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HEART HEALTH

DHA Lowers Triglycerides in Patients Taking Statins: More Evidence

In the June issue of Fats of Life, we reported that patients taking statin medications to lower their LDL-cholesterol ("bad") levels experienced additional heart health benefits when they added EPA (eicosapentaenoic acid, a long-chain omega-3 fatty acid) to their treatment. Besides lowering their LDL-cholesterol levels, they had significantly fewer major coronary events, such as a heart attack or coronary bypass surgery, less unstable angina (chest pain because of heart disease) and fewer other non-fatal heart problems. What made these findings even more surprising is that they occurred in a large sample of Japanese patients with high cholesterol and triglyceride (blood fat) levels who already consume much more fish and long-chain omega-3 fatty acids than most people in western countries. In these 61-year-old patients, increased intake of EPA improved their heart health.

A new study from Australia reported that in a sample of 45 patients taking statins to improve their blood lipids, the addition of tuna oil to their treatment provided greater heart health benefits than statins alone. These patients had both high cholesterol and triglyceride levels. They were divided into 3 groups: one taking just over 1 g/day of DHA (docosahexaenoic acid, a long-chain omega-3 fatty acid abundant in tuna oil), another taking just over 2 g/day of DHA and a control group consuming olive oil. Tuna oil also contains about 25% EPA in addition to DHA. After 3 and 6 months, the investigators measured their patients’ blood lipid levels.

Over the course of the study, all patients consuming tuna oil saw their blood triglyceride levels fall. Those taking the highest dose, 2 g of DHA/day, experienced a significant drop in their triglycerides after only 3 months. At 6 months, their triglycerides remained significantly lower, but did not decrease further. In the group taking 1 g/day of DHA, their triglycerides fell at both 3 and 6 months, but the drop did not reach statistical significance.

These 2 studies and previous reports of fish oil and blood lipids indicate that patients taking statin medications may obtain additional heart health advantages by consuming marine omega-3s—the long-chain ones, EPA and DHA—found abundantly in fatty fish or fish oil supplements. These fatty acids have the advantage over other drugs in being well tolerated, safe and without adverse side effects. In this case, food can be your medicine!

High Fish Intake Linked to Stroke in Swedish Men

No one expected to find that people with higher fish intakes would be more likely to develop ischemic stroke, but that was the observation from a study in Sweden. Why? Several studies have reported that people with greater intakes of seafood are less likely to develop ischemic stroke, the type of stroke related to clogged blood vessels typical of atherosclerosis. This might be expected from the knowledge that the omega-3 fatty acids in fish improve blood flow and blood vessel function and help slow the progress of atherosclerosis.

In this study, the investigators from Umea, Sweden, examined the dietary intakes of patients who suffered a stroke over a 5-year period and compared them with patients of the same sex and age who did not have a stroke. In this region, people consumed fish on average 1.4 times/week, much more often than in much of Europe and North America. They observed that men with high fish intakes were 25% more likely to have a stroke than women or those with low fish intakes.

When the investigators examined whether DHA,
a long-chain omega-3 fatty acid in seafood, or mercury were related to stroke, they came up empty-handed. There was no relationship with any of these substances in either men or women. These results are puzzling because people in this region with higher intakes of EPA and DHA have a lower chance of heart attack. Although this report is not the only one to have observed higher risk of stroke with greater fish consumption, the investigators themselves found it difficult to suggest a plausible explanation. It is also curious that the observations occurred only in men, not women. Fish consumption is thought to reduce the risk of stroke in women, but in this study it was unrelated to women’s chance of developing stroke. Sometimes, in science and people not everything turns out as expected. In this example, different types of evidence may be needed to clarify these observations.

We now have good evidence of the benefits to the developing fetus, infant and mother of consuming sufficient amounts of the omega-3 fatty acids found in fish and shellfish during pregnancy and lactation. DHA is essential for brain growth and development, proper visual function and long-term behaviors and learning. Omega-3s may also be important for reducing the infant’s chance of developing allergies. Instead, some women avoid eating fish because of worries about contaminants. They overlook the fact that they are also missing critical nutrients their baby needs. In fact, infants of mothers who eat plenty of fish and shellfish during their pregnancy have better developmental outcomes than infants whose mothers do not eat fish.

