also contains EPA. EPA suppresses the immune system and increases lipid peroxidation. Since DHA produces most of the benefits of fish oil, whereas EPA produces most of the harm, it makes sense to take a high DHA formulation rather than fish oil.

DHA can benefit your mind. Fish has been called "brain food", but DHA deserves the credit. DHA is highly concentrated in membranes of brain synapses and in the retina of the eye. DHA declines in brain cell (neuron) membranes with aging may result in declining mental function. DHA requirements for brain development in the late-stage foetus and newborn are so critical that slight deficiencies can have a life-long impact on intelligence.

WHAT IS DHA?

DHA is an omega-3 fatty acid, so-called because it has a double-bond 3 carbon atoms away from the methyl end of the molecule. All the fatty acids which are essential in the human diet are either omega-3 or omega-6. Although DHA can be synthesized in the body from alpha-linolenic acid (a simpler omega-3 found in linseed oil and perilla oil), the capacity for synthesis declines with age. So the older you are (beyond infancy), the more you can benefit from DHA.

The omega-3 and omega-6 family of fatty acids are essential because they cannot be synthesized in the body, but must be obtained in the diet. Fatty acids are contained in the membranes of every cell in your body, but the essential fatty acids are particularly concentrated in the membranes of brain cells, heart cells and immune-system cells.

The most important long-chain fatty acid in the omega-6 family is **arachidonic acid**. Arachidonic acid has 20-carbons and 4 double-bonds. Arachidonic acid, gives rise to a whole group of 20-carbon, biologically-important substances known as the **eicosanoids** (**eicosa-** is Greek for "20"), including prostaglandins, thromboxanes, lipoxins and leukotrienes -- which affect immunity, inflammation and blood clotting (among other actions).

In the omega-3 family, the most important long-chain fatty acids are EPA (EicosaPentaenoic Acid, 20 carbons and 5 double-bonds) and DHA (DocasaHexaenoic Acid, 22 carbons and 6 double-bonds). Like arachidonic acid, EPA gives rise to its own class of eicosanoids. The EPA-generated eicosanoids are in the omega-3 family, as distinct from the omega-6 eicosanoids derived from arachidonic acid. The omega-3 eicosanoids reduce the inflammatory and allergy-producing effects of the omega-6 eicosanoids. Many people believe that excessively high omega-6 rather than omega-3 in the modern diet is responsible for an increase in allergies and the need to take aspirin to reduce the risk of heart attack (myocardial infarction).

ESSENTIAL FATTY ACIDS IN THE DIET

The primary source of omega-6 fatty acid in the diet is linoleic acid from the oils of seeds and grains. Sunflower, safflower and corn oil are particularly rich sources of linoleic acid, which is at the root of the omega-6 fatty-acid family. Evening primrose oil and borage oil are high not only in linoleic acid, but the omega-6 derivative gamma-linolenic acid (GLA).

Omega-3 fatty acids, on the other hand, are more frequently found in green leaves. The leaves and seeds of the perilla plant (widely eaten in Japan, Korea and India) are the richest plant source of alpha-linolenic acid, although linseed oil is also a rich source. Fish oil contains very little alpha-linolenic acid, but is rich in the omega-3 derivatives EPA and DHA.

Although most fish oils are high in EPA and DHA, there are some fish oils which are not. Flounder, swordfish and sole are particularly low in EPA and DHA. Fish oils with the highest levels of EPA and DHA include mackerel, herring and

salmon. Some fish, such as cod and haddock, store most of their fat in the liver, therefore the liver oils of these fish should be taken rather than oil from the fillet.

DHA PROMOTES A HEALTHY HEART

Fish oil has achieved medical prominence primarily due to its ability to reduce heart disease in fish-eating populations such as Eskimos and Japanese. Even in Japan, fishermen have lower blood pressure and lower incidence of heart disease than do farmers. The omega-3 fatty acids EPA and DHA are the fish oil components held responsible for these benefits. EPA and DHA are elevated in blood plasma and in cell membranes at the expense of the omega-6 fat arachidonic acid in Eskimos and Japanese.