In many countries, including the United States, much of Europe and Australia, DHA intakes are inadequate. To address this concern, an international group of experts in maternal and child health, nutrition and lipid metabolism developed recommendations for intakes of fat and specific fatty acids during pregnancy and lactation. They also realized the importance of detecting dietary shortcomings early in pregnancy and recommended screening women early in their prenatal care. This recommendation could be especially important in countries, such as the United States, where fish consumption is low.

The group emphasized that pregnant and nursing women need to consume DHA already formed, not as its precursor, alpha-linolenic acid from plants (e.g., flax oil). This is because the conversion of this fatty acid to DHA is almost negligible, no matter how much the woman consumes.
Here is a simplified summary of the group’s recommendations:

**Recommendations for Fat and Fatty Acid Intakes In Pregnancy and Lactation**

*On behalf of the Perinatal Lipid Intake Working Group*

- Fat intake during pregnancy and lactation, as a proportion of energy, should be the same as for the general population.

- The omega-3 fatty acid, docosahexaenoic acid (DHA), must be deposited in adequate amounts in brain and other tissues during fetal and early postnatal life. Several studies have shown a relationship between maternal intake of oily fish or oils during pregnancy and/or lactation and the infant’s visual and cognitive development and other functions.

- Pregnant and lactating women should consume enough seafood omega-3s to reach a DHA intake of at least 200 mg/day. Consuming up to 1g/day DHA or 2.7 g/day total seafood omega-3s is without significant adverse effects.

- Women of childbearing age can meet the recommended intake of DHA by eating one to two portions of sea fish per week, including oily fish, which is a good source of omega-3s. This intake of oily fish rarely exceeds the tolerable intake of environmental contaminants. Dietary fish should be selected from a wide range of species without giving preference to large predator fish (such as swordfish and shark), which are more likely to be contaminated with methylmercury.

- Alpha-linolenic acid, the plant-based omega-3, is far less effective with regard to supplying DHA to the fetal brain than the intake of preformed DHA.

- There is no evidence that women of childbearing age whose dietary intake of linoleic acid is adequate need additional dietary arachidonic acid.

- Some studies have shown that mothers who eat fish, fish oils or omega-3s have a slightly longer gestation time, a somewhat higher birth weight and a lower chance of early preterm delivery.

- Mothers should be screened for dietary inadequacies during pregnancy, preferably during the first trimester. If less than desirable dietary habits are detected, individual counseling should be offered during pregnancy and lactation.
The expert group acknowledged concerns about contaminants in seafood. However, they emphasized that the benefits of fish consumption far outweigh the risks and that avoiding seafood carries its own dangers. They recommended eating a variety of fish and shellfish, especially those known to be low in contaminants, such as salmon, herring and mackerel.

**Essential Fatty Acids in Breast Milk From Around the World**

The composition of a mother’s milk depends on what she eats, but some nutrients, such as polyunsaturated fatty acids, are more variable than others. This is especially true for the omega-3 fatty acids found in fish and shellfish, notably for DHA, a long-chain omega-3. Because of the importance of the mother consuming DHA preformed, rather than as the precursor alphalinolenic acid, the level of DHA closely reflects the mother’s fish consumption. Women who do not eat fish, including vegetarian women, have significantly less DHA in their milk than women who eat fish. By eating seafood more often, a mother can increase her breast milk DHA as much as 10-fold.

A group of investigators at Cornell University, USA, wondered how much DHA and its counterpart in the omega-6 family, arachidonic acid, was present in breast milk in different countries. They confined their data search to reports of single samples of breast milk from mothers of full term infants. By carefully defining the samples they included, the investigators ensured that the data were based on typical mature breast milk.

The results are based on 84 studies of human milk from nearly 2,500 mothers in over 30 countries. The study revealed that, on average, arachidonic acid is more abundant than DHA and that DHA levels vary much more than arachidonic acid. This observation suggests that dietary DHA requires attention to ensure that levels meet the needs of the young infant. We know that very little DHA is obtained from alphalinolenic acid and if the infant does not receive DHA from the mother’s diet, he will try to meet his needs from the mother’s own tissues.

Women in countries where eating fish is common have much higher amounts of DHA in their breast milk compared with women in countries with low fish consumption. For example, in Japan breast milk DHA averaged 1.0% of all fatty acids, but in Germany and the United States, it was about 0.2%, a fifth of the Japanese level.

Studies have also shown that when infants are provided additional DHA in their formula, they have higher performance scores than infants consuming unsupplemented formula. Infants whose mothers increased their DHA intake also compare more favorably than infants whose mothers who eat little or no fish and have low DHA intakes. The bottom line is that babies need DHA for proper brain growth and development. Their mothers can provide a head start by ensuring that they, too, have plenty of DHA in their diet. They should aim for at least 200 mg of DHA a day from fish or fish oil supplements.

**Improved Outcomes in Women with High-Risk Pregnancies Who Take Fish Oil**

Women who are more likely to give birth before term because of past early delivery, multiple births or other reasons are usually monitored very carefully. There are limited things a mother can do to minimize the likelihood of preterm delivery, but one of them may be increasing her fish consumption. Fish, especially fatty species such as salmon, sardines, rainbow trout and herring, are rich in long-chain omega-3s. These fatty acids are needed by the growing fetus for brain development and function. The mother also needs them for her own tissues and breast milk production. Chances are they may lower the risk of preterm delivery, too.
Several studies have reported that women who consume fish often are more likely to have longer gestation times. Overall, gestation time does not increase very much—about a day or two. But some reports have found no difference in gestation time. These modest and mixed findings suggest that if there is an effect, it is likely small.

In this report, investigators in Denmark, where fish consumption is common, wanted to know whether the mother’s usual fish-eating habits had anything to do with her responses to fish oil supplementation during pregnancy. An earlier report from a large number of pregnancies indicated that women who consumed no fish in the first or second trimesters were 20 times more likely to give birth early, compared with women who ate fish. This finding that a woman’s usual fish eating habits might affect her response to consuming fish oil in pregnancy.

Accordingly, the investigators re-examined the data from a large study of fish oil supplementation in women with high-risk pregnancies. Originally, the study reported that taking fish oil reduced the chance of preterm delivery, but not in women carrying twins or experiencing intrauterine growth retardation. The investigators divided the women into 4 groups: those with a previous pregnancy complication, those carrying twins, women currently having trouble, such as pre-eclampsia (pregnancy-induced high blood pressure and protein excretion), and a control group given olive oil. All women were given nearly 4 g/day of long-chain omega-3s from the 20th week of gestation until delivery. Women with current difficulties were given an even larger dose, just over 6 g/day. Women were interviewed to assess their fish consumption habits.

The investigators found that women with previous or current pregnancy difficulties who consumed fish oil were significantly less likely to have a spontaneous preterm delivery. The chance of preterm birth was 31% lower in women with a previous problem and 45% lower in women presently having trouble. Delivery time was unaffected by fish oil consumption in women expecting twins.

When the investigators examined the delivery times of the women with a previous pregnancy problem, taking into consideration their usual fish-eating habits, it became clear that women with low or medium fish intakes responded to fish oil consumption more dramatically than women with high fish intakes. This effect was not observed in women currently experiencing difficulties. The effect of customary fish-eating habits was also observed in the control group who were not given fish oil.

In these women, those with low or medium fish intakes had significantly higher chances of preterm delivery than women with high fish consumption.

The study was unable to determine what actual fish intakes were, but in similar studies in this population, low levels represented never or rarely, medium consumption was once in 2 weeks and high intakes were more than once in 2 weeks. Assuming these levels would be similar in this study, the implication is that consuming fish at least once a week could be important in reducing the chance of preterm delivery.

You may wonder, is preterm delivery a problem? It can be, depending on how much before term the baby is born. Babies born before 32 weeks of gestation face the greatest risk of complications that usually affect the lungs, gastro-intestinal system, vision or hearing. In addition, babies born preterm have less fat stores and have not received as many essential fatty acids from the mother as term babies. Thus, preterm babies need special nutrition to promote healthy development. If prenatal care and the mother’s diet can make a difference, everyone benefits.
IMMUNE FUNCTION

Eating Fish During Pregnancy Linked to Lower Chance of Allergic Rhinitis

It is becoming clearer that the foods a woman eats during her pregnancy may affect the development of allergies in the infant. Some nutrients in foods may influence the maturation of the immune system in a way that makes allergies less likely. Other factors, such as the environment, tobacco smoke, urban living and family history of allergies, contribute to the increase in allergic diseases seen around the world. In infants, allergies appear most often as eczema and breathing difficulties. Less often, allergic rhinitis with symptoms typical of hay fever may develop.

In Japan, however, allergic rhinitis has become common. Nearly 20% of the population is affected and no one knows why it occurs so frequently there. To find out more about the development of allergies in women and children, a large study is being conducted in the Osaka region. The investigators have collected medical history information from pregnant women and details of their diet during and after pregnancy. They also collected health information about the offspring. Particular attention was given to the mothers’ fish intake and the development of allergies in their infants. In this report, only the relationship between the mother’s fish consumption and her chance of developing rhinitis was described.