There has been controversy over whether the cardiovascular benefits of fish oil are more due to EPA or DHA or whether both are of equal benefit. Some studies have indicated that EPA is more effective for lowering blood triglycerides. But a recent large, double-blind, placebo-controlled trial showed a triglyceride decrease of 26% for subjects taking DHA, in contrast to a 21% decrease for those taking EPA [*1]. Both DHA and EPA lower triglycerides by reducing the rate of fatty acid synthesis in the liver [*2].

Purified DHA has been shown to lower blood pressure and reduce blood viscosity. The evidence indicates that DHA increases red blood cell membrane fluidity, thereby increasing the deformability of the blood cells so that they can move through capillaries more easily and thereby lower blood viscosity and blood pressure [*3]. DHA may also reduce blood pressure by lowering cortisol [*4].

The most dramatic effects of fish oil on the heart, however, are in connection with cardiac arrhythmias (irregular heartbeats). In the United States, a quarter of a million people die annually within an hour of a heart attack as a result of arrhythmia. The protective effect of fish oil against cardiac arrhythmias has been strikingly illustrated by two similar experiments, one performed on rats [*5] and the other on marmoset monkeys [*6]. Middle-aged animals were fed sheep fat (saturated fat), sunflower seed oil (omega-6) or fish oil (omega-3) for 12 weeks (for rats) or for 24-30 months (for monkeys). With both rats and monkeys arrhythmia was produced in over 40% of the animals fed sheep fat, roughly 10% of the animals fed safflower oil and in none of the animals who were fed fish oil.

Phosphatidylethanolamine (an important phospholipid of the inner layer of cell membranes) from monkey heart tissue showed 5 times more (over 25% total) DHA in the fish-oil fed monkeys than in the other two groups. EPA accounted for over 6% of the fatty acid phosphatidylethanolamine of fish-oil fed monkeys, and was undetectable in the other two groups. A similar experiment on rats using purified DHA and purified EPA, rather than fish-oil, indicated that DHA is responsible for most of the anti-arrhythmic effect [*7]. DHA is more readily incorporated into heart cell membranes than EPA [*8]. It is the DHA in heart cell membranes, rather than DHA in the bloodstream, which is protective [*9].

DHA IS BRAIN FOOD

Most of the dry weight of the brain is lipid (fat) because brain activity depends greatly upon the functions provided by lipid membranes. Compared to other body tissues, brain content of DHA and arachidonic acid is very high. DHA is particularly concentrated in membranes that are functionally active, namely in synapses and in the retina.

The ability of enzymes to produce the omega-6 and omega-3 family of products of linoleic and alpha-linolenic acid declines with age. One experiment showed that desaturase enzyme function in old rats was only 44% of the desaturase function in young rats [*26]. Because DHA synthesis declines with age, as we get older our need to acquire DHA directly from diet or supplements increases.

Because of the decline in DHA synthesis, it is not surprising that DHA content of brain cell membranes declines. DHA is also reduced when the brains of rats are experimentally exposed to high oxygen levels. Free-radical oxidation probably causes the depletion in both cases. Vitamin E treatment protected the rats from neuron damage from the oxygen. This suggests that Vitamin E may be important for prevention of neurodegeneration in humans [*25].

The greatest dependence on dietary DHA occurs in the foetus during the last third of pregnancy and (to a lesser extent) in the infant during the first 3 months after birth. It is during this period that brain synapses are forming most rapidly, and an infant's demand for DHA exceeds the capacity of the enzymes to synthesize it [*11]. The additional requirements are fulfilled by mechanisms believed to concentrate DHA absorption from the mother's placenta [*12].

After birth, the additional needed DHA comes from the nursing mother. Rapid brain growth in the human infant requires large amounts of omega-3 and omega-6 essential fatty acids. Human milk contains (in total fatty acids by weight) 12% linoleic acid, 0.5% alpha-linolenic acid, 0.6% arachidonic acid and 0.3% DHA [*13]. Infant formulas frequently have not contained arachidonic acid or DHA. One study showed that by (or just before) age 8, children who had been breast-fed as infants had an 8.3-point IQ advantage over children who had received formula [*14]. The study corrected for the education and social class of the mother.