The investigators observed that fish consumption was not related to the mother’s chance of developing rhinitis, but when they examined the omega-3 fatty acid intakes of the mothers, a clear relationship emerged. Fish, as Fats of Life readers know, are the main source of long-chain omega-3s in the diet. Women with the greatest intakes of EPA or DHA (the long-chain omega-3s in fish) were 40% less likely to develop allergic rhinitis compared with women who ate fish infrequently or not at all.

A lower risk of allergic rhinitis has also been reported in German adults with the highest levels of red blood cell EPA. Fish consumption was also linked to a 55% lower chance of allergic rhinitis in Norwegian children who ate fish in their first year and likewise in Swedish children who ate fish before the age of 1. Now, we await the results of the occurrence of allergic diseases in the children whose mothers participated in the Osaka study. If eating more fish or long-chain omega-3s helps reduce the chance of allergies, that will be nothing to sneeze at.

Children Whose Mothers Ate Fish During Pregnancy Have Less Eczema and Wheeze

The most common allergic condition in young infants is eczema, an itchy skin rash. Children whose parents have or had allergies are more likely to develop them as well. There are no certain ways to prevent allergies, but modification of the mother’s diet during pregnancy, when the infant’s immune system is developing, may be a promising strategy. Omega-3 fatty acids, the kind found mainly in fish and shellfish, appear to reduce the chance of some childhood allergies if the mother eats fish or fish oil supplements during pregnancy. However, as with many promising efforts, not all studies have demonstrated beneficial effects. In some cases, if the child eats fish during his first year, the chance of allergic conditions is reduced. Other studies suggest that pregnancy may be a better time for the mother to influence her child’s immune function.

In this report from Spain, over 450 mothers provided information about their food habits during pregnancy and children’s allergies at 6, 14 and 24 months after birth. In Spain, it is common for women to eat fish, a tradition verified in this study. On average, mothers ate fish one and a half times a week. However, women with asthma ate significantly less fish than women without the condition.

When the children were 1 year old, it was apparent those whose mothers ate fish more frequently were significantly less likely to develop eczema compared with children whose mothers ate fish infrequently.
If mothers increased their fish consumption from once a week to two and a half times a week, the chance of eczema fell by 37%. All children benefited, regardless of whether their mothers had allergic conditions or not. These observations are similar to those from another study in Australia where children whose mothers consumed fish oil during their pregnancy were less likely to have a positive skin prick test for allergies by the age of 1.

At the age of 6, the children whose mothers ate fish during pregnancy were also significantly less likely to develop allergic wheeze, a symptom of asthma. This association suggests, but does not prove, that maternal fish consumption affects the development of the infant’s immune system, perhaps by hastening its maturation. The investigators indicated that they will continue to monitor the children. Doing so will provide much-needed long-term data about the potential importance of eating fish during pregnancy.

**Increasing Omega-3 Intake From 6 Months to Age 3 Does Not Reduce Allergies**

Readers of the preceding articles in this section will know that in 2 recent studies, a mother’s fish consumption during pregnancy was linked to reduced allergies in her child. These studies suggest a beneficial effect of increasing omega-3 exposure very early in life—before birth—in reducing childhood allergies. Some studies have reported that children who eat fish in their first year of life are less likely to develop allergic responses than those who begin eating fish later. However, not all studies have reported an effect of childhood diet or omega-3 consumption on allergic responses.

An example of a contradictory report is the latest findings from the Childhood Allergy Prevention Study in Australia. This is one of the largest studies of childhood allergies ever undertaken. The study enrolled over 600 six-month-old infants and by the time they were 5 years old, over 500 remained in the study. All infants had either a parent or sibling with allergic asthma. In this trial, families were provided cooking oils and spreads that were enriched with monounsaturated fatty acids. The infants consumed fish oil with their formula or first foods. The study made great effort to limit the intake of omega-6 fatty acids because they compete with omega-3s and can be pro-inflammatory.

By the time the children were 3 years old, the incidence of wheeze, a symptom of asthma, was reduced. However, at age 5, this reduction disappeared. Even though the treated children raised their blood omega-3s levels and reduced their omega-6 fatty acids, they were just as likely to develop allergies as the children not taking the omega-3s. It is possible the intervention was too late in the development of the child’s immune system or that the change wasn’t large enough. However, the changes were practical in a home setting. And it is possible that omega-3 consumption has very little to do with the development of childhood allergies when there is a family history of these conditions. The study cannot answer these questions.

There is a caution about this report, however. Only a little over half the families and children complied with the dietary changes, even though several foods were given to the families. This is a difficulty encountered in many intervention studies, whether they are with adults or children. With such a relatively high rate of non-compliance, the investigators had a much lower chance of detecting differences in outcomes. Whether this aspect doomed the study is not easy to confirm.

**MENTAL HEALTH**

**In Major Depression Brain Has Reduced DHA**

There are now many reports of improved symptoms in patients with depression who have taken supplementary long-chain omega-3 fatty acids, DHA and EPA. These fatty acids are found mainly in fish and shellfish. Not all studies have reported improvements, but most have described clinical benefits where omega-3 fatty acids were used along with medications appropriate for the
patient. The findings have been positive enough that the American Psychiatric Association recently concluded that 1 g/day of EPA and DHA may be useful in patients with mood disorders. These conditions include depression, postpartum depression, anxiety, bipolar disorder and closely related conditions.

More recently, brain researchers have developed safe methods to determine whether there are physical changes in the brain in some of these conditions. We reported in the June 2007 issue of Fats of Life that scientists at the University of Pittsburgh, USA, measured volume changes 3 regions of the brain cortex associated with Alzheimer’s disease. In people with greater consumption of DHA and EPA, these regions were larger. Whether this means that they are also healthier remains to be established, but it goes along with other studies linking brain DHA with reduced likelihood of this condition.

In this report, another group of investigators led by Dr. Robert MacNamara at the University of Cincinnati College of Medicine, USA, measured different regions of the frontal cortex in patients with major depression who died. They focused their attention on a part of the frontal cortex known as Brodmann’s area 10 (illus). This region is thought to be involved in the emotional processes linked to major depression. The researchers measured different fatty acids in this region and compared the results with control patients matched for age, who died without evidence of depression.

Of all the fatty acids examined, only DHA, a long-chain omega-3 fatty acid concentrated in brain, differed between the two groups. In the depressed patients, DHA content was 22% lower compared with the controls. Further, concentrations were two times lower in female patients than in males. These findings provide direct evidence that some regions of the brain are altered in major depression and that these alterations are linked directly to DHA. We know that DHA

There is now direct evidence that patients with major depression have significantly reduced levels of DHA in their frontal cortex.

Figure. Cross-section of the human brain showing Brodmann’s areas by number. Image reproduced courtesy of Professor Mark Dubin, University of Colorado.

is important in neurotransmission, in the way brain cells “talk” to each other, and the functions such “cell talk” triggers. These observations provide additional rationale for the American Psychiatric Association’s recommendation to ensure adequate consumption of long-chain omega-3s.

COGNITIVE DECLINE

Loss of Cognition in Elderly Men Slowed with Omega-3s

As the pace of life slows in aging, so does the brain’s memory and some of its abilities. There is a distinction, however, between healthy aging and the cognitive decline associated with dementia (formerly called senility). In the latter, a person’s ability to handle executive functions (planning and carrying out tasks) and to recall verbal and spatial details declines noticeably. These losses appear as getting lost in familiar places, repetitive questioning, odd behaviors, personality changes and so on. Cognitive decline is barely detectable in some people, while others eventually become dysfunctional. Alzheimer’s disease is the most common type of dementia among the elderly.
Is there a way to prevent cognitive decline or at least slow it down? Avoiding tobacco, keeping socially and physically active and in good health all make a difference. Good diet is also becoming an important factor and regular fish consumption appears to be beneficial. Observational studies have suggested a link between fish consumption and lower risk of Alzheimer's disease and cognitive loss, but other data are needed to establish whether fish or their long-chain omega-3 fatty acids are causally linked to lively brain function. One study of omega-3 supplementation reported some benefit in slowing cognitive decline in the early stages of Alzheimer's disease, but not later.

Here, Dutch investigators took another look at data from a study that has been monitoring the diet and health of elderly men in the Netherlands for years. The investigators now have updated information about fish omega-3 fatty acids (EPA and DHA), so they examined the 5-year trend in cognitive function in these men. Participants ranged from 70 to 89 years of age when their diets and mental health were assessed. Of the 210 participants, 24% did not eat fish, with the remainder eating amounts ranging from very little to more than 20 grams (almost 1/2 of an ounce) each day. Five years later, their cognitive function was re-assessed.