Further support for the idea that DHA is critical for brain development came from an experiment which studied the effects of adding DHA (in the form of fish oil) to infant formula. At both 16 and 30 weeks of age the breast-fed and supplement-formula-fed infants showed significantly better visual acuity than the placebo-formula-fed infants [*15]. Arachidonic acid supplementation is also needed because DHA supplementation given alone lowers arachidonic acid levels [*16] and because arachidonic acid is essential for growth [*17,*18]. Deficiency of arachidonic acid during brain development is less reversible than deficiency of DHA [*19]. Recent reviews have firmly recommended the inclusion of both arachidonic acid and DHA in the formula of premature babies [*20].

Even in the best formulations the efficiency of DHA and arachidonic acid absorption by an infant is inferior to what is seen for breast milk. Therefore, the best way to ensure adequate DHA and arachidonic acid would be for a pregnant/nursing mother to take a DHA supplement. The content of DHA and EPA in human milk has been increased experimentally by giving fish oil supplements to lactating women [*21]. The diet of the mother may contain enough omega-6 fat to allow her to synthesize sufficient arachidonic acid. DHA supplementation would be particularly important for mothers who have consumed excessive alcohol, because alcohol inhibits the desaturase enzymes necessary for DHA synthesis [*22].

Arachidonic acid is similar to glutamate (glutamic acid) in that it can be harmful in conditions of restricted blood circulation (ischemia), but it is essential for normal brain function. It is the EPA (not DHA) in fish oil that can reduce arachidonic acid synthesis. Where pure DHA, rather than fish oil, has been used in infant formulas, inhibition of growth has been much less [*22]. The best infant formula should contain both DHA and arachidonic acid, however, because arachidonic acid improves growth.

An experiment studying maze-learning in rats demonstrated that, after training, the rats showed less cholesterol and more membrane fluidity in the hippocampal and cortical regions of the brain [*23]. Adult mice fed fish oil for 12 months showed more brain DHA, less brain arachidonic acid, more synaptic membrane fluidity and higher maze-learning ability [*24].

Fatty acid in phosphatidylethanolamine of human gray matter cell membrane is roughly 25% DHA, 25% stearic acid, 14% arachidonic and 12% oleic acid. In the outer segments of retina photo-receptors of the eye more than 50% of the fatty acid content is DHA. It is DHA's special properties of permeability and perhaps fluidity that probably accounts for this high concentration [*10].

In contemporary diets, omega-6 fatty acids typically exceed **all** omega-3s (alpha-linolenic, EPA or DHA) by 6 or 7 times. A study on guinea pigs showed that both insufficient and excessive dietary DHA resulted in less than optimal visual acuity. The problems with excessive DHA were attributed to oxidative damage. This result is not too surprising because DHA, with six double-bonds, is the most highly unsaturated fatty acid found in significant quantities in the human body. The researchers did not include Vitamin E in their experiment, which is unfortunate because Vitamin E would be expected to reduce lipid peroxidation [*27].

OXIDATIVE DAMAGE AND DHA

EPA and DHA are the most unsaturated fatty acids found in large quantities in the bodies of animals and therefore are likely to be more vulnerable to lipid peroxidation than any other fats. Early experiments showed that extremely

high levels of cod liver oil in experimental animals can produce enough oxidative damage to result in muscle lesions. Subsequent experiments showed that these lesions can be prevented with vitamin E [*28].

More recent and more careful studies have shown that the oxidative damage due to fish oil -- and the ability to protect against it -- varies greatly between tissues. Vitamin E is least able to protect against oxidation of either EPA or DHA in blood plasma [*29]. The alpha-tocopherol form of vitamin E protects red blood cell membranes of young animals more effectively than those of old animals [*30]. Although both alpha- and gamma-tocopherol protect against lipid peroxidation, they do so by different mechanisms. Generally, gamma-tocopherol is only 30% as effective as the alpha form as an anti-oxidant, but gamma-tocopherol is particularly effective against peroxynitrite [*31].

Alpha-tocopherol protects against oxidative damage from fish oil far more effectively in the liver than in the kidney [*32]. But the kidney is less vulnerable to oxidative damage because kidney cell membrane composition is much less subject to alteration by changes in dietary fat. Although a four-fold increase in alpha-tocopherol above normal dietary levels has been shown to reduce fish oil-induced peroxidation in monkey livers, peroxidation was not completely eliminated. The experimenters suggested that higher levels of vitamin E or other anti-oxidants might reduce the damage further.