Those who did not eat fish had lower cognitive scores (1.2 points lower) compared with their scores 5 years earlier, while men whose fish consumption was in the middle range had less decline (0.3 points). Men with the highest fish consumption actually had slightly (but not significantly) improved scores. The same pattern was observed when the calculations were made using EPA and DHA. In this case, the decline in cognition with low fish intake was statistically significant, meaning that it was unlikely due to chance.

The conclusion was easy: eating fish frequently was associated with slower loss of cognition in men over the age of 70. Doesn’t it add up to give fish a regular place on the menu at least twice a week?

### Link Between Slower Mental Decline and Intake of Polyunsaturated Fatty Acids

A large study in the United States has been monitoring groups of middle-aged adults in several centers throughout the country for various risks of atherosclerosis over time. The study is also well suited to examine the factors involved in cognitive decline as people grow older, as this report from participants in Minnesota indicates.

More than 2,250 men and women between the ages of 50 and 65 took part. They had their blood lipids, cognitive abilities and dietary intakes assessed when they enrolled and again after 3 and 6 years. There were 3 measures of cognition: delayed word recall, psychomotor speed and verbal fluency. The researchers related these cognitive scores to blood lipid levels and various clinical conditions, such as diabetes, high blood pressure and heart disease.

Several characteristics distinguished those who showed signs of declining cognition from those who did not. The participants with such signs were older (58 vs 56 years), less physically active, and had higher scores for depressive symptoms (9.7 vs 8.1), verbal recall and fluency compared with those who showed no signs of decline. Their blood coagulation profile was also significantly higher, suggesting greater risk of heart disease. These participants had higher levels of palmitic acid (a saturated fatty acid) and arachidonic acid, a long-chain omega-6 fatty acid in their blood. These fatty acids are associated with higher risk of heart disease.
In contrast, people with higher omega-6 fatty acids, particularly linoleic acid, which is plentiful in American diets, were less likely to show signs of cognitive loss.

When the investigators examined the participants’ blood levels of EPA and DHA—long-chain omega-3 fatty acids—they observed that people with the highest levels of EPA and DHA had about 25% less decline in verbal frequency. Other measures of cognition were not related to these omega-3s. Once again, an association does not establish causality, but it adds to the evidence that long-chain omega-3s may protect mental function as well as eye and heart health.

**Long-Chain Omega-3s of Little Clinical Benefit in Alzheimer’s Symptoms**

Sometimes research seems to take two steps forward and one or two back. Can’t we just progress in an orderly manner? Of course, not! Study participants vary considerably, research designs differ widely and there are always confounding variables that can be controlled only to a certain extent. On top of these matters, chronic diseases are complicated and the interactions among various conditions and their treatments make it difficult to see a clear picture.

Nowhere are these circumstances better illustrated than in the study of Alzheimer’s disease. The occurrence of this nasty deterioration of brain function in aging is increasing rapidly as the number of older people soars. The Alzheimer’s Prevention Foundation International points out, however, that if we can slow the progression of the disease by 5 years, we can cut the number of cases in half. The group suggests that diet, stress management, exercise and “brain aerobics” along with appropriate pharmaceuticals may help prevent the onset of this disease. The organization also noted the commonalities between heart disease and Alzheimer’s.

**Fats of Life** has reported several studies that suggest an important connection between the brain’s content of DHA, a long-chain omega-3 fatty acid in fish, and the chance of developing Alzheimer’s disease. Detailed studies of brain cells of Alzheimer’s patients (not covered in this issue) have shown that DHA is used to make substances that protect brain cells in the hippocampus, where Alzheimer’s hits hardest. Other studies have linked fish consumption to a lower chance of developing the disease.

A big question is, once Alzheimer’s disease is diagnosed, is it too late for seafood or long-chain omega-3s from seafood to benefit the brain? Some studies suggest that increased omega-3 consumption may be helpful only in the early stages of the disease and before. A new report from researchers who have been studying the treatment effects of omega-3s in Alzheimer’s patients described some effects of these fatty acids on various symptoms.

One of the conditions that increases the chance of developing Alzheimer’s is the presence of a particular genotype—certain genetic variations—known as APO-E. In patients with this genotype, treatment with about 2 grams of long-chain omega-3s for a year resulted in improved symptoms of agitation. In patients without this genotype, agitation symptoms were unaffected, but there were small improvements in their depression scores.

Overall, this study showed little effect of long-chain omega-3s in improving Alzheimer’s disease symptoms. We do not know, however, whether a higher dose would have been any different. The suggestion is that once the disease is established, boosting the intake of seafood omega-3s may have little impact on its course. That means it is wiser to make fish consumption a regular habit today, not wait until tomorrow.
VISUAL FUNCTION

Long-Chain Omega-3s Promote Healthy Retinas Damaged by Disease

From the earliest stages of visual development in infancy to the problems of impaired vision typically found as people age, the importance of polyunsaturated fatty acids (PUFAs) in the eye is becoming better understood. In the retina, PUFAs with 20 or more carbons and 4 or more “double bonds,” a reflection of how unsaturated they are, matter most. The retina has very high concentrations of these PUFAs, which are vital to turning light signals into visual information the brain can process. These PUFAs can be converted to other substances that protect retinal cells from damage, reduce inflammation and ensure a healthy blood supply. A new report from the National Eye Institute in Bethesda, USA, describes how the PUFAs of the omega-3 family promote the growth of healthy new blood vessels when the retina becomes damaged.

The retina is a thin lining of neurons at the back of the eyeball (illus). It can be damaged from low oxygen, products of fatty acid metabolism and inflammation, to name a few dangers. Retinal damage occurs in diabetic retinopathy, age-related macular degeneration, ischemia and other conditions. One way the retina protects itself is to make protective substances from the long-chain omega-3 PUFAs it has available. In this report, the investigators described how animals that did not have sufficient long-chain omega-3 PUFAs in their diet were less able to recover from a period of low oxygen.

The investigators compared mice fed diets high in either omega-6 or long-chain omega-3 PUFAs. The mice were kept in an atmosphere with less oxygen than usual for 5 days and then returned to room air. A low-oxygen environment is a model for what happens during reduced blood flow, as occurs in ischemia (reduced oxygen). In these circumstances, some blood vessels are damaged or destroyed, while new blood vessels develop to compensate. If conditions in the retina are poor, the new blood vessels may be abnormal or develop in places where they do not belong.

When the two groups of mice were compared the mice fed the omega-3 PUFA diet developed significantly more new blood vessels than the omega-6 PUFA group, even though the loss of damaged blood vessels was the same in both groups. This observation suggests that the long-chain omega-3s promoted the development of healthy new blood vessels, rather than merely limiting the loss of them. The investigators also detected protective substances in the omega-3-fed mice, but not in the omega-6 animals. These substances are made from long-chain omega-3s; they protect retinal cells from injurious conditions and stop inflammation.

These important studies show that long-chain omega-3s not only limit the cellular damage from ischemia, they promote healing responses, such as the growth of healthy new blood vessels and the production of guardian substances. These findings help explain why long-chain omega-3s reduce the risk of age-related eye diseases and those associated with diabetes and cardiovascular disease, conditions characterized by ischemia and inflammation. Heart, brain and eye health: 3 good reasons to see your way to eating fish or the omega-3s found in them regularly.
**Omega-3 PUFAs and Cataracts: Links Unclear**

Whether omega-3 polyunsaturated fatty acids (PUFAs) protect vision when problems develop outside the retina is uncertain. To date, there is only a handful of studies to suggest that they might. These include reports on cataracts and dry eye. Cataracts (Figure) target the lens, making it cloudy and blurring vision. A large observational study among Boston nurses reported a 12% lower chance of having cataract surgery in women with the highest intakes of long-chain omega-3s. In contrast, consumption of total fat and linoleic acid, the main omega-6 polyunsaturated fatty acid in the diet, was linked to an 8% greater risk of cataracts. Although these risks are not particularly large, they may be a warning.

A report from an Australian study of visual function in aging examined the relationships between fatty acid consumption and cataracts in nearly 2,000 middle-aged people. Two notable observations emerged. First, people with higher protein intakes had a significantly lower chance of subcapsular cataracts compared with people having low intakes. Second, those with the highest consumption of total omega-3s had a 40% lower chance of developing nuclear cataracts. Omega-6 fatty acids were unrelated to the chance of any cataracts.

It should be noted that in Australia, as in the United States and elsewhere, most omega-3s in the diet come from plant sources, not fish. The main and richest source of long-chain omega-3s is fish.

In a follow-up to the original study in Boston nurses, investigators observed in 440 women that only one fatty acid was related to the density of the lens: alpha-linolenic acid, an omega-3 fatty acid found in some plants and oils. Women with the highest consumption of this fatty acid experienced a 70% greater increase in the density or opacity of their lenses compared with women having the lowest intakes. Long-chain s were not linked to changes in lens density.