Oxidative damage to the heart due to fish oil, however, is much less than oxidative damage to the liver or even the kidney. When incorporated into heart muscle membranes, both EPA and DHA promote alpha-tocopherol being incorporated into the membranes as well. In fact, a high omega-3 fatty acid diet increases the alpha-tocopherol content of heart muscle membranes by **five** times, and this effect is most prominently associated with DHA [*33,*8].

Vitamin E provides more anti-oxidant benefit to the heart and spleen than selenium, beta-carotene or coenzyme Q10. In fact, at the maximum effective dose of Vitamin E, the other anti-oxidants offer no additional benefit. Selenium, however, gives the most anti-oxidant protection to the kidney. Under certain oxidative stresses coenzyme Q10 gives the most protection to the liver, with little additional benefit from the other anti-oxidants [*34].

DHA's most remarkable effect on oxidation is in the brain, where increasing tissue levels of DHA in the cerebral cortex causes significant increases in the anti-oxidant enzymes catalase and glutathione peroxidase. The induction of anti-oxidant enzymes by DHA in the brain is so dramatic that the researchers actually have referred to DHA as an anti-oxidant [*35].

DHA AND IMMUNE FUNCTION

Fish oil has been used for its anti-inflammatory effects in rheumatoid arthritis. Researchers have shown that anti-inflammatory action by DHA (not EPA) helps prevent cardiovascular disease because blood vessel inflammation plays a role in atherosclerosis [*36]. An experiment on human volunteers showed that fish oil concentrate was able to reduce inflammatory cytokines produced from monocytes by at least one third [*37].

The inflammatory response is closely linked to the immune system, and there has been concern that fish oils suppress the immune system along with inflammation. Lipid peroxidation suppresses lymphocyte proliferation, but it has been shown that when adequate amounts of alpha-tocopherol are given with fish oil, lymphocyte proliferation is not reduced [*38]. Fish oil increases the allergenic immunoglobulin IgE, but alpha-tocopherol opposes this increase [*39]. These results indicate that Vitamin E can be used to prevent some of the immune-suppressant effects of fish oil.

Not all of the immune-suppressing effects of fish oil are due to oxidation, however. Incorporation of certain fatty acids into cell membranes affects second-messenger systems (molecular signalling systems within cells) that can modify gene expression. An experiment that studied the individual effects of EPA and DHA found that EPA reduced natural killer (NK) cell activity and cell-mediated immune response, but that DHA does not. This study concluded that the immune-suppressing effects of fish oil are mainly due to EPA, not DHA [*40].

DHA SUPPLEMENTS FOR YOUR HEALTH

Although fish oil has been widely used and widely recommended for its benefits for heart and circulation, DHA is responsible for most of those benefits. Since excessive fish oil can be harmful, it makes sense to maximize the benefits and minimize the hazards by taking DHA rather than fish oil. Is there a supplement offering more benefit to you and your family than one protecting against sudden death due to heart attack -- the number one killer in Western society? DHA provides that benefit, while greatly reducing the hazards of immune-suppression due to EPA.

Mothers in their last third (trimester) of pregnancy or who are breastfeeding a newborn may contribute to the development of their child's brain by taking DHA in consultation with their physician. Others may want to take DHA supplements to guard against the decline of brain DHA normally seen with aging.

Dosages of 6 grams per day of DHA for 120 days have been used by adult males under close bio-medical supervision with no evident side effects [*41]. So 1 or 2 grams of DHA daily should be quite safe for nearly anyone. In comparison with some extremely high dosages of DHA used in animal experiments, 6 grams per day is modest.

But DHA (and fish oil) should be taken with Vitamin E (at least 400 IU), selenium (at least 100 micrograms) and coenzyme Q10 (at least 30 mg) to minimize oxidation. Fish oil is a natural component and health-promoting component of diet, so cautions about oxidation should be heeded in the spirit of avoiding the "more is better" attitude of many people who take supplements. Taken with mindfulness of reducing oxidation, DHA can prevent arrythmia and maintain neural function.

FOOTNOTES

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