It is much too soon to rush to the conclusion that alpha-linolenic acid may be harmful to vision or cataracts. There is no clear explanation for this observation and it has only been reported in one or two studies. Observational studies do not establish causation. It will take much more research and direct evidence before we can confirm whether all omega-3s behave in a similar way, or, for that matter, any can influence cataract development.

**Clinical Conditions**

**Heart Disease and Depression: Are There Common Links?**

Patients who have had a heart attack or have heart disease are more likely to develop depression than people with healthy hearts. The reverse seems also true. Unfortunately, a person who develops heart disease and depression is at even greater risk of subsequent heart “events” (angina, heart attack, heart failure etc.). Both conditions are more common in people whose blood and tissue levels of omega-3 fatty acids are low. Another common feature of the two conditions is enhanced inflammatory responses. Several investigators have wondered how important altered immune function and omega-3 fatty acid status are in these conditions. It is no easy matter to untangle these closely related effects.

An approach taken by Dutch investigators, who monitored the health of group of elderly men in the Netherlands for many years, was to evaluate the mortality of those who died over a 10-year period in terms of whether the men had depression or heart disease and how much...
seafood-based omega-3s they consumed. The men were 70 to 90 years old when they enrolled in the study and were free of heart disease and diabetes at the time.

At baseline, 22% of the men had mild to severe symptoms of depression. Those with the highest intakes of seafood-based omega-3s (the long-chain ones) were the least likely to be depressed. Men in the highest third of omega-3 consumption were about 50% less likely to have symptoms of depression than those in the bottom third. After 10 years, half the participants died, 28% from heart disease. However, their chance of dying from heart disease was unrelated to their consumption of omega-3s. The investigators concluded that omega-3s could not explain the link between depression and heart disease. These observations do not tell whether a lifetime’s habit of eating fish regularly contributed to the men’s low rate of heart disease or kept inflammation at bay.

Another study in the Netherlands looked at patients who had survived a heart attack and compared those who developed depression with those who did not in terms of their blood levels of C-reactive protein. This is a marker of inflammation somewhere in the body. The investigators also measured two fatty acids in the patients’ blood, arachidonic acid (a long-chain omega-6 fatty acid) and eicosapentaenoic acid (EPA), a long-chain omega-3. These men were younger than in the study mentioned above (average age 55 years).

In this study, arachidonic acid levels were higher and EPA levels lower in the patients with depression. However, depressed patients were no different from their counterparts without depression when it came to C-reactive protein levels. This observation may mean that there really were no differences or that both groups of patients, who were taking statin medications, had responded to the statins with reduced C-reactive protein levels. That is a common effect (benefit) of these drugs. The differences in fatty acids observed support other studies showing similar results in heart patients with depression. Omega-3s are typically low in heart disease patients as well. Both studies confirm a relationship between depression and omega-3s in heart patients.

A third study in Canada, also tried to untangle the relationships between heart disease, depression and inflammation. They did not examine fatty acids. Patients with acute coronary syndrome were recruited 2 months after they left the hospital. Patients were assessed at enrolment for symptoms of depression and markers of inflammation. Their health was monitored for the next 2 years. Depression was observed in 27% of the participants and was more prevalent in women than men (35% vs 25%).

Over the following 2 years, 14% of the patients incurred at least one additional major heart problem, including death, heart attack and by-pass surgery. Participants with depression were significantly more likely to develop a heart problem compared with patients without depression. C-reactive protein content was also higher in the depressed patients than the others. Higher levels of this protein (above 2 mg/Liter) were also linked to a 36% greater chance of developing a heart problem compared with outcomes in patients whose levels were below 2 mg/Liter. Further, the effect of C-reactive protein was greater in depressed patients than those without depression. However, the two conditions combined did not appear to make the condition worse. Because of that, the investigators concluded that depression probably does not aggravate the heart health through inflammatory responses.

A common link with inflammation, depression and heart disease is long-chain omega-3s. These studies provide some suggestions that these fatty acids may lessen the severity of these conditions, even if men without heart disease and higher omega-3 levels were not less likely to die from heart disease. Omega-3s have been shown repeatedly to reduce mortality in people with the disease. These studies illustrate the complexity of the issues, different approaches to understanding the relationships between co-existing conditions, and the importance of looking at the whole picture. It appears that diet and drugs will be part of the prescription for some time to come